Improving Access and Outcomes in Living Kidney Donor Transplantation

Camilla Sara Hanson

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Declaration

This is to certify that to the best of my knowledge, the content of this thesis is my own work. This thesis has not been submitted for any degree or other purposes.

I certify that the intellectual content of this thesis is the product of my own work and that all the assistance received in preparing this thesis and sources has been acknowledged.

Signature: ……………………………… Date: ………………………………..

Camilla Sara Hanson

Author's Contribution

The work presented in this thesis has been carried out by the author under the supervision of Associate Professor Allison Tong and Professor Jonathan Craig of the Sydney School of Public Health, The University of Sydney.

The author planned the research, designed the studies, obtained ethics approval, collected, managed and analysed the data, interpreted results, drafted and revised the manuscripts for submission to peer-reviewed journals, and wrote and compiled this thesis.

As supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

Signature: ………………………………. Date: ………………………………..

A/Professor Allison Tong

Ethical Clearance

The study presented in Chapter 4 was approved by the Human Research Ethics Committee at the University of Sydney.

The studies presented in Chapters 4 and 6 were approved by the Western Sydney Local Health District Human Research Ethics Committee, Monash Health Ethics Committee, and the University of British Columbia and Providence Health Care Research Ethics Board.

All participants gave written informed consent for participation in the study.

Abstract

Shortages in deceased organ donation have necessitated widespread acceptance of living donor kidney transplantation, which offers better outcomes in terms of graft survival, life expectancy and quality of life for many patients with end-stage kidney disease, compared with deceased donor kidney transplantation and dialysis. However, there are barriers and challenges that exist in the current practice of living kidney donor transplantation. Overall, the rates of living kidney donor transplantation have decreased or plateaued, with ethical and socio-economic disparities in access to living kidney donation reported in many countries, that remain largely unexplained. Living donors must accept risks associated with undergoing nephrectomy, despite the evidence on the long-term risks of living kidney donation remaining uncertain. In response, there have been efforts to identify and describe the barriers and disparities in living kidney donor transplantation, and to assess a range of outcomes for living donors. Yet, little is known about the donors' priorities for outcomes. A comprehensive understanding of the values, beliefs, experiences, priorities and preferences of the key stakeholders, including donors and health professionals involved in their care, is needed to ensure that research, clinical practice and policy in living kidney donations address their needs and priorities.

The first part of this thesis (Chapters 3 to 6) consists of qualitative studies that describe in-depth the perspectives and experiences of kidney transplant recipients, living kidney donors and nephrologists. These studies address recipient decision-making, donors' experiences of the evaluation process, and nephrologists' perspectives on recipient eligibility and disparities in living kidney donor transplantation.

Chapter 2 provides an overview of qualitative health research methods and principles including participant selection, data collection and analysis. The approaches used to demonstrate rigour are discussed in terms of credibility, confirmability, dependability and transferability.

In Chapter 3, to understand recipient expectations and attitudes regarding living kidney donor transplantation, a systematic review and thematic synthesis of primary qualitative studies that examined recipient perspectives was conducted. Six themes were identified, including prioritising own health, guilt and responsibility, ambivalence and uncertainty, seeking decisional validation, needing social support, and cautious donor recruitment. A new conceptual schema of the barriers and facilitators was developed, highlighting the need to address patients' concerns regarding donor outcomes, guilt, relationship tensions and donor recruitment.

Chapter 4 examines how donors sustain commitment to donation during the evaluation period, including their experiences with informed consent, and their medical and psychosocial assessment. From focus groups conducted in Australia and Canada, themes were identified that reflected the challenges they experienced, including underlying fears for their health, obstructive system shortfalls and lifestyle interference. Their emotional investment, feeling undeterred by low risks, and mental preparation for possible donation outcomes sustained their commitment throughout the evaluation process, despite facing these challenges.

Chapter 5 describes nephrologists' attitudes towards recipient eligibility and access to living kidney donor transplantation. Nephrologists from Australia and New Zealand participated in a semi-structured interview study. The themes identified reflected nephrologists' competing priorities - to achieve optimal recipient outcomes, ensure the risk to the donor was justified, and to protect their transplant unit's integrity. Nephrologists also considered disparities to be entrenched and difficult to address within their roles and limited resources. This analysis led to recommendations to promote more equitable decision-making and help nephrologists address disparities and advocate for disadvantaged patients.

The second part of this thesis (Chapters 6 and 7) is focussed on outcomes for living kidney donors. These studies sought to identify the outcomes most important to donors and evaluate the spectrum and consistency of outcomes reported in trials and observational studies of living kidney donors.

In Chapter 6, outcomes most important to living kidney donors and the reasons for their choices were elicited using nominal group technique – a mixed methods approach that incorporates quantitative ranking and qualitative focus group discussion. The top five most important outcomes included kidney function, time to recovery, surgical complications, donor-recipient relationship and lifestyle restrictions. The themes that explained their rankings included unfulfilled expectations, heightened susceptibility, confidence and empowerment, downplaying risks and harms, and worthwhile sacrifice.

Chapter 7 presents the scope and frequency of outcomes reported in recent trials, and observational studies in living kidney donors based on a systematic review. The top five most frequently reported domains were kidney function, time to discharge, blood loss/transfusion, operative time and blood pressure. There was also large heterogeneity in the measures used to assess the same outcomes.

The latter two chapters highlight a mismatch between outcomes that were most frequently reported in contemporary studies in living kidney donors and outcomes explicitly identified to be most important to donors, such as time to recovery, clinical outcomes including pain and mortality, and psychosocial outcomes including the donor-recipient relationship, lifestyle restrictions, life satisfaction and family life.

In conclusion, this thesis identifies potential strategies to address the tensions and challenges in the pathway to living kidney donor transplantation for recipients, donors and nephrologists. The findings highlight the need for culturally sensitive, family-oriented educational and psychosocial support to resolve recipient ambivalence, and help patients find an acceptable approach to engaging in discussions with potential donors. They also highlight the need to help nephrologists to better advocate for their patients. To facilitate equitable decision-making, and resolve tensions and uncertainties for nephrologists, it was demonstrated that there is a need for greater consensus and standardized practice regarding complex medical psychosocial cases, and greater transparency of centre practices. Focus groups with living donors showed that more attention is needed to the psychosocial challenges of live donor evaluation; including preparing donors for surgery and recovery, minimising anxiety and lifestyle burdens, ensuring donors feel comfortable expressing their fears and concerns, and making explicit the responsibilities of donors in their assessment process.

This thesis also provides greater understanding of the outcomes that are most important to donors, and a framework for improving the relevance of outcomes reported in trials and observational studies to clinical and donor decision-making. It was demonstrated that consistent reporting of outcomes relevant to decision making is needed to better inform and prepare donors for outcomes after donation. Overall, the acknowledgement of stakeholder perspectives in guidelines, education, research and practice needs to address the real tensions faced by nephrologists, recipients and donors, to ensure equitable decision-making, alleviate barriers and disparities, and improve outcomes for recipients and their donors.

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I thank my family and friends, particularly Mum, Dad, Guy and Tim for their endless support and encouragement. Thank you for keeping me company while I finished off the last few papers, cooking my meals, and providing the captive audience to hear my talks and the motivation to hurry up and get the thesis done.

I would like to dedicate this thesis to my paternal grandmother, Anita Hanson, whom I never met. She died of renal failure in 1954 – the year of the first living kidney donor transplant.

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First Author Publications Arising from this Thesis

This thesis is presented for examination as a thesis containing published work. Chapters 2, 3 4, and 5 have been published in international peer-reviewed journals, Chapter 6 is under revision, and Chapter 7 has been submitted for publication. The candidate is the first and corresponding author of each of these papers.

Chapter 2	**Hanson CS**, Craig CC, Tong A. In their own words: the value of qualitative research to improve the care of children with chronic kidney disease". Pediatric Nephrology 2016; 1-7. (October 15th 2016, PMID: 27744620 DOI10.1007/s00467-016-3526-y
Chapter 3	**Hanson CS**, Chadban SJ, Chapman JR, Craig JC, Wong G, Ralph AF, Tong A. The expectations and attitudes of patients with CKD towards living kidney donor transplantation: a thematic synthesis of qualitative studies. Transplantation 2015; 99 (3): 540-544. (December 2nd 2014, PMID: 25463967 DOI: 10.1097/TP.0000000000000433
Chapter 4	**Hanson CS,** Ralph AF, Manera KE, Gill JS, Kanellis J, Wong G, Craig JC, Chapman JR, Tong A. The lived experience of 'being evaluated' for organ donation: focus groups with living kidney donors. Clinical Journal American Society of Nephrology (In press, accepted July 17th 2017)
Chapter 5	**Hanson CS,** Chadban SJ, Chapman JR, Craig JC, Wong G, Tong A. Nephrologists' perspectives on patient eligibility and access to living donor kidney transplantation. Transplantation 2014; 199 (4): 943-953. (Accepted 3rd May 2015, PMID: 26425873, DOI: 10.1097/TP.0000000000000921).
Chapter 6	**Hanson CS,** Chapman JR, Gill JS, Kanellis JK, Wong G,

	Craig JC, Teixeira-Pinto A, Chadban SJ, Garg AX, Ralph AF, Pinter J, Lewis JR, Tong A. Identifying outcomes that are important to living kidney donors: a nominal group technique study. (Submitted, August 2017)
Chapter 7	**Hanson CS,** Sautenet B, Craig JC, Chapman JR, Knoll G, Reese, PP, Tong A. Informative for decision-making? The spectrum and consistency of outcomes following living kidney donation reported in trials and observational studies. (Submitted, August 2017)

Conference Proceedings Arising from this Thesis

Hanson CS, Chadban S, Chapman JR, Wong G, Craig JC, Tong A. Patients’ attitudes towards living kidney donation: systematic review and thematic synthesis of qualitative research. Australian and New Zealand Society of Nephrology 29th Annual Scientific Meeting, 9-11 September 2013, Brisbane, Australia.

Hanson CS, Chadban SJ, Chapman JR, Wong G, Craig JC, Tong A. Patients' attitudes towards living kidney donation: systematic review and thematic synthesis of qualitative research. 12th Congress of the International Society for Organ Donation and Procurement, 21-24 November 2013, Sydney, Australia.

Hanson CS, Chadban SJ, Chapman JR, Craig JC, Wong G, Ralph AF, Tong A. Patients' attitudes towards living kidney donation: systematic review and thematic synthesis of qualitative research. The Transplantation Society of Australia and New Zealand 32nd Annual Scientific Meeting, 11-13 June 2014, Canberra, Australia.

Hanson CS, Chadban SJ, Chapman JR, Craig JC, Wong G, Tong A. Everyone's got their own threshold. Nephrologists' perspectives on patient eligibility and access to living donor kidney transplantation. World Transplant Congress, 26-31 July 2014, San Francisco, United States.

Hanson CS, Chadban SJ, Chapman JR, Craig JC, Wong G, Ralph A, Tong A. Patients' attitudes towards living kidney donation: systematic review and thematic synthesis of qualitative research. World Transplant Congress, 26-31 July 2014, San Francisco, United States.

Hanson CS, Chadban SJ, Chapman JR, Craig JC, Wong G, Tong A. "Everyone's got their own threshold". Nephrologists' perspectives on patient eligibility and access to living kidney donor transplantation. Australian and New Zealand

Society of Nephrology 50th Annual Scientific Meeting, 25-27 August 2014, Melbourne, Australia.

Hanson CS, Chadban SJ, Chapman JR, Craig JC, Wong G, Tong A. "Everyone's got their own threshold". Nephrologists' perspectives on patient eligibility and access to living kidney donor transplantation. 13th Congress of the International Society of Organ Tissue and Donation, 17-20 October 2015, Seoul, Korea.

Hanson CS, Kanellis J, Chadban SJ, Chapman JR, Craig JC, Wong G, Pinter J, Garg AX, Gill JS, Lewis JR, Tong A. Living Kidney Donor Priorities for Outcomes: A Nominal Group Technique Study. 34th Annual Scientific Meeting of the Transplant Society of Australia and New Zealand, April 10-12, 2016, Sydney, Australia.

Hanson CS, Kanellis J, Chadban SJ, Chapman JR, Craig JC, Wong G, Pinter J, Garg AX, Gill JS, Lewis JR, Tong A. Living Kidney Donor Priorities for Outcomes: A Nominal Group Technique Study. The 4th Ethical, Legal and Psychosocial Aspects of Organ Transplantation Congress, April 22-25, 2016, Rome, Italy.

Hanson CS, Kanellis J, Chadban SJ, Chapman JR, Craig JC, Wong G, Pinter J, Garg AX, Gill JS, Lewis JR, Tong A. Living Kidney Donor Priorities for Outcomes: A Nominal Group Technique Study. 2016 American Transplant Congress, June 11-15, 2016, Boston, United States.

Hanson CS, Kanellis J, Chadban SJ, Chapman JR, Craig JC, Wong G, Pinter J, Garg AX, Gill JS, Lewis JR, Tong A. Living Kidney Donor Priorities for Outcomes: A Nominal Group Technique Study. The 26th International Congress of the Transplant Society, Hong Kong, August 18-23, 2016.

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The Transplant Society International Society of Organ Donation and Transplantation Scientific Award, June 2017

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List of Abbreviations

CINAHL	Cumulative Index for Nursing and Allied Health Literature
COREQ	Consolidated Criteria for Reporting Qualitative Health Research
CKD	Chronic Kidney Disease
ENTREQ	Enhancing Transparency for Reporting Qualitative Health Research
ESKD	End-Stage Kidney Disease
GFR	Glomerular Filtration Rate
HDI	Human Development Index
KDIGO	Kidney Disease Improving Global Outcomes
LKDT	Living Kidney Donor Transplantation
MeSH	Medical Subject Headings
NGT	Nominal Group Technique
OMERACT	Outcomes Measures in Rheumatology
OPTN	Organ Procurement Transplant Network
QOL	Quality of Life
RELIVE	Renal and Lung Living Donors Evaluation
SIPAT	The Stanford Integrated Psychosocial Assessment for Transplantation

Chapter 1: Introduction

1.1 Overview

"A rising demand for organs exists without enough organs to meet it, making the urgency for those willing and able to donate even more critical and the need for innovation and support even more imperative."

- Barak Obama, April 1st 2016

This thesis is presented as a series of papers that address the overall aim of improving access and outcomes in living kidney donor transplantation. In this chapter, background literature is reviewed to provide an overview of living kidney donor transplantation. This is followed by a discussion of important gaps in research and practice in addressing barriers and disparities in living kidney donor transplantation, and ways to improve the donation pathway and outcomes for living kidney donors. This chapter also includes justification for this research, the value of qualitative research methods, and an outline of the aims of each study.

1.2 Living kidney donor transplantation

The first successful living kidney donor transplantation was performed in 1954 in Boston Massachusetts, between identical twin brothers. Living kidney donor transplantation is now the preferred treatment option for many patients with end-stage kidney disease, as it is associated with superior graft survival, patient survival and quality of life outcomes.[1,2] Moreover, the unresolved shortages in deceased organ donation have necessitated widespread acceptance of living kidney donor transplantation.[3] In 2014, 23,233 transplants were made available by living kidney donors, comprising 42% of all kidney transplants worldwide.[4]

The rate of living kidney donor transplantation varies widely across countries, and differences in transplant policy and practice are apparent.[5] In high income countries, including Australia, Canada, the United Kingdom and the United States, living kidney donor transplantation comprises up to 40% of kidney transplants.[6] Spain's highly successful deceased donor program has resulted in a very low proportion of living kidney donors, at less than 10%.[7] In contrast, living donors comprise 90% of all kidney transplantations in Japan, due to legal restrictions on deceased donation (which were revised in 2010).[3] In Saudi Arabia, high rates of living donation are thought to be related to a large uptake of unrelated donors.[3] In Hong Kong and Taiwan, emotionally related donation is restricted. Furthermore, living unrelated donation is prohibited in many countries in Asia.[8]

Reimbursement practices for donors differ substantially, ranging from the provision of paid leave (e.g. Australia), reimbursement for out-of-pocket expenses (e.g. Canada) and government regulated compensation in Iran.[9] In most countries, payment for donation is illegal[10], although organ trafficking and transplant tourism are still practised[11].

Major innovations in transplantation have transformed and improved access and outcomes in living kidney donor transplantation for both patients and donors. Advances in immunosuppression and recipient desensitization techniques have enabled unrelated donors, who are blood-type or human leukocyte antigen incompatible, to donate.[12,13] However, immunologically matched donor-recipient pairs are preferable as these techniques come with increased risk of infection and rejection for the recipient.[12] Laparoscopic nephrectomy, introduced in 1995, improved surgical outcomes for donors by reducing the length of stay in hospital, the size of their incision and their overall convalescence period. Many countries have introduced a living kidney donor exchange scheme.[3,12] Incompatible donors, and in recent times also compatible donors, enter the paired donation scheme and 'swap' donors in order to receive a compatible or better matched kidney.

There are various types of kidney donors. 'Directed donation' refers to donation between relatives or friends, wherein there is an emotional or biological relationship.[12] In many countries the demographic of living donors is changing, to include unrelated donors from the patient's broader social network.[14] There has been substantial growth in non-directed (altruistic) donors in recent years, particularly in the United States, the Netherlands and the United Kingdom.[15] Kidney donations from non-directed donors are usually allocated to a recipient on the waiting list, as determined by a computer algorithm[16], or to a recipient to initiate a chain in a paired exchange program, allowing a kidney to be allocated to someone on the waiting list[13]. Many transplant centres do not accept non-directed donors due to concerns about the psychosocial impact of donation, ulterior motives and commercialisation.[15] More recently, the process of donating directly to a stranger has been allowed, often identified through social media or public pleas, whereby a donor can respond to the request for a kidney donation of a specific person with whom they have no prior connection.[12] This has been legalised in the United Kingdom and United States but is not currently practised in many other countries, including Australia.

1.3 Ethical considerations

The practice of living kidney donation entails unique ethical issues. Living kidney donor transplantation requires a healthy person to undergo surgery for the benefit of the patient[17], who is thus exposed to the risks associated with nephrectomy. For clinicians, the practice of living kidney donation can be perceived to be in tension with the fundamental principle of medical ethics, to do no harm (*primum non nocere*). However, the transplant community recognises that there are not only benefits for the patient, but also a range of non-medical benefits for the donor.[18]

Ultimately, clinicians must make decisions to ensure that the risks to donors are sufficiently small, and at the same time may have to trade off these potential risks with the potential benefits for the recipient and the donor.[19,20]

The ethical principles of autonomy, justice, beneficence and non-maleficence are often used as a framework to guide practice in living kidney donor transplantation.[21,22] Autonomy, the right of individuals to make their own decisions, is actualised by obtaining informed consent from potential donors.[22] However, patient and donor autonomy must be balanced or tempered by medical judgement.[20]

Beneficence refers to the need to protect the welfare and interests of the donor and recipient, while non-maleficence entails the protection from harm, and minimisation of risk.[20] Rigorous medical screening and assessment, informed consent incorporating education about long-term outcomes, and access to long-term health care are critical to ensuring these principles are upheld.

1.4 The living kidney donor transplant pathway

This thesis examines the living kidney donor transplant pathway to understand barriers and disparities in living kidney donation, and determine strategies to better donors for surgery and recovery and satisfaction with the donation process. An overview of the main components of the pathway to living kidney donor transplantation is provided in this section, and are summarised in Figure 1.1.

In most jurisdictions, living kidney donor transplant programs are organised and overseen by individual transplant centres, without the same level of oversight as deceased donor transplant programs, which are typically governed by nationally or regionally operated waiting lists and allocation criteria.[23] This, in part, explains the substantial variability across centres and countries in the practices and policies in living kidney donor transplantation, particularly in terms of eligibility criteria and assessment practices.

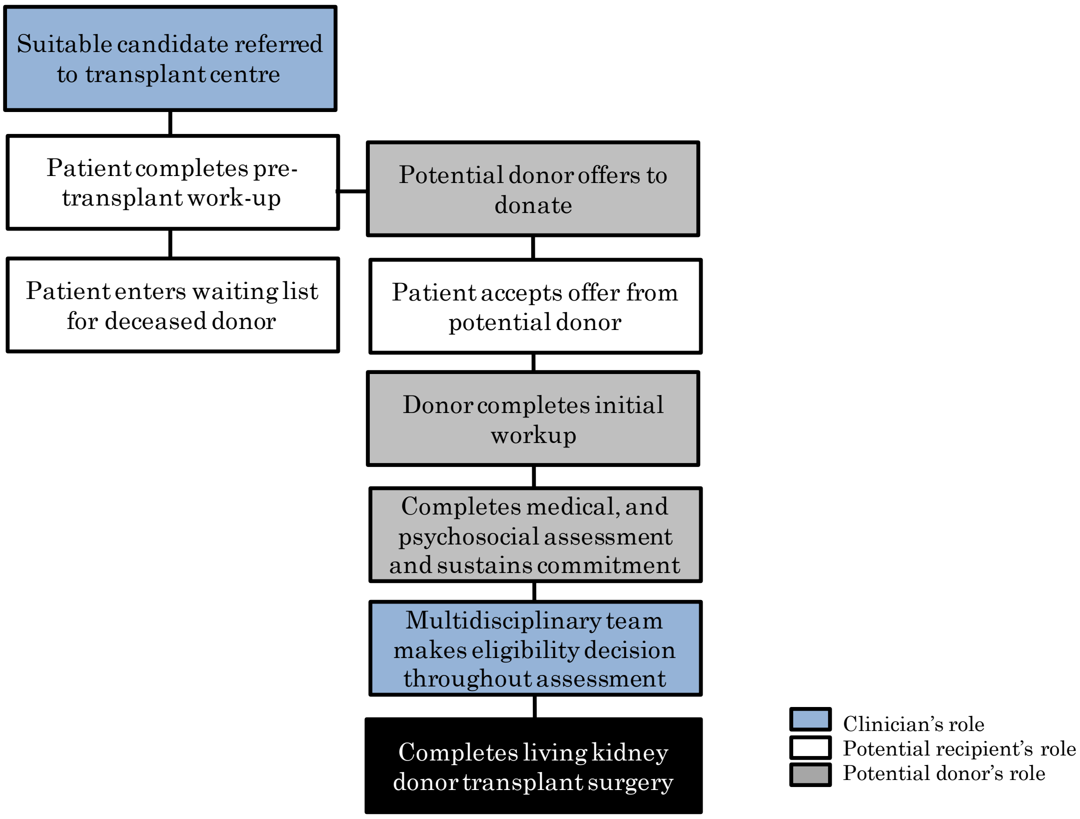

Figure 1.1. Key steps in the living kidney donor transplantation pathway*

*Adapted from Renal Resource Centre. An introduction to kidney donation by live donors Kidney Health Australia. (http://kidney.org.au/cms_uploads/docs/rrc-kidney-donation-by-live-donors.pdf) Published 2010. Accessed January 1st 2017.

Live donor evaluation

Comprehensive evaluations involving medical and psychosocial screening and informed consent are necessary to safeguard donor voluntarism and minimise harm for living kidney donors.[21,23] The Kidney Disease Improving Global Outcomes (KDIGO) guidelines state that the primary goal of the live donor evaluation is to determine individual suitability for donation, ensure donors are making an informed choice, and determine whether their kidney is suitable for the intended recipient.[24]

National guidelines for live donor assessment are available, but practices differ substantially among different units.[12] It is widely recommended that the team evaluating the potential donor should be independent from the team evaluating the potential recipient, to minimise a conflict of interest.[18] The duration of assessment varies substantially, due to the available resources at each unit. A generic example of the live donor evaluation is provided below in Table 1.1:

Table 1.1: Living kidney donor evaluation and education

Assessment stage	Details
1. Initial assessment	• Blood group and tissue typing compatibility • Full medical assessment
2. Education	• Informed consent – understand risks and benefits
3. Live donor cross-matching	• HLA leukocyte antigen typing • ABO compatibility testing • Cross-matching by two different methods
4. Assessment of renal function	• 24-hour urine collection and/or nuclear medicine scan and/or renal laboratory test • Renal ultrasound
5. General health assessment	• Chest x-ray and ECG, sometimes echocardiogram and stress test • Blood tests (electrolytes, liver function, full blood count, fasting glucose, lipids, oral glucose tolerance test) • Blood tests for transmissible disease, Epstein-Barr virus and CMV • Females > 50 require pap smear and mammogram, males > 50 require PSA
6. Renal angiogram	• 3D Helical CT angiogram, magnetic resonance imaging MRI, angiogram or formal arteriogram
7. Psychosocial evaluation	• Social worker: emotional support, advice on practical, organisational, and financial matters • Psychologist/psychiatrist: assesses capacity to cope with process or a poor outcome
8. Surgical assessment	• Surgeon provides information about operation and risks, reviews CT renal angiogram and obtains informed consent
9. Review by renal physician	• Renal physician discusses test results, answers questions, notifies recipient's renal physician that workup complete, plans surgery date

* Adapted from Renal Resource Centre. An introduction to kidney donation by live donors Kidney Health Australia. (http://kidney.org.au/cms_uploads/docs/rrc-kidney-donation-by-live-donors.pdf) Published 2010. Accessed January 1st 2017; HLA: Human Leukocyte Antigen; ECG: Electrocardiography; CMV: Cytomegalovirus; PSA: Prostate-specific antigen; CT: Computed tomography scan; MRI: Magnetic resonance imaging.

Donor eligibility criteria

Guidelines specify some absolute and relative contraindications to living kidney donation. Most countries require donors to be over the age of 18 years.[12] Caution with respect to donors under 30 years of age is often applied due to a lack of evidence on lifetime risks.[25] In Australia, relative and absolute contraindications include cancer, diabetes, high blood pressure, infection disease, lung and heart disease, kidney disease, obesity, psychiatric disorder and major abdominal surgery.[26] Obesity and lifestyle related problems are generally considered to be relative contraindications that can be addressed.[18] Lack of evidence for determining risk factors for medical and psychosocial outcomes may explain some of the variability in assessment and acceptance of donors, particularly regarding age, measured glomerular filtration rate (GFR), body mass index and hypertension.[27,28] The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend that each centre "strives to develop and communicate a quantitative threshold of 'acceptable risk' for each post-donation adverse outcome they wish to avoid".[29] In practice, the decision to accept a donor is complex and involves weighing the risks to the donor against the benefits for the donor and the intended recipient.[21]

Informed consent

Informed consent aims to ensure that donors are making a voluntary, intentional decision and understand the potential consequences of donating. The most recent KDIGO guidelines indicate that potential donors should understand the "likely medical, psychological, social and economic outcomes of donation, potential risks and benefits to themselves, and anticipated outcomes for the recipient".[24] Moreover "uncertainty in the risk estimates should be discussed when risk cannot be accurately quantified based on available data". Informed consent practices have been shown to vary widely.[30] The information conveyed to donors is complex, and may be difficult for donors to process and completely comprehend prior to donation.

Various strategies have been used to implement informed consent. To ensure donors make a considered decision, some transplant programs implement a 'cooling off period' and deliberately delay the process.[27] Dew et al[31] designed a motivational interviewing intervention to address donor ambivalence prior to donation, which showed reductions in ambivalence, fatigue, physical symptoms, pain, shorter recovery times, anxiety symptoms, and family-related problems after donation. Since 2007, the Organ Procurement and Transplant Network in the United States has mandated the independent living donor advocate to assist with informed consent by providing education, support and advocacy to potential donors.[32] Home-based education programs have been developed to improve education about living kidney donor transplantation, particularly among ethnic minority groups.[13,33,34]

Psychosocial evaluation

Psychosocial evaluation assesses how the donation will potentially impact on the donor's life and wellbeing i.e. the non-medical aspects of donation.[21] The gift of a transplant can impact the donor's sense of self, their roles, and their relationships.[35,36] The psychosocial assessment ultimately aims to ensure donors are prepared for the challenges they may face, and donors are ruled out if they are deemed unlikely to cope.

Specific components of the psychosocial evaluation include an assessment of donors'[12,37]:

- motives for donation (reasons for volunteering, decision-making process, coercion or inducement, ambivalence)
- relationship with the recipient (nature of existing relationship, degree of closeness, perceived obligations and expectations)

- knowledge about surgery/recovery (understanding and expectations of risks and outcomes)
- social support (emotional and practical support, pressure or opposition from family, social network and workplace), and
- financial status (financial stability, insurance coverage, resources for unexpected expenses).

Many of the issues explored in the psychosocial evaluation are considered relative contraindications that can be overcome prior to donation.[30] However, guidelines offer limited advice regarding specific tools to conduct psychosocial assessments and address these issues.[26]

Previous studies have shown that the donor evaluation process can be lengthy, invasive and anxiety provoking.[28,38-40] Donors have reported a fear of being deemed ineligible, uncertainty about their eligibility status and surgery date, and difficulty navigating an unfamiliar healthcare system.[38-40] These experiences can cause considerable stress during the evaluation. Many donors report anxiety and residual ambivalence about undergoing surgery.[31,41,42] Previous studies have found that donors attempt to manage how they are perceived throughout evaluation, to ensure that they are accepted as donors.[43] There are, therefore, concerns that donors may not disclose their apprehensions and anxieties in order to protect their eligibility.[43]

1.5 Barriers and disparities in living kidney donor transplantation

Living kidney donor transplant programs are an important strategy to improve access to kidney transplantation. In recent years, the number of living kidney donor transplants has decreased or plateaued, particularly among disadvantaged populations[44], prompting concerted efforts to understand and reduce disparities and inequities in transplantation[45]. This problem was highlighted in the quote by Barak Obama at the start of this chapter, who called for increased support and innovation in transplantation. Such strategies to increase living kidney donor transplantation require greater understanding of the barriers preventing uptake of living kidney donation.

While the term ‘disparities’ describes health differences between subgroups, equity is an ethical concept.[46] The World Health Organisation defines *health inequities* as “differences in health that are unnecessary, avoidable, unfair and unjust”.[47] Health equity, therefore, entails the dismantling of systematic health disparities between social groups with different degrees of social advantage or disadvantage.[46] While poor health outcomes may relate to biological variation between populations, it is argued that we have a responsibility to do something about the health gaps that are caused by systematic disparities.[48]

Disparities in the rates of living kidney donation have been reported both within and across countries worldwide, but the reasons remain largely unexplained.[44,45] Ethnic minority status, socio-economic disadvantage, female gender and older age have been associated with a lower probability of living kidney donor transplantation.[49-51] However, the associations between cultural, demographic and socio-economic factors with living kidney donor transplantation are not completely understood.[52]

Living kidney donor transplantation involves the private gift exchange between two individuals; therefore, the barriers are thought to be different to those relevant to deceased donor transplantation.[53] Patients must be deemed eligible for transplantation and be able to navigate the transplant pathway, but they also depend on the eligibility and willingness of a healthy donor.[54] A clear understanding of the range of barriers to living kidney donation and reasons for disparities is needed to inform strategies to overcome them. Importantly, it is important to identify solutions “that do not require ‘encouraging’ people to donate who would otherwise be unwilling or unlikely to consider donation”.[55]

Theoretical framework

The socio-ecological model[56] adapted from Bronfenbrenner's ecological systems theory (1998) informs the aims of this thesis, to describe barriers and facilitators impacting on access to living kidney donor transplantation from different perspectives. This model examines the influence of personal values, family, extended social network, health care system, and cultural or societal (including government regulations and policy) values on health care decision-making and behaviour. Barriers and disparities in living kidney donor transplantation are complex, and multifactorial, thus many studies have utilised this model.[57] The 'pathway approach' to understanding disparities in living kidney donor transplantation was also utilised, which emphasises the importance of understanding barriers in the context of the entire disease and transplant process.[48] The pathway to living kidney donor transplantation was outlined above in Figure 1.1 (section 1.3).

Patient perspectives

Patients with chronic kidney disease (CKD), the potential transplant recipients, have various attitudes and beliefs that can pose barriers to receiving a living donor transplant. Previous studies have identified patients' reluctance to ask someone to donate a kidney, or to accept a relative's offer to donate, as a common barrier to pursuing living kidney donor transplantation.[58,59] Surveys have found that potential recipients would feel guilty accepting a kidney from a living donor because they have concerns for the donor's health and wellbeing, financial implications and fear that the graft might fail. Potential recipients may also lack knowledge about living kidney donor transplantation.[59-61]

In general, cultural perspectives on living kidney donor transplantation are not well understood.[62] A willingness to approach potential living kidney donors has been found to be lower among ethnic minorities and uneducated, older and female populations.[59,63] Qualitative studies and surveys, mostly conducted in North America and Europe, suggest that a patient's cultural background may influence their communication with clinicians[64], their trust of medical information[64], their propensity to actively seek information[65] and their willingness to communicate with their family and potential donors about living donation[59,63,66-68]. Within some cultures, decision-making is a family-oriented process which operates according to rules of family hierarchy.[69] Discussions about disease and illness are sometimes considered unacceptable and taboo.[65] Concerns about the donor's reproductive and marriage potential may be more prevalent among certain communities.[69,70] Poor health literacy may also limit comprehension of information among patients of ethnic minority background.[62]

Although most religions are not actually opposed to living or deceased donor transplantation, religion is still thought to be a potential barrier to receiving or undergoing living kidney donor transplantation.[71] For example, a patient may perceive their kidney disease as fate or spiritual punishment, and therefore not feel worthy of receiving a kidney from a donor.[63,69] Some religions believe in maintaining bodily integrity and being buried whole; therefore, some people view kidney donation as incompatible with this principle.[72] However, many religions also espouse the principles of altruism and saving a life, which are often used to justify kidney donation.[71]

Donor perspectives

The 'differential access' hypothesis to explain disparities in living kidney donor transplantation is prominent in the literature, suggesting that ethnic disparities are primarily underpinned by the lesser availability of medically suitable or compatible potential donors.[73,74] However, this has only been demonstrated in single-centre studies, and these studies have only included the potential donors who approach the transplant unit for evaluation.[73] Research suggests that many people, including people of ethnic minority backgrounds, may face some modifiable barriers to becoming a donor.

Most studies have found that living kidney donors have a high tolerance for medical risks associated with donation, such that they are willing to accept more risk and uncertainty on medical outcomes, including kidney disease, cardiovascular disease and hypertension, than health professionals.[75,76] Donors are usually highly motivated to donate, and their decisions are instantaneous and stable, compelled by moral duty, perceived responsibility and social expectation, spiritual confirmation, and personal benefits including improved quality of life, relationship and lifestyle.[36,40,77,78] Non-directed donors report a similar resoluteness and determination to their decision.[79] They believe they are able to live with one kidney, trust in the medical system, perceive themselves to be genetically and physically resilient, and are willing to accept mild inconvenience.[79] Simmons et al (1987) identified that some donors undergo a more deliberative and postponed decision-making process.[80]

It is estimated that up to 22% of candidates undergoing assessment for donation choose to opt-out.[81] Some of the key barriers are thought to include education and misconceptions about donation, financial burdens, and concerns about the health risks of donation.[81] Financial barriers may be a deterrent for potential donors of low socio-economic status, as donation assessment and recovery can incur travel and accommodation expenses, time away from work, unpaid leave, lost income and, in some countries, medical costs for assessment and post-operative care.[82-84] However, research on donor decision-making mostly includes retrospective studies on those who actually donate.[36] Donors who have gone on to complete the donation have reported feelings of ambivalence and anxiety prior to the donation, and inadequate knowledge of donation procedures and outcomes.[31,41,42]

Clinician perspectives

Nephrologists play a central role in facilitating access to kidney transplantation, through educating patients about transplant options, referring them to a transplant program, completing transplant evaluations and participating in recipient acceptance meetings.[48,54,85] In the absence of a standardised pre-transplant assessment pathway and eligibility criteria, nephrologists' recommendations and eligibility decisions may vary according to their attitudes, preferences, ethical values, priorities and competing responsibilities.[86]

Nephrologists are generally in favour of living kidney donation, but may have differential views regarding thresholds for patient and donor eligibility and their suitability for living kidney donor transplantation.[87,88] Their decision to accept a donor and recipient involves a number of tensions and challenges: to adhere to ethical principles; increase access to transplantation; ensure equitable access; ensure donor safety and voluntariness; and provide optimal outcomes for the patient.[88]

Decision-making about transplantation may be more complex in disadvantaged populations which are more likely to present with medical and psychosocial risk factors.[48,57,86,89-91] Previous research suggests that clinicians' interactions with disadvantaged patients may reflect their inherent biases regarding patients' interest in transplantation, their likelihood of finding a donor, completing evaluations or adhering to treatment, and the expected survival benefit of transplantation compared to dialysis.[90,91] Clinicians also report difficulties in communicating and establishing trust with people from different backgrounds to them, and completing their referral and evaluation processes.[90,92]

Nephrologists' decisions and promotion of living kidney donation may also be influenced by the centres in which they work. In 2014, the proportion of living kidney donor transplants in Australian hospitals ranged from 16-

52%.[93] Many countries have demonstrated inter-unit variability in the utilization of living kidney donor transplantation, after adjusting for the characteristics of a centre's patient population.[52,94,95] Previous research has identified various centre factors associated with higher rates of living kidney donor transplantation, including a higher annual volume of transplant candidates, longer waiting times for deceased donor transplantation, higher percentages of laparoscopic donor nephrectomy, greater use of unrelated donors, and programs to overcome biological incompatibility.[49,52,95-97] Centres with higher rates of living kidney donor transplantation are likely to have mechanisms that particularly encourage living kidney donation, such as better education programs, formalised procedures to help patients and donors complete transplant evaluations and more support to alleviate financial burdens.[52,94]

1.6 Outcomes of living kidney donation

This thesis also addresses problems relating to research and the assessment and discussion of living kidney donor outcomes, particularly during donor evaluation and post-donation care. Living kidney donors undergo a "medically unnecessary procedure"[98]; therefore, their safety and long-term outcomes are a primary concern for donors, recipients and their clinicians. Living donor transplantation has long been thought to incur minimal risk to donors who are deemed to be healthy and suitable to donate, and the social and emotional benefits to the donor have been considered to outweigh the risks for a medically suitable donor. [18] Recent evidence supports the view that short term risks of morbidity and mortality after donation are very low.[99,100] In a recent study of 80,347 donors in the United States, the 90-day all-cause mortality rate was 0.03%, and 2.5% of donors experienced major complications.[100] Donors are usually advised of the minimal risks associated with surgery, and that they can expect to live a long and normal life. However, an understanding of long-term donation outcomes is evolving, with recent publication of more robust longitudinal data.[21,23] These studies suggest a small increase in the absolute risk of end-stage kidney disease, hypertension, hypertension in pregnancy and all-cause mortality in the three years after donation, compared to the general or healthy population.[12,101-106] Despite some methodological limitations, these studies have changed how risk is discussed with living donors to include discussion of uncertainty regarding individualised risk and long-term outcomes.[24]

Limitations of living donor outcomes research

Our knowledge of long-term risks is considered incomplete due to several limitations in the evidence currently available. Observational studies have obtained less than ten years follow-up data on long-term outcomes, and been limited to retrospective data collection, recall bias, insufficient sample sizes to estimate effects, significant loss to follow-up and inappropriate control groups.[21,107,108] Therefore, the lifetime risks of long-term health outcomes are uncertain and cannot be accurately extrapolated to young donors. Prospective studies which include a healthy non-donor control group are needed to determine the risks attributable to living kidney donation[23] as this control group can simulate life without donating[109]. There is also limited data to estimate risks on an individual level based on specific risk-factors. This is becoming increasingly important as criteria for donation have been expanding, such that donors with comorbidities and older candidates are increasingly being accepted as donors.[12]

Long-term data collection and monitoring of living donors remains a challenge for transplant units, globally. More recently, emerging data from larger donor databases and linkage to population databases have enabled longer follow-up, larger samples and comparison with matched controls.[13,23,110,111]

Long-term clinical outcomes

After nephrectomy, the donor's remaining kidney adapts by undergoing hyper filtration, which may adversely impact kidney function and blood pressure in the long-term.[108] Two large registry studies from North America and Europe indicate that the relative risk of kidney failure is higher among donors compared to healthy matched non-donors.[101,112] In a US study, 96,000 donors were followed for a median of 7.6 years, and compared to 20,000 healthy non-donors. Living donors had eight times the risk of end-stage kidney disease (ESKD) compared to healthy non-donors; however, the absolute risk was 0.3%.[105] In a Norwegian study, living donors had 11 times the risk of ESKD compared to healthy non-donors, and a similar absolute risk of 0.47% for non-donors.[101] However, there is considerable uncertainty in these estimates due to issues with the analysis and comparison cohorts.[21] Most studies have found that donors have similar mortality risks to healthy matched non-donor controls.[103] The Norwegian study reported a higher mortality rate in kidney donors compared to healthy controls, and a 5% increase in all-cause mortality after 25 years, attributable to donation.[101] Table 1.2 provides a summary of the recent evidence on other outcomes in living kidney donors compared with healthy controls.

Table 1.2. Recent evidence on donor outcomes compared to healthy controls

Outcome	N donors	N healthy matched donors	Median donor follow-up (years)	Incidence donors (%)	Incidence controls (%)	HR (95% CI)
All-cause mortality						
Mjoen et al. (2014)[101]	1901	32,621	15.1	11.8	7.4	1.30 (1.11-1.52)
Reese et al. (2014)[103]	3,368	3,368	7.8	3.4	4.5	0.90 (0.71-1.52)
End-stage kidney disease						
Mjoen et al. (2014) [101]	1901	32,621	15.1	0.47	0.067	11.38 (4.37 – 29.63)
Muzaale et al.	96,217	96,217	7.6	0.10	0.037	Not reported

(2014)[105]						
Hypertension						
Garg et al. (2008)[113]	1,278	6,369	6.0	16.3	11.9	1.4 (1.2-1.7)
Major cardiovascular events						
Garg et al. (2012)[104]	2,028	20,280	6.8	1.3	1.4	0.85 (0.57-1.27)
Pre-eclampsia or gestational hypertension						
Garg et al. (2015)[106]	85	510	11.0	11.5	4.8	2.4 (1.2-5.0)
Gout						
Lam et al. (2015)[114]	1,988	19,880	8.8	3.4	2.0	1.6 (1.2-2.1)

Donor-reported outcomes

There is also a range of possible psychosocial and surgical related outcomes that can result after donation. Previous studies have generally shown that quality of life is good or better for living donors compared to the general population, and few donors regret their decision to donate.[115] Some qualitative studies support the view that donors gain a number of benefits from donation, including a new appreciation of life, personal growth and self-worth, and strengthened relationships with the donor and family.[36] Many studies have found that only a minority of donors (5-25%) experience negative psychological outcomes after living kidney donation.[116] The majority of donors report no depression or anxiety, but instead an improved relationship with the recipient, increased self-esteem and no change or improvement in their psychosocial health.[117]

However, qualitative research indicates that some donors experience challenges in their relationships and emotional wellbeing, particularly related to recipient death, recipient non-adherence and a lack of medical follow up.[36] An Australian study found evidence of psychological distress or a diagnosable psychiatric disorder in 25% of living donors, including donors with no prior history of mental illness.[118] After donation, up to 25%

of kidney donors report financial hardships attributable to donation. The financial impacts include out-of-pocket expenses related to travel to the transplant centre, lost wages, lost employment, and difficulties obtaining/retaining health or life insurance.[119] Up to one third of donors report that their health is poor or worse after donation, complaining of fatigue and pain.[119] Recent studies have also suggested that donors who experience medical complications, or their recipient, have an adverse outcome, and may be more likely to experience negative psychosocial impacts. The Renal and Lung Living Donors Evaluation (RELIVE) Study, found that pre-donation psychiatric diagnoses, younger age, a longer recovery from surgery and dissatisfaction with medical attention were associated with worse mental health after donation.[120] A prospective study from the Netherlands found that donor or recipient medical complications were associated with a decline in donors' mental health up to 12 months post-donation.[121] Adverse outcomes may lead to depression and feelings of disappointment, guilt, conflict in the donor recipient relationship.[117] However, it is likely that differences in psychosocial reactions among donors also reflect donors' different coping styles.[121]

There are some limitations of research on post-donation psychosocial outcomes. These studies have typically only assessed psychosocial outcomes in the short-term (i.e. less than twelve months). The surveys used are usually generic, facilitating obtaining data from general population controls, but lacking donation-specific items.[117] In most studies, population-based surveys were used as controls, rather than matching for health and demographic characteristics; therefore, psychosocial morbidity may be underestimated among donors. Additionally, donors have been found to be reluctant to express negative feelings in regard to their donation experience, possibly due to social desirability bias.[117]

Which outcomes are important to donors?

Living donors undergo rigorous medical screening and assessment; they must provide informed and voluntary consent and have access to long-term health care.[21,29,102] Informed consent assumes that donors receive reliable data about the outcomes they regard as important and relevant to their decision. Living kidney donors experience a broad range of outcomes that span their health, physical function, relationships, wellbeing and livelihood. Follow-up care may not address the outcomes that are most important to donors.[122] Donor priorities for outcomes have not been systematically identified.

Research may also not include outcomes that are important to donors, making it difficult to provide reliable and useful information to donors, and provide appropriate clinical care after donation.[122] Various initiatives have been developed to improve the selection and reporting of outcomes in trials and observational research[123,124], including the aim to ensure they are more relevant to consumers, clinical and policy decisions. These groups have worked towards establishing a minimum set of outcomes to be measured and reported across research in specific health areas e.g. kidney transplantation, dialysis and rheumatology.[125] The process typically involves steps to identify priorities for key stakeholders, the scope of the outcomes frequently measured in research, and consensus methods to reach agreement on the most important 'core' outcomes. The Outcome Measures in Rheumatology (OMERACT) initiative, led by independent international health professionals, has demonstrated improvements in the reporting and measurement of outcomes in trials.[123]

1.7 Justification for the study

The perspectives of kidney transplant recipients, living kidney donors and nephrologists are fundamental to improving access and outcomes in living kidney donor transplantation. However, the values, perspectives and beliefs that shape their decisions and actions have not been studied in-depth, particularly in the areas of donor recruitment by potential recipients, nephrologists' decisions on recipient eligibility and donors' perceptions of donation risks and experiences of the evaluation process. Nephrologists are also uniquely placed to provide insight to understand barriers and disparities across the transplant pathway. In addition, little is known about what outcomes are critically important to donors, and whether research, informed consent, education, and follow-up care address these outcomes. This study needed to ensure that these standard-of-care processes address outcomes and provide information that is meaningful and relevant to kidney donors.

As well, these perspectives of donors, recipients and nephrologists need to be considered when planning and delivering ethical and equitable strategies to improve access, outcomes and satisfaction with the donation process. Qualitative research is a powerful tool for eliciting stakeholder perspectives, utilizing rigorous and systematic methods with practical recommendations for living kidney donor transplantation clinical care and policy.

1.8 Qualitative research methods used in the study

In this thesis, qualitative research methods were used, including thematic synthesis of qualitative studies (Chapter 3), focus groups (Chapter 4), semi-structured interviews (Chapter 5) and the nominal group technique, a mixed-methods approach (Chapter 6). A systematic review of patients' perspectives was performed, given the plethora of existing research, including patients' perspectives on living kidney donor transplantation. Primary interviews were performed with clinicians to gain in-depth insight into their perspectives on barriers and disparities in living kidney donor transplantation, and to understand varying individual perspectives. There were no pre-existing studies addressing the research questions posed in this study. Focus groups were considered more appropriate for living donors because rapport among participants can encourage more open and honest discussion about the donation experience. The nominal group technique was also used with living donors to elicit their priorities for outcomes. Adapted grounded theory and thematic analysis/synthesis were applied to the qualitative studies in this thesis, as they are suited to questions around health care problems and solutions, and their results are directly applicable to practice and policy development.[126]

Chapter 2 contains an overview of qualitative research methods, including interview and focus groups methods. Grounded theory and thematic analysis, synthesising qualitative research in systematic reviews, and the use of the nominal group technique (NGT) for focus groups are expanded upon below.

Use of grounded theory and thematic analysis

Grounded theory is a commonly used methodological approach in qualitative health research, due to its focus on problems and how participants resolve them.[127] Grounded theory describes a theory that was derived from the data, and gathered and analysed in a systematic and inductive process.[128] Strauss and Corbin (1990) describe theory as “a set of well-developed concepts related through statements of relationship, which together constitute an integrated framework that can be used to explain or predict phenomena”.[128] The data analysis process is an iterative process, such that the data is analysed concurrently with data collection, and subsequent participants are chosen due to their potential to confirm or test the emerging theory (i.e. theoretical sampling).[128] Through the constant comparative method data are continuously compared across participants, to enable a deeper level of interpretation and development of more analytical themes from descriptive categories.[128] The research question or the interview questions may also change throughout the data collection process.[129]

Thematic analysis is commonly used to analyse grounded theory studies[127], because it is "theoretically flexible" i.e. not linked to a specific methodological approach.[126] Thematic analysis is a systematic approach to developing themes that identify "patterns of meaning" in the data and generate models of human attitudes, experiences and behaviours.[130] These themes answer a specific research question, and are developed into more analytical concepts through interpretation and comparison within the data set.[126,131] A thematic analysis can generate results that are accessible to lay persons and useful for policy development.

Synthesising qualitative research

A synthesis of qualitative research is presented in this thesis. Methods for synthesising qualitative research are not as developed and standardised as they are for quantitative research, with many different approaches emerging and evolving.[132] However, there has been increased recognition of their value in providing evidence to inform patient-centred care, and implementing and evaluating health care interventions.[133] A qualitative systematic review involves systematically searching for qualitative studies that address a specific research question, and synthesising their findings.[134] Their findings are useful for identifying research gaps, and generating comprehensive models of a phenomenon, with broad and in-depth insight from various cultural and health care contexts.[134]

Meta-ethnography[135] was the first proposal for the synthesis of qualitative research that informed the development of various other approaches, including thematic synthesis, grounded theory synthesis and critical interpretive synthesis. Each is associated with different methods and approaches for searching and selecting studies to include in the review, for appraising the quality of the included studies, synthesising findings from the included studies, and determining the type of output that is produced. Thematic synthesis developed by Thomas and Harden[132] was used in this thesis. A thematic synthesis is suited to questions of participants' experiences and perspectives, supports a systematic and transparent approach, and produces practical recommendations.[132] Other methodologies, such as critical interpretive synthesis and meta-ethnography, often produce more complex, "conceptually rich", theoretical findings which may require further interpretation of readers to directly apply their findings to policy or practice.[133,136]

Focus groups using the nominal group technique

Focus groups and NGT are used in the studies in this thesis. The NGT is a variation of a focus group, utilizing both quantitative and qualitative components (i.e. mixed-methods). The NGT was first developed to identify strategic problems and develop strategies to solve them[137] and has been used to identify consumers' preferences and priorities[138-140], and reach group consensus.[141] It involves a highly structured face-to-face meeting lasting up to two hours.[142] The process begins with a structured 'brainstorming' discussion to develop ideas, followed by individual voting on the prioritised list of options.[141] Finally, reasons for divergent and similar opinions are explored through group discussion. By voting confidentially as an individual, each participant is able to offer their own viewpoint without the pressure to converge to the mainstream viewpoint.[141] Generally speaking, the quantitative analysis of the NGT involves analysing the scores or rankings of participants, as well as the frequency of votes for each outcome.[142] Thematic analysis is often used to analyse the qualitative discussion from the NGT.[137] The qualitative data should be compared to the priority scores (quantitative data) to contextualise and explain group priorities, explore where they converge or contract each other, and inform policy implications.[137,143]

1.9 Aims of the research

This thesis can be divided into two related parts, reflecting the aims of the studies:

a) the pathway to living kidney donor transplantation (chapters 3 to 5), and
b) living kidney donor outcomes (chapters 6 and 7).

The specific aims of each study are:

1. to identify and describe the beliefs, attitudes and expectations of patients with CKD (stages 1-5) regarding living kidney donation (Chapter 3)
2. to describe kidney donors' experiences of the evaluation process (Chapter 4)
3. to describe nephrologists' perspectives on barriers to living kidney donation and disparities in access to living kidney donor transplantation (Chapter 5)
4. to identify living kidney donors' priorities for outcomes and describe the reasons for their choices (Chapter 6), and
5. to determine the scope and heterogeneity of outcomes in adult living kidney donors reported in randomised trials and observational studies (Chapter 7).

1.10 Structure of the thesis

This chapter, Chapter 1, includes a summary of existing literature regarding the pathway to living kidney donor transplantation (including barriers and disparities and the evaluation process), and outcomes for living kidney donors. An overview of the thesis structure is provided in Figure 1.2. The studies presented in this thesis are identical copies of the published peer-reviewed articles (Chapters 2, 3, 4, 5), and submitted articles (Chapters 6 and 7).

Chapter 2 provides an overview of qualitative research methods and the principles of rigour.

Chapters 3 to 5 include qualitative studies on the perspectives of patients, living kidney donors and nephrologists on different aspects of the pathway to living kidney donor transplantation. In Chapter 3, the expectations and attitudes of patients with CKD regarding living kidney donor transplantation are described, based on a systematic review and thematic synthesis of qualitative studies. Chapter 4 presents donors' experiences of the evaluation process elicited through focus groups in Australia and Canada. Chapter 5 provides in-depth insights on nephrologists' attitudes and perspectives regarding recipient eligibility and access to living kidney donor transplantation, which were generated through semi-structured interviews.

Chapters 6 and 7 focus on donor outcomes. Chapter 6 elicits living kidney donors' priorities for outcomes using the nominal group technique, and describes the reasons underpinning their preferences as derived from the focus group discussion. Chapter 7 provides a comprehensive, systematic, and detailed evaluation of the scope, consistency and measurement of outcomes reported in randomised trials and observational studies on living kidney donor outcomes.

In Chapter 8, the concluding chapter of this thesis, the key findings from each study are integrated and considered as a whole. These findings were compared with existing literature. The strengths and limitations of studies are discussed. Finally, the implications of these studies for improving access and outcomes in living kidney donor transplantation are outlined.

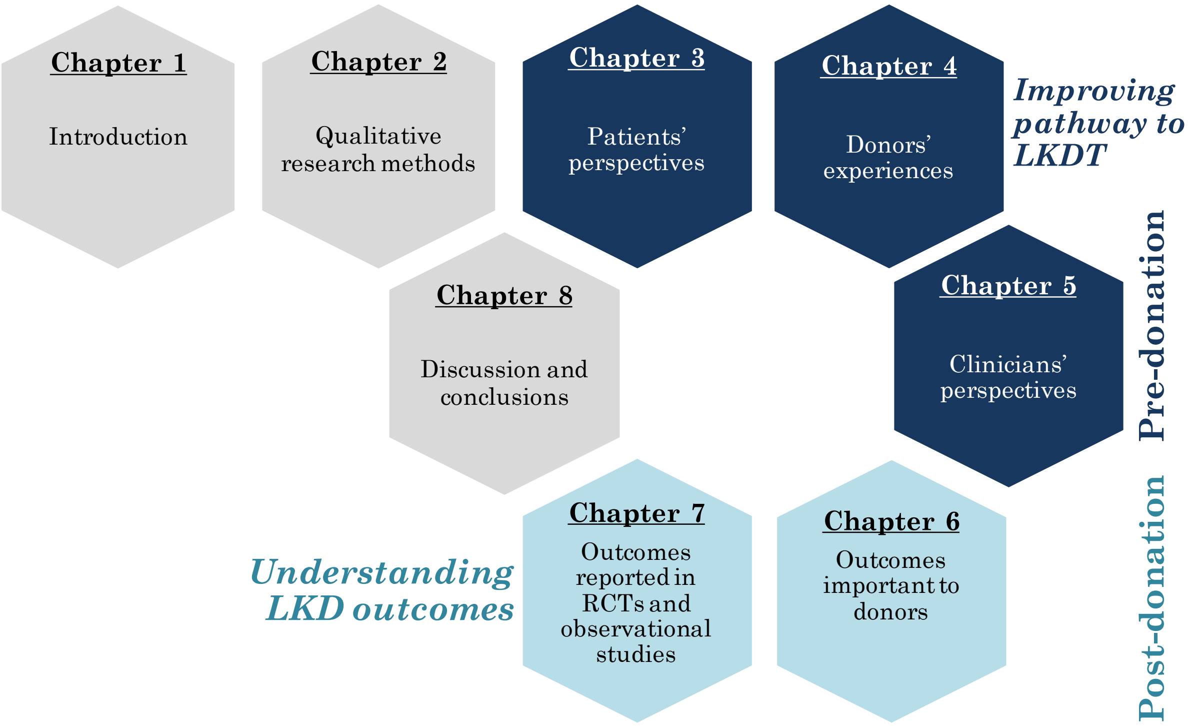

Figure 1.2. Thesis chapter outline

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Chapter 2: Qualitative research: methods and rigour

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The chapter is structured as per the journal article.

NB. This invited paper details the qualitative methods applied in this thesis (to the adult population). Given the target audience of the journal, considerations in conducting qualitative research in children were included but have been removed from this chapter.

2.1 Introduction

Qualitative research aims to describe, understand or explain social phenomena using a systematic and scientific process.[1] Qualitative methods are designed to answer 'why' questions. For example, to explain why adolescent kidney transplant recipients do not take immunosuppression medications as prescribed, particularly given their higher rates of graft loss due to non-adherence during transition.[2,3] While quantitative research tests hypotheses, qualitative research generates hypotheses and provides detailed and nuanced understandings about health behaviours, decisions and experiences. Qualitative methods may also be conducted in a mixed-methods framework (i.e. combined with quantitative research), for example, to inform survey design or explain survey responses, or used in process evaluations to guide the design, conduct, evaluation, and implementation of clinical trials.

Qualitative research is a broad term for various approaches of inquiry. Depending on the research question, researchers may use a methodological framework to guide their choice of methods used to collect and analyse data (e.g. grounded theory, phenomenology or ethnography).[1] Common methods used in qualitative research are outlined in Figure 2.1. In the following section, we describe the methods of participant selection, data collection and analysis in qualitative research.

2.2 Participant selection and recruitment

In qualitative research, participants are sampled for meaning, not for statistical power. Typically, purposive sampling (e.g. to include a range of demographic, clinical characteristics, experience and backgrounds) of information-rich informants, is used to gain a broad insight relevant to the phenomenon being investigated.[4,5] Qualitative interview studies generally include 20 to 50 participants, while focus group studies usually report around 6 or more groups, with 6-8 participants per group to optimize participant interaction. Generally, recruitment will cease when data saturation is achieved i.e. when subsequent data collection does not provide new insights.[5] Unlike quantitative studies, qualitative findings are not 'generalisable' or 'representative' across all patients, however, the findings (or concepts) may be transferable to other contexts.[1]

2.3 Data collection

Interviews and focus groups are commonly used in qualitative health research. Semi-structured or in-depth interviews are suited to research that aims to understand individual perspectives, for example, a person's decision-making about medicine taking or the impact of disease on their identity. Semi-structured interviews use a flexible question guide, which can evolve during data collection. The question guide includes open-ended questions related to the study topic, and prompts to encourage participants to elaborate and clarify their responses. In-depth interviews are unstructured, inviting participants to share their narratives with occasional prompts from the researcher. In contrast, focus groups harness the dynamics of group interaction to elucidate reasons for similar or disparate views and experiences, or to brainstorm ideas, for example to develop a new transition program. Audio-recording and transcription ensure accuracy and allow researchers to concentrate on interacting and engaging with participants. Field notes on contextual information and non-verbal communication may be recorded.

2.4 Data analysis

The aim of qualitative data analysis is to develop a description or explanation of a phenomenon that captures the breadth and depth of the data collected. The output is usually themes (e.g. thematic analysis), or a theory (e.g. grounded theory analysis). Coding is the basis of most forms of qualitative data analysis, involving an iterative process of data reduction by identifying and interpreting the meaningful sections of text and synthesizing the data into themes or concepts. Usually, the concepts are identified inductively. However, content analysis involves coding of the data into pre-defined categories or existing theories and is usually done when there is a meaningful denominator (e.g. the number of websites with a focus on specific pre-determined topics). Coding can be performed within a software program to facilitate analysis of qualitative data. Multiple investigators may be involved to ensure the analysis is comprehensive (investigator triangulation). Researchers may identify conceptual relationships and patterns among the concepts or themes identified.

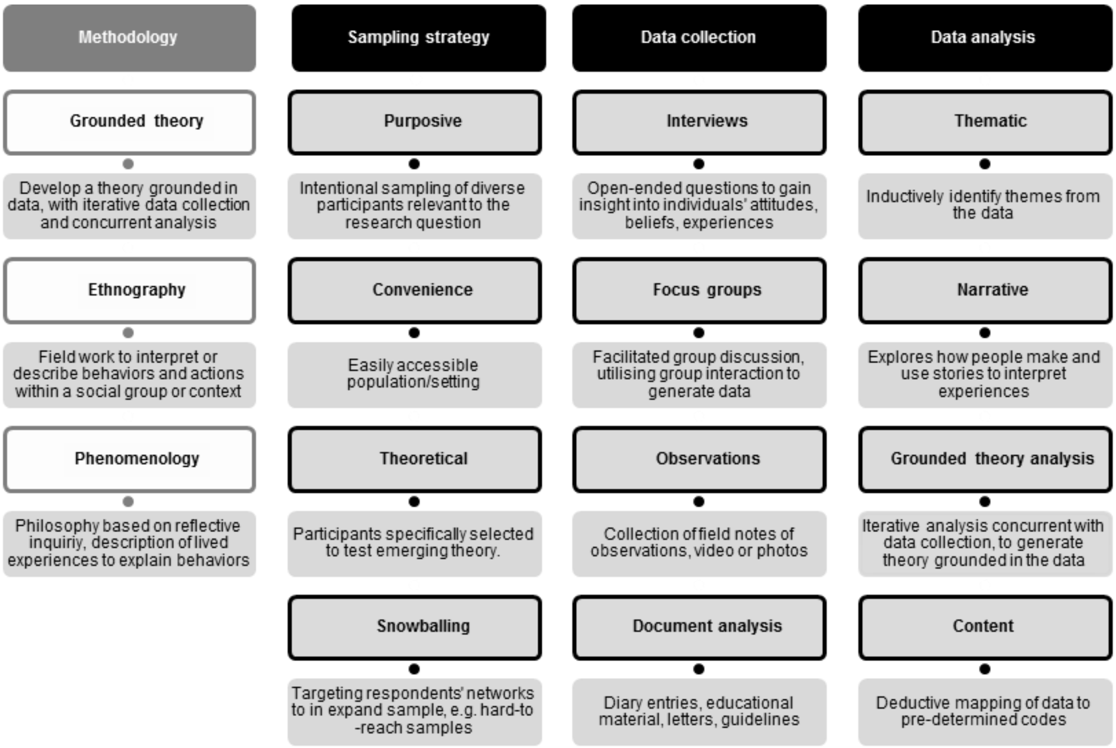

Figure 2.1. An outline of common methodologies and methods used in qualitative research

2.5 Appraising qualitative research

Several guidelines suggest criteria for appraising qualitative research though this remains contentious as there is no empiric basis to demonstrate that a given approach (e.g. use of software) improves the quality of a qualitative study.[5-7] To guide the appraisal of qualitative research, we suggest the use of four constructs proposed by Guba and Lincoln[8]: credibility (are the findings trustworthy?), confirmability (are the interpretations linked to the data?) dependability (is the process logical and auditable?), and transferability (are the findings relevant to other settings and contexts?).

Credibility: The credibility of a study's findings considers how comprehensive, truthful and reasonable the findings and interpretations are. Qualitative data collection involves the co-construction of meaning among the researchers, participants and research process[9,10]; and is not designed to measure a single objective reality. Providing a detailed description of the research team and their roles, study setting, question guide and findings can help readers determine whether these may have influenced participant responses and the researchers' interpretations. The question guide should be relevant to the research question and designed to facilitate in-depth discussion. Purposive sampling and data saturation ensures that sufficient data has been collected to captures the diversity of views and experiences relevant to the research question. Triangulation using multiple methods of data collection, or multidisciplinary investigators in the analysis can ensure more comprehensive insight and interpretations.[5] Member-checking (obtaining participant feedback on the results) can also ensure that the findings reflect the complete range and depth of opinions.[6]

Confirmability: The confirmability of a study convinces the readers that the findings reflect the participant's perspectives, rather than the researcher's predetermined assumptions or agenda. Reflexivity involves researchers recognizing any undue influence on the their interpretations of the data.[6] Strategies to demonstrate confirmability include independent coding by multiple investigators who are familiar with the data (e.g. by reading all the transcripts), and presenting raw data such as participant quotations to support themes and concepts that are developed.[5,11]

Dependability: Dependability establishes that the study followed a rigorous and systematic approach by demonstrating a coherent link between the findings and the methods and methodology. Qualitative research methods are iterative and interpretive, and impossible for another researcher to replicate[12], therefore the concept of ‘reliability’ is not applicable[6]. Audio recording, transcription of data, and use of software for coding can ensure a transparent and auditable documentation of the research process. This can allow the raw data, and analysis process to be reviewed by others.

Transferability: Transferability describes the extent to which the themes or concepts can be considered relevant to other settings.[5,13] Details about the study setting, participant characteristics, and health care framework can help readers to ascertain whether the findings are applicable to their own context.[6] Also, demonstrating some similarities to other studies conducted in different regions and populations, or to existing theory can help demonstrate the broader relevance of their findings.[14]

The Consolidated Criteria for Reporting of Qualitative Research (COREQ) [13] provide a framework for reporting qualitative studies using interviews or focus groups, so readers can assess study quality.

2.6 Conclusions

In summary, qualitative methods are valuable for providing in-depth understanding the values, beliefs, attitudes, priorities and preferences of the key stakeholders involved in living kidney donor transplantation. Authors can ensure the value of qualitative studies by demonstrating the principles of credibility, confirmability, dependability and transferability. Qualitative research is also useful for developing hypotheses, for example, to develop interventions to address disparities in living kidney donor transplantation.[12] By using rigorous and systematic qualitative research methods, the research in this thesis intends to gain in-depth insight into donor, recipient and nephrologists perspectives to identify strategies to improve access, outcomes and satisfaction with living kidney donor transplantation.

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Chapter 3: The expectations and attitudes of patients with chronic kidney disease towards living kidney donor transplantation: a thematic synthesis of qualitative studies

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3.1. Abstract

Background: Living kidney donation offers superior outcomes over deceased organ donation, but incurs psychosocial and ethical challenges for recipients because of the risks imposed on their donor. We aimed to describe the beliefs, attitudes, and expectations of patients with chronic kidney disease toward receiving a living kidney donor transplant.

Methods: We conducted a systematic review of qualitative studies of patients' attitudes toward living kidney donation using a comprehensive literature search of electronic databases to February 2013. The findings were analysed using thematic synthesis.

Results: Thirty-nine studies (n = 1791 participants) were included. We identified six themes: prioritising own health (better graft survival, accepting risk, and desperate aversion to dialysis), guilt and responsibility (jeopardising donor health, anticipating donor regret, and causing donor inconvenience), ambivalence and uncertainty (doubting transplant urgency, insufficient information, confronted by unfamiliarity, and prognostic uncertainty), seeking decisional validation (a familial obligation, alleviating family burden, reciprocal benefits for donors, respecting donor autonomy, external reassurance, and religious approval), needing social support (avoiding family conflict, unrelenting indebtedness, and emotional isolation), and cautious donor recruitment (self-advocacy, lacking self-confidence, avoiding donor coercion, emotional vulnerability, respecting cultural, and religious taboos).

Conclusion: Enhanced education and psychosocial support may help clarify, validate, and address patients' concerns regarding donor outcomes, guilt, relationship tensions, and donor recruitment. This may encourage informed decision-making, increase access to living kidney donation, and improve psychosocial adjustment for transplant recipients.

3.2. Introduction

Critical shortages in the rates of deceased organ donation have necessitated widespread acceptance of living organ donors for transplantation.[1,2] In 2011, 42% of the 76,118 kidney transplants registered across more than 80 countries were from living donors.[3] Ethnic and socioeconomic variations in access to living donor kidney transplantation have been reported in many countries[4-8], but the barriers are poorly understood.

While living donor kidney transplantation offers optimal recipient survival outcomes, [9-11] the risks posed to their living donor make decision-making ethically and emotionally complex for potential recipients [1,9,12]. Patients report concerns about the long-term health problems and financial burdens for their donor, the possibility of graft failure, family conflict, feelings of guilt and indebtedness and initiating discussions with potential donors.[13-19]

Guidelines offer limited recommendations to address the psychosocial issues faced by potential recipients[20,21], and educational and psychosocial resources vary considerably among transplant centres. [22,23] We aimed to describe the attitudes and expectations of patients with chronic kidney disease (CKD) regarding living kidney donation, to inform strategies to support decision-making that addresses patients' perspectives and priorities.

3.3. Methods

We followed the Enhancing Transparency of Reporting the Synthesis of Qualitative Research (ENTREQ) framework.[24]

Selection criteria

Qualitative studies were included that explored the perspectives of adult patients ($\geq$ 18 years of age) with CKD (stages 1-5, 5D, and 5T) towards living kidney donation (including related, unrelated, altruistic, commercial, and paired exchange donation). Non-English articles were excluded to avoid misinterpretation of meaning.

Data sources and searches

The search strategy is provided in Appendix A.1. The searches were performed in MEDLINE, Embase, PsycINFO, and CINAHL from inception to the 19th February 2013. Google Scholar and reference lists of relevant articles were also searched. CSH screened the titles and abstracts and discarded articles that did not meet the inclusion criteria. Full-text articles of potentially relevant studies were obtained and assessed for eligibility.

Quality of reporting assessment

For each study, two reviewers (CSH/AFR) independently assessed the explicitness of reporting of each study using the Consolidated Criteria for Reporting Qualitative Health Research (COREQ) framework for interview and focus group studies.[25] Disagreements were resolved through discussion. This framework enables readers to assess the transferability of each study to their own setting.

Data analysis

Thematic synthesis, the inductive generation of analytical themes, was used to synthesise the findings.[26] All text in the "results/findings" and "discussion/conclusion" sections were extracted and entered into HyperResearch (ResearchWare, INC 2009 version 3.5.2), software for qualitative data management. CSH performed line-by-line coding of all text relating to patients' perspectives regarding receiving a living kidney donation, to identify preliminary concepts. These concepts were translated between studies by coding data into existing or new themes as they emerged. AT independently reviewed these themes to ensure they incorporated all of the concepts. We mapped relationships between themes to develop a conceptual analytical framework.

3.4. Results

Literature search and study characteristics

Our search yielded 1325 articles. We included 39 studies ($n \geq 1791$) involving participants with CKD stages 1-5 (n = 108), 5D (n = 912), 5T (n = 766) and unspecified (n = 5) (Figure 3.1). At least 444 (60%) of the transplant recipients had received (or were undergoing evaluation for) a living donor transplantation. At least 39 (5%) of the transplant recipients received a pre-emptive transplant. Persons of ethnic minority status were recruited by purposive sampling in 16 (46%) studies. Data was collected using in-depth or semi-structured interviews, focus groups and open-ended surveys. The studies were conducted across 13 countries. The study characteristics are provided in Table 3.1.

Comprehensiveness of Reporting

Studies reported between 6 and 21 of the 27 items included in the COREQ framework (Table 3.2). Twenty-four studies described the participant selection strategy, 24 studies provided the questions or topic guides, and all studies included participant quotations. Eighteen studies reported researcher triangulation, and four reported on theoretical saturation.

Synthesis

We identified six major themes: prioritising own health, guilt and responsibility, ambivalence and uncertainty, needing social support, seeking decisional validation and cautious donor recruitment. Selected quotations for each theme are provided in Table 3.3. Conceptual links among themes are depicted in Figure 3.2. Perceived urgency and desperation fostered a pro-active pursuit of a living donor. Participants were conflicted between choosing the best treatment to improve their survival and quality of life (QOL), and their concerns regarding their donor's health, the emotional challenge of asking someone to donate, the burdens of guilt, responsibility, indebtedness and family conflict. These concerns were minimised with emotional support and reassurance, internal and external decisional validation and shared responsibility.

Prioritising own health

Better graft survival: Living donor kidney transplantation was perceived to be the "best way forward"[27], as the graft was expected to last longer than a deceased donor graft, particularly a related donor which could provide "the best match"[14]. Participants' derived comfort from knowing the origin and quality of a living donor kidney.

Accepting risk: The risks to the donor were perceived to be minimal, and it was thought that a person could spare one kidney. Some coped with uncertainty by avoiding focussing on risks that "may never happen"[28] or identifying "standby donors"[29] in case the graft failed.

Desperate aversion to dialysis: Some felt desperate for a living donor, believing they were waiting "in vain"[30] on the transplant list, facing imminent death on dialysis, or could no longer cope with dialysis. Pre-dialysis participants hoped for a pre-emptive living donation to avoid dialysis. Some participants considered paying for a kidney from an overseas donor.

Guilt and responsibility

Jeopardising donor health: Participants expected that guilt would constantly play "at the back of [their] mind"[13] if their donor was harmed. Older participants felt it was "selfish"[13] to potentially shorten a young person's life. Parents believed it was their inherent duty to protect their children from harm.

Anticipating donor regret: Participants feared that their donor might blame and resent the recipient for their "bad decision"[15] if the donor experienced health problems. The donor might regret their unnecessary sacrifice if the graft failed. Some were reluctant to accept their partner's[15] kidney in case their children ever needed a transplant, particularly if polycystic kidney disease was diagnosed in the family.

Causing donor inconvenience: Participants would feel guilty for causing their donor to incur financial loss, career disruption, dietary restrictions, pain or impaired self-esteem due to scarring. They believed that those with a "busy job"[17], young children or sporting aspirations should not risk their health and take time away from their commitments.

Ambivalence and uncertainty

Doubting transplant urgency: Some found it difficult to consider pre-emptive transplantation if they were asymptomatic, still producing urine, and living a normal life. Some believed their "kidney [function] might be coming back"[31] with adherence to medication or dialysis. A living kidney donation could be a "last resort"[32] if their illness became "life threatening".[33]

Insufficient information: Some felt there was insufficient information about donor acceptance criteria, financial and insurance issues, risks to the donor, the surgical procedures, the exchange program, and the possibility of overseas donors. Participants from diverse cultural and linguistic backgrounds felt that the information provided was difficult to understand and could be more culturally sensitive. Turkish, Moroccan and Cape Verdean patients from the Netherlands explained that they would not "dig any further for information"[33] and relied on clinicians to provide information. Participants did not feel they had enough time with their doctor to discuss their concerns. Families could help them to comprehend information, but some thought family members may be unwilling or unable to attend education sessions.

Confronted by unfamiliarity: Living donation was unfamiliar and confronting to Mexican participants, portrayed as "strange", "outside of [their] world", and "something for rich people".[31] Some felt uneasy about incorporating a living person's kidney into their own body.[34] African and Turkish patients felt their communities were unfamiliar with living donation, thus discussions with family members were met with resistance.[33,35]

Prognostic uncertainty: Despite knowing that the risks to the donor were low, the potential consequences were considered severe. Some were concerned that their donor might die during surgery, have a shortened life expectancy, or develop kidney failure and require dialysis.[36] They feared that donation might cause fertility and pregnancy complications. Some preferred a deceased donor transplant to spare their loved one from possible harms.

Seeking decisional validation

A familial obligation: Donation between blood relatives was perceived to be "fair"[37] and obligatory, and participants with volunteering relatives thought that there was a mutual understanding that the participant would have donated if the roles had been reversed.

Alleviating family burden: Living kidney donation was expected to alleviate the restrictions and caregiver burdens placed on family members, enabling the flexibility to travel and socialise.

Reciprocal benefits for donors: Some believed their donor might experience increased self-esteem from helping a loved one.[38] Spousal donors were thought to benefit from alleviated caregiver burdens and improved QOL.

Some recipients felt these benefits for the donor could be better communicated during decision-making.[39]

Religious approval: Muslim, Christian and Buddhist participants believed that living kidney donation aligned with the altruistic values of their religion.[33,40,41] Some were concerned that their religious community might condemn interfaith or unrelated living donation. Some Muslim participants argued that their beliefs did not prohibit living donation, and the notion of bodily integrity was irrelevant as "it's the soul which goes to God not the body".[40]

Respecting donor autonomy: Participants believed that motivated donors had the "right to donate"[42], and would feel disappointed if their offer was rejected or were deemed ineligible. Refusing an offer would therefore be perceived as "selfish"[42].

External reassurance: Participants wanted reassurance from their doctor that their donor was going "to be ok".[33] Patient advocates were described as a valuable source of emotional support.

Needing social support

Avoiding family conflict: Some felt that accepting or rejecting a relative's offer could ignite family conflict. Refusal to donate created resentment and tension. Some participants concealed their feelings to preserve relationships. Participant's valued decisional-support from their families, fearing blame for potentially harming their loved one or losing their kidney.

Unrelenting indebtedness: Participants expected to feel eternally indebted to their donor, particularly sibling donors, and be unable to refuse what their donor might ask of them, for fear of appearing ungrateful. Young participants felt that accepting their parent's kidney meant their parents would have even greater control over their lives. Some rejected offers which they suspected came with "strings attached"[43] such as financial obligations. They preferred the "neutrality"[43] and anonymity of deceased donation.

Emotional isolation: Participants felt there was limited support to cope with depression, anxiety about uncertain donor or graft outcomes, guilt, or accept their diagnosis. Participants explained that they concealed their "miseries"[30] from their donor, family or health care providers. Refusal from family members to donate led some participants to feel isolated, as they felt their friends and family withdrew from them.

Cautious donor recruitment

Self-advocacy: Participants believed that being honest and informing family members about the possibility for living kidney donation was respectful, but would also maximise their chances of finding a donor. Some believed that clinicians could convey the "legitimate"[33] need for donation to potential donors more effectively. Some felt they had to "promote" their own cause with "a really good story"[33] or by offering incentives[33].

Lacking self-confidence: Participants lacked confidence in finding a willing living donor, particularly if they had been refused in the past. Participants were unsure how to approach the topic and were worried about misleading or misinforming potential donors. Pre-dialysis patients were uncertain about their ability to justify the need for pre-emptive transplantation to a potential donor without immediate medical urgency. Some were willing for clinicians to hold family information sessions, mediate discussions or make requests on their behalf.

Avoiding donor coercion: Some participants preferred to "wait and see"[33] if a donor volunteered, in case the donor might feel too guilty to refuse. Others preferred an indirect approach like using humour, providing information, or "cautiously [dropping] the subject".[44] Providing information to potential donors early was thought to facilitate informed decision-making. Some believed that donors were nominated and pressured by other family members, and participants sought reassurance that their motives were genuine.

Emotional vulnerability: Initiating discussions with potential donors was expected to be "emotionally excruciating"[31] as participants expected refusal to be devastating. Asking would feel like "beg[ging]"[33], and was considered "pathetic"[33], "awkward"[33] and embarrassing. Clinician-mediated discussions were suggested.

Respecting cultural and religious taboos: Turkish, Dutch Antillean, Moroccan and Surinamese patients expressed that discussing illness was considered to be "taboo"[33], and thus donation requests would be considered disrespectful. African participants mentioned that they had to seek permission from their senior relatives prior to discussing donation with family.[35,41]

3.5. Discussion

For patients with CKD, decisions regarding living donor kidney transplantation involve complex tensions between prioritising their own health and concerns about the risks to their living donor. A preference for living kidney donation was based upon maximising graft survival, a desperate aversion to dialysis, and confidence in the transplant community to protect their donor from harm. Patients justified accepting a donation from a living donor to reduce caregiver burdens and to demonstrate respect for the donor's choice to donate. However, decision-making can be challenging for patients' harbouring concerns about the donor's vulnerability to physical harm, coercion and financial hardship. Patients anticipated bearing burdens of guilt, responsibility and indebtedness, and causing conflict among family members. They also faced the challenge of initiating sensitive discussions about live donation with friends and family. Patients who were unable to accept or understand their diagnosis of CKD were reluctant to contemplate pre-emptive transplantation. The inability to communicate and resolve these anxieties intensified decisional-conflict in potential recipients.

The themes identified in our review might explain some of the psychosocial and cultural barriers underpinning ethnic disparities in living donor kidney transplantation.[5,6] Previous studies have found that patients from minority ethnic backgrounds are less likely to initiate discussions with potential living donors than non-minority patients [19,45]. Our findings indicate that patients emphasise various cultural values which underpin reluctance to seek potential donors including the impropriety of discussing illness, rules of family hierarchy, and suspected community unfamiliarity and ambivalence about living donation. A sense of medical urgency and desperation mobilised patients to initiate discussions with potential donors. Previous studies, however, have found that African American patients have difficulty accepting their diagnosis of renal failure and the need for transplantation.[4,19,45-47]

Our study has certain strengths. We performed a comprehensive literature search and an independent appraisal of study reporting[9,25], and used software to facilitate the auditable development of themes. A novel conceptual schema was developed depicting the facilitators, barriers and challenges influencing patients' decisions about living donor kidney transplantation. This review included participants from a range of clinical, ethnic, cultural and religious backgrounds. However, the exclusion of non-English studies, and the predominance of studies from high income countries with a high human development index (HDI)[48] may limit the overall transferability of our findings.

Education directed at potential living kidney donor transplant recipients should seek to identify and address patients' valid concerns and mitigate misconceptions. Patients are anxious about donors having an increased risk of ESKD[36], perioperative mortality[13], a shortened life expectancy[13], pregnancy complications[17], erectile dysfunction[41], pain[13], and facing long-term lifestyle modifications[49]. Evidence-based information about the potential risks and benefits should be communicated to patients. Recent data suggests that donors may be at an increased risk of ESKD[50,51], gestational hypertension during pregnancy[52], and have a 0.03% risk of perioperative mortality[53]. Studies also show that living donors can derive various personal benefits from donation including an improved relationship with the recipient, increased quality of life due to reduced caregiver burdens, and gain an increased sense of self-worth.[54]

Informing patients about efforts to safeguard donors such as independent donor advocates, reimbursement schemes, psychological evaluation, and rigorous donor acceptance criteria may provide reassurance to patients. To help patients engage in discussions about pre-emptive transplantation, transplant education should emphasise the benefits of pre-emptive transplantation and ensure that patients understand that while CKD can be asymptomatic, the disease can progress to ESKD requiring renal replacement therapy. Clinicians may also be confronted with the patient's preference for commercial or deceased donor transplantation due to desperation, or to avoid exposing their loved ones to the possible risks associated with living donation; and resources to educate patients about the risks of commercial transplantation are available.[55]

Interventions should be evaluated that specifically address patients concerns about guilt, indebtedness, family conflict, donor coercion, uncertain donor outcomes and donor recruitment. Quality of life therapy, which aims to identify specific areas of dissatisfaction and problem-solving strategies, can improve QOL and psychological functioning for patients awaiting living donor kidney transplantation.[56] Our findings can inform possible coping-strategies such as sharing responsibility for possible risks. Mediated open-communication between patients, their family and potential donors might resolve interpersonal concerns and facilitate family support, shared responsibility and decisional validation.[29,57] A randomised controlled trial[58,59] found that a culturally-sensitive home-based family education program improved patients knowledge and willingness to discussion living kidney donation, decreased patients concerns about living donor kidney transplantation, and led to increased donor inquiries, evaluations and actual living kidney donor transplant rates. Family-oriented interventions may be particularly effective for culturally and linguistic diverse patients to facilitate social support, information comprehension and address family ambivalence.[57,60]

Reticence to initiate discussions with potential donors is one of the most frequently reported barriers among patients waitlisted for transplantation.[19,61] Indirect discussions about donation, rather than direct requests to donate, have been found to be effective for donor recruitment[32], and may alleviate concerns about disrespecting, pressuring potential donors. This might be achieved through family-oriented education, led by a health professional independent from the transplant team[57,60,62]. The Talking about Living Kidney Donation Educational and Social Worker intervention encourages patients to identify and resolve self-identified barriers to discussing and pursuing pre-emptive living kidney donor transplantation. This intervention increased discussions about living kidney donation with family and clinicians, and the identification of potential donors.[57,60] Boulware and colleagues[60] developed model conversations to help patients initiate such discussions with potential donors (http://diseasemanagementboulware.org/talk-materials/). Similarly, a rubric with example phrases and role-playing exercises could be offered to potential recipients for making direct donation requests. The provision of a medical 'alibi' to excuse unwilling potential donors has been widely advocated[63], and may also protect the patient's self-esteem and preserve family relationships. We also recommend providing patients access to counselling to cope with the disappointment of refusal to donate and develop resilience for making subsequent requests.

Research is needed to inform strategies for identifying and addressing the specific challenges experienced by living donor kidney transplant recipients. We suggested further adaptation to validated psychosocial screening tools, for example The Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT)[21] to capture additional domains identified in our review such as guilt, indebtedness and donor recruitment. Identifying the priorities and preferences of patients from ethnic minorities is needed to inform culturally sensitive interventions. Further research is needed in low and middle HDI countries where treatment is less readily available. Previous studies have identified socioeconomic disparities in access to living donor kidney transplantation[6,7,64], but barriers from the patients' perspective require more in-depth exploration. Also, more understanding is needed about patients' attitudes towards pre-emptive transplantation, paired kidney exchange, altruistic living donation and the perspectives of patients who are likely to face a longer waiting time for a deceased donor kidney, for example highly sensitised patients.

Living donor kidney transplantation is appreciated by patients as the optimal treatment for CKD, but carries inherent psychosocial and ethical challenges implicated in asking another person to accept risks on their behalf, as well as coping with guilt, responsibility, indebtedness, potential coercion and family resistance. We propose culturally sensitive, family-oriented educational and psychosocial strategies to resolve guilt, ambivalence, decisional-conflict and interpersonal problems and help patients find a personally acceptable approach to engaging in discussions with potential donors. Recognising and addressing patients' concerns may encourage informed decision-making, increase access to living kidney donation, and improve recipient's psychosocial wellbeing.

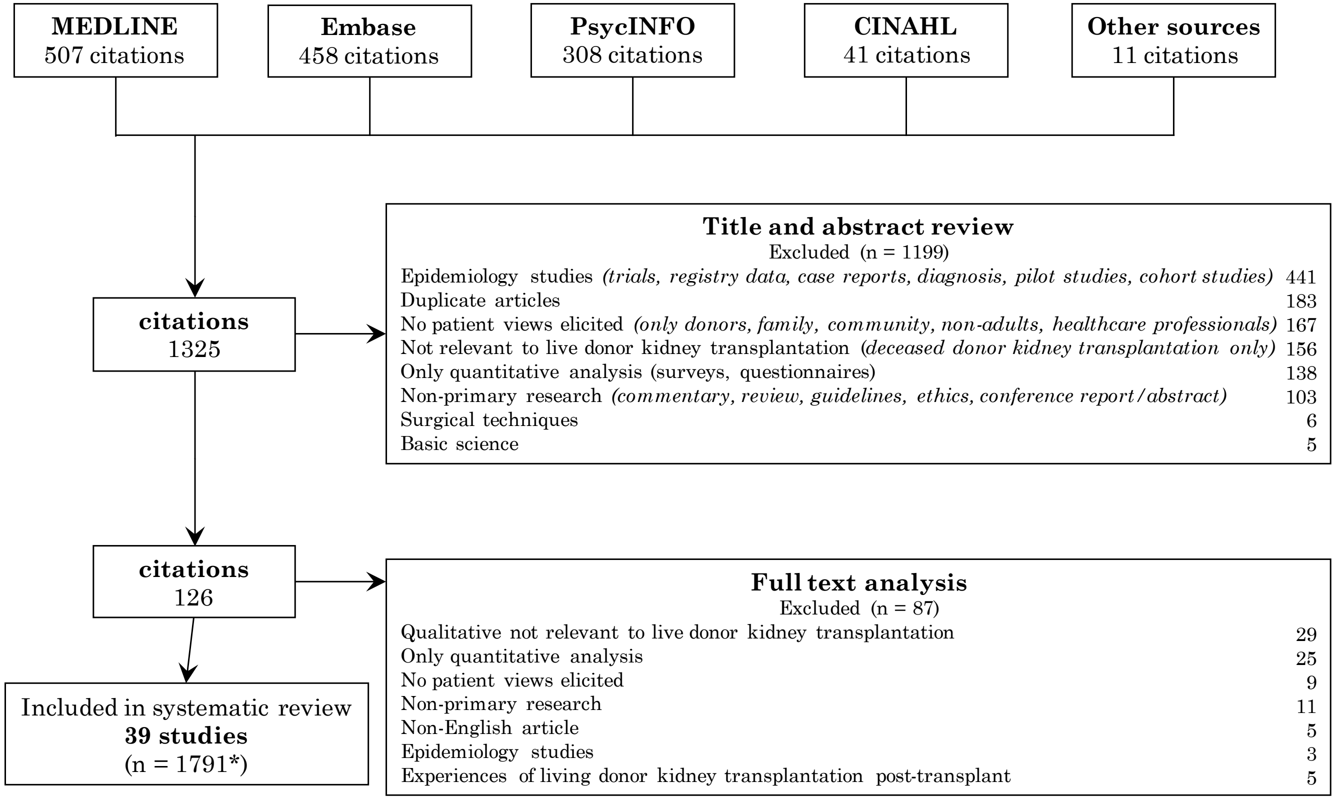

Figure 3.1. Search Results

* Minimum 1769 CKD 1-5, dialysis and transplant patients (Gill 2008 and 2012; Gordon 2001a and 2001b; Ismail 2010, 2011 and 2012; Mazaris 2012a and 2012b used the same participants in each study).

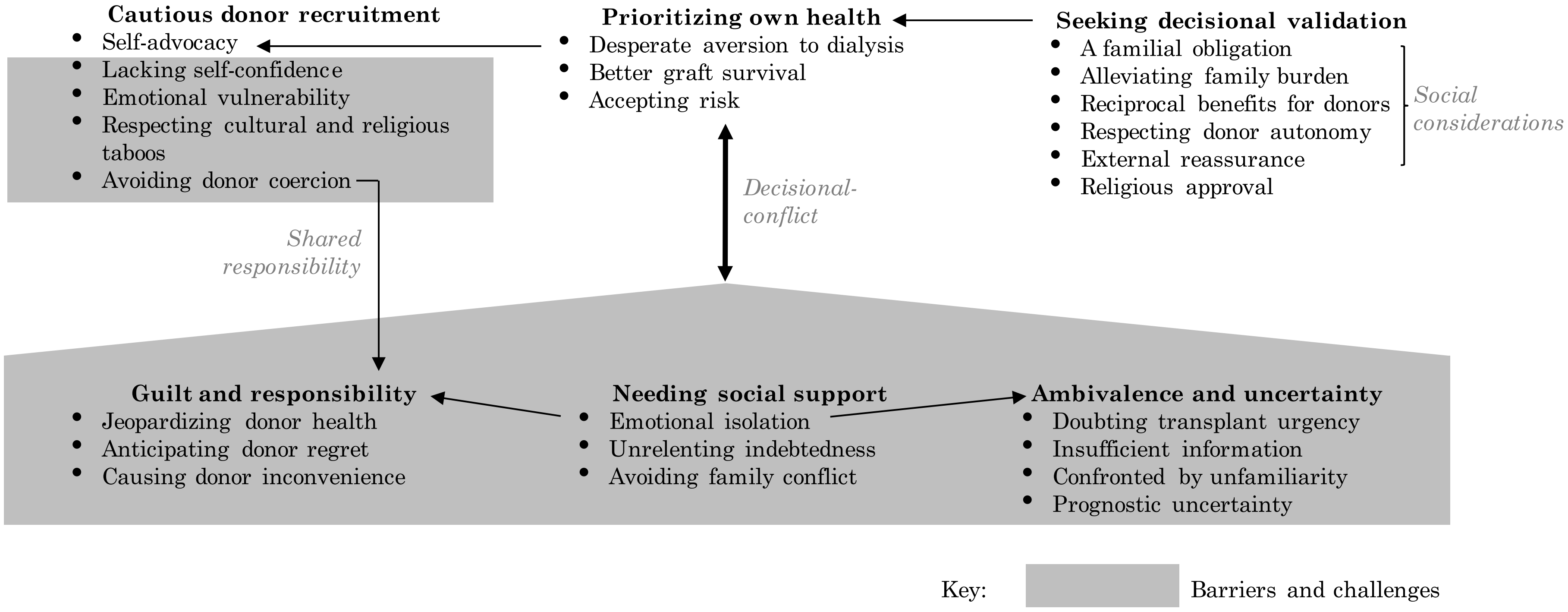

Figure 3.2. Thematic schema representing adult CKD patients' expectations and attitudes towards living kidney donor transplantation

Table 3.1. Characteristics of included studies (grouped by country)

Study	Country	*n*	Age range (years)	Gender M:F	CKD stage					Data collection	Methodological framework	Analysis	Research questions relating to living kidney donor transplantation
					1-5	5D	DD	LD	Pre-				
Martin-McDonald 2003	**Australia**	10	22-68	5:5		●				Face-to-face, in-depth interview	Narrative inquiry	Thematic	Medical concerns for donor
Tong 2009	**Australia**	63	20-78	31:32	●	●	●	●		Focus groups	-	Thematic	Psychosocial considerations
Barnieh 2011	**Canada**	145	-	83:62	●	●				Survey with open-ended response	-	Thematic	Knowledge, psychosocial barriers
Hilton 1994	**Canada**	10	20-60	-				●		Interviews	Grounded theory	Content	Family decision-making
Schweitzer 2003	**Germany**	67	-	40:27				●		Prospective, face-to-face open-ended interview	-	Content	Psychosocial and medical concerns
Lock 1999	**Japan**	21	-	-			●	●		Face-to-face open-ended interview	-	-	Cultural beliefs and attitudes
Crowley-Matoka 2005	**Mexico**	50	17-62	28:22			●	●		Prospective, face-to-face, in-depth interview	Ethnography	Content	Socio-cultural, political and economic issues
Martin 2013	**New Zealand**	193	19-77	104:87		●			●	Open-ended survey	-	-	Barriers to finding a donor
Alnaes 2012 (15)	**Norway**	18	-	-				●		Face-to-face, semi-structured interview	Narrative inquiry Gift theory	-	Psychosocial and cultural barriers among ethnic minority patients
Alnaes 2012 (21)	**Norway**	18	-	-				●		Prospective, face-to-face, unstructured interview	Narrative inquiry	-	Psychosocial and cultural barriers for Asian and African immigrants
Frade 2011	**Portugal**	35	-	22:13				●		Open-ended survey	-	-	Psychosocial concerns
Ndlovu 1998	**South Africa**	14	19-48	6:8			●	●		Face-to-face, semi-structured interview	-	-	Religious and cultural beliefs
Ekelund 2010	**Sweden**	39	26-84	30:9		●				Face-to-face and phone semi-structured interview	-	Thematic	Psychosocial issues
Sanner 2003	**Sweden**	12	46-59	7:5				●		Face-to-face open-ended interview	-	Content	Preferences, psychological barriers
Sanner 2011	**Sweden**	214	-	124:90			●	●	●	Survey with open-ended responses	-	Content	Experiences during evaluation
de Groot 2012	**The Netherlands**	27	-	17:10			●	●		Focus groups	I-change model	Content	Motivations. social concerns
Ismail 2010*	**The Netherlands**	50	21-74	26:24		●				Focus groups, In-depth interview	Grounded theory	-	Attitudes, communication and knowledge among ethnic minorities
Ismail 2012*	**The Netherlands**	50	21-74	26:24		●				Focus groups In-depth interview	Grounded theory	-	Religious attitudes among ethnic minority patients
Ismail 2013*	**The Netherlands**	50	21-74	26:24		●			●	Focus groups In-depth interview	Grounded theory	-	Cultural barriers among ethnic minority patients
Kranenburg 2005	**The Netherlands**	61	-	35: 26		●				Face-to-face, semi-structured interview	-	-	Preferences, medical and psychosocial concerns

Kranenburg 2007 (20)	**The Netherlands**	48	-	25: 23				●		Face-to-face and phone structured interview	-	-	Psychosocial issues for patients in kidney exchange program
Kranenburg 2007 (27)	**The Netherlands**	151	18-75	95:49		●				Face-to-face, in-depth structured interview	-	Content	Psychological and communication barriers
Kranenburg 2009	**The Netherlands**	84	19-76	61:23		●				Face-to-face, semi-structured interview	-	Thematic	Barriers to finding a living donor
Franklin 2003	**United Kingdom**	20	-	8:12				●		Face-to-face, semi-structured interview	Phenomenology	Content	Beliefs about risks to the donor and expected relationship changes
	United Kingdom	30	-	14:16				●		Face-to-face, semi-structured interview	Ethnography	Content Thematic	Socio-cultural barriers
Gill 2008*	**United Kingdom**	11	32-63	6:5				●		Face-to-face, semi-structured interview	Phenomenology hermeneutical	Thematic	Psychosocial issues related to gift exchange
Gill 2012*	**United Kingdom**	11	32-63	6:5				●		Face-to-face, semi-structured interview	Phenomenology hermeneutical	Thematic	Stressors and coping mechanisms
Mazaris 2012(44)*	**United Kingdom**	16	-	-		●	●	●		Focus groups	Grounded theory	-	Pre-surgical experiences
Mazaris 2012(27)*	**United Kingdom**	16	-	-		●	●	●		Focus groups	Grounded theory	-	Donor recruitment
Boulware 2011	**United States**	8	34-71	5:3	●				●	Structured group interview	-	Thematic	Communication barriers among African American patients
DePasquale 2012	**United States**	29	37-72	12:17		●			●	Face-to-face, semi-structured interview	-	Content	Medical, psychological and economic barriers
Gordon 2001(15)*	**United States**	79	19-73	39:40		●				Face-to-face, semi-structured interview	Ethnography	Content	Medical, social and cultural issues and personal attitudes
Gordon 2001* (53)	**United States**	79	19-73	39:40		●				Face-to-face, semi-structured interview	Ethnography	Content	Socio-cultural issues and medical concerns
Humphreys 2011	**United States**	9	39-64	5:4		●				Face-to-face, semi-structured interview	Grounded theory		Cultural attitudes and personal beliefs
Murray 1999	**United States**	115	26-75	63:51**		●				Face-to-face, semi-structured interview	Constant comparative method	Thematic	Knowledge, preferences and expectations
Pradel 2003	**United States**	13	26-72	6:7	●	●		●		Focus groups	Phenomenology	Content	Expectations and beliefs about laparoscopic nephrectomy
Simmons 1972	**United States**	83	-	-			●	●		Prospective, face-to-face interview	-	-	Family communication patterns in the search for a kidney donor
Waterman 2006	**United States**	26	-	14:12				●		Focus groups	-	Content	Psychological concerns, donor recruitment, educational needs.
Wilson 2012	**United States**	12	-	7:5			●	●		Focus groups	-	Content	Improvements to education

(-) not stated, unclear, or unable to ascertain; (*) Other studies included in this review have used the same sample ; (**) One participant in this sample did not indicate gender Abbreviations: CKD 1-5, not undergoing renal replacement therapy; CKD-5D, dialysis patients (peritoneal or haemodialysis patients, and those undergoing transplant evaluation or waitlisted); LD, received, or being evaluated for a living donor transplant; DD, received or are being evaluated for a deceased donor transplant; Pre, received, or being evaluated for a pre-emptive transplant. Definitions: I-change model, predisposing social factors determine a person's self-efficacy, intention and motivation to carry out certain behaviours; gift theory, gift exchange is a cycle bound by three key obligations i.e. giving, receiving and reciprocating.

Table 3.2. Comprehensiveness of reporting of included studies

Items	**Studies reporting each item**	**n(%)**
Personal characteristics		
Interviewer/facilitator identified	13,17,27,28,30,31,33-35,40,41,43,44,65-70	19(54)
Occupation	15,27-29,36,40,57,65,67,69-73	14(40)
Gender	17,27,28,30,31,35,41,43,65,67,72	11(31)
Qualitative research experience	14,15,33,36,40,44,71	7(20)
Relationship with participants		
Relationship established prior to study commencement	17,27,28,31,44,65,67	7(20)
Participant selection		
Selection strategy (snowball, purposive, convenience)	17,27,28,30,31,33-37,40-44,65,67,69-75	24(70)
Method of recruitment	14,15,17,27,28,31,33-38,40-42,44,65,67,69,70,73-76	24(70)
Sample size	13-15,17,27,28,30,31,33-38,40-44,57,65,67-79	34(97)
Number/reasons for non-participation	14,15,17,30,34-37,42,44,57,70,74,75	14(40)
Setting		
Venue for data collection	13-15,17,27-31,33-37,40-43,67-70,73,75,77	25(71)
Presence of non-participants	15,27-31,33,40-42,44,57,70-75	18(51)
Description of the sample	13-15,17,27-31,33-38,40-42,44,57,65,67-77,79	33(94)
Data collection		
Questions or topic guide	13-15,17,27-30,34-36,40,42,44,57,65,67,69,71-75,77	24(69)
Repeat interviews	13-15,27-31,33,34,37,40-44,57,65,67,69-71,73-75,77,78	27(77)
Audio/visual recording	13-15,17,27-31,33-35,38,40-42,44,57,67,70,71,74,76,79	24(69)
Field notes	13,31,33,35,41-43,65,67,70,74,79	12(40)
Duration	13,15,17,28,31,33-37,40,44,57,65,67,69,71,72,74	19(54)
Data/theoretical saturation	33,40,44,74	4(11)
Transcripts returned	41,67,69	3(9)
Data analysis		
Researcher triangulation	14,15,27-29,33,36-38,42,44,57,65,71,72,74,76,79	18(51)
Derivation of themes or findings	13-15,17,27-31,33,34,36-38,40,42,44,57,65,67,69-72,74,76,79	27(77)
Protocol for translation	33,37	2(6)
Protocol for data preparation and transcription	13-15,17,27,28,30,31,33,34,38,40-44,57,67,69,71,73-76	24(69)
Use of software	31,33,40,42,44,67,74	7 (20)
Participant feedback on findings	17,34,41,67,69,73,75	7 (20)
Reporting		
Participant quotations or raw data provided	13-15,17,27-31,33-38,40-44,57,65,67-79	35(100)
Range and depth of insight into participants perspectives	13-15,28,33,35-37,40,41,44,57,70-72,74,79	17(49)

Note: References Barnieh (2011), Frade (2011), Martin (2013) and Sanner (2011) were not included as COREQ is not applicable to survey studies.

Table 3.3. Illustrative quotations

Themes	Participants quotations (italicised) and/or authors' explanations	References
	Prioritising own health	
Better graft survival	*When my wife offered to give me her kidney, it's not that you're ungrateful but I didn't want her to go through that for me. But we talked it over and eventually decided that it was the best way forward and reluctantly, but gratefully, I've accepted it.* – UK [27] *One can keep the kidney from a living donor longer than that of a deceased.* – The Netherlands [33] *He's flesh of my flesh and blood of my blood. Half my gene set comes from her.* – Sweden [37]	13,14,27,28,33,37,44,66,74,77,79
Accepting risk	*The worst-case scenario is very rare.* – UK [76] *We've been both guilty of heads in the sand approach, until we've needed to come to the next hurdle and then we cope with it and move on. But we try not to worry too much about things that may never happen.* – UK [28] Some had developed "*emergency plans*" such as selecting a second "*standby donor*". – Germany [29]	13,28,29,76
Desperate aversion to dialysis	One patient commented that he would accept a kidney *"even from my worst enemy"*. – The Netherlands [17] *I did not want my children to see their father this way. I was prepared to go to great lengths for that.* – The Netherlands [74] *I am tired of that whole dialysis thing. I hate those needles and such; sometimes it hurts so much that I do not want to go to the dialysis centre anymore.* – The Netherlands [33]	13,14,17,31,33,36,41,44,49,57,70,74,80
	Guilt and responsibility	
Jeopardising donor health	*I've had a pretty full life, so I wouldn't want to take a kidney, like, from my daughter or my wife, which might shorten their life.* – US [57] *It's a selfish thing of me to ask of my family or others to give me what God gave them to survive. I had my kidney…* – US [34] *… He's having an operation he doesn't need. If anything happens to him by giving me a kidney, I'd never forgive myself.* – UK [28] *My son is healthy and [has] my same blood type, but he has two young children. How could I, when they tell us the risks involved…* - US [79] *To take a transplant from either of my two daughters is anathema to me because I don't want to violate their bodies.* – Australia [42]	13-15,17,27-29,33,34,36,37,42-44,49,57,61,65,68,77,79
Anticipating donor regret	*I didn't want to increase their likelihood of having problems in the future and then have them say, "Oh my God! I gave my dad my one kidney".* – US [15] *We're all young and we're all just getting married and looking at starting families and…I wouldn't want any of my friends to have this resentment if they had a child that needed it for a husband or another family member of theirs.* – US [15] *I know for myself that what I have is hereditary, and my concern was if my husband was my donor and I had a child who needed it and who happened to match him as well, would there be an issue? You have no more spares.* – US [15] *I would be more upset [if the kidney failed] because I put them through all that … I'd be afraid they would think they made a bad decision.* – US [15] *I'm afraid that the donor someday will ask for his kidney back* – The Netherlands [44]	13-15,17,28,29,33,36,42-44,49,57,66,68,70
Causing donor inconvenience	*You know, most of them are younger and have little kids, you know my parents are too old at this point… so, you know what I'm saying… like everybody has such busy lives, so having to bring it up, it's just so, you know, it's disrupting their life so much…* – US [49] *Because I heard it's really hard for the donor (they break the ribs [to get to the kidney]), the donor is in the hospital longer than the recipient, and I don't want him to go through that.* – US [13] *I've told my two daughters that they should maintain their health so that they can take care for their own children.* – The Netherlands [44]	13-15,38,42-44,49,80
	Ambivalence and uncertainty	
Doubting transplant	*However, if an emergency arises and I really need a kidney, then I will ask someone to donate.* – US [13] *Maybe when I'm really sick!* – US [36]	13,14,17,28,31,33,34,36,41,44,49,57,80

urgency	*I've been doing really well on dialysis and I think there is a chance that my kidneys might be coming back… so I think maybe I'm getting better and I won't even need one.* – Mexico [31] *I didn't want to accept it… I was in denial, I refused to believe my kidneys were packing up… I thought maybe I'll feel better tomorrow.* – UK [28]	
Insufficient information	*You have questions that come up and you are so overwhelmed by what is going to be happening to you that when you go finally to see the doctor and he gives you 3 minutes of his time, you don't have time to ask all of these questions.* – US [15] *The collaboration between the hospital and foreign people is bad; they do not give us all the information we need.* – The Netherlands [33] *I do not think that they [my family] would come to such a meeting, it would really help them understand my situation.* – The Netherlands [33] *My wife was with me, and then she turned out to be the living donor. So her education was far more important than mine.* – US [79] *I'm more interested on like if you have a donor somewhere else, like a different country. That wasn't really covered.* – US [79]	15,33,40,79
Confronted by unfamiliarity	*My doctor mentioned the idea of a transplant to me when I was first diagnosed, but I thought, that's not for me, I suppose it seemed like something for rich people, movie stars, people who can go up there [to the US] not for me.* – Mexico [31] *The Mosque isn't negative about it; it's the people that are. Because they are not experts on this issue…* – The Netherlands [40]	31,33-35,40
Prognostic uncertainty	*I have to talk to her doctor. What would be her health down the road? Is that extra kidney going to help her along better?* – US [13] *As I look back on it... the actual event wasn't anywhere near as bad as the anticipation* – US [13] *I'm afraid that I will get to live and the donor will die, I heard that it already happened once, so I've heard.* – The Netherlands [44] *I'm afraid to take it from my family because a friend of mine gave a kidney and now she's on the machine. I don't want that for my family.* – US [36] *Uncertainty and waiting are big problems, but I also feel split regarding the question of whether I really do want to receive a living organ.* – Sweden [30]	13-15,17,27-30,33,34,36,37,42-44,57,61,65,67-70,72-77,79,80
	Seeking decisional validation	
A familial obligation	*I think my brothers and sisters had gone through their life having a slightly ill little sister but not quite realising how ill and when I had a total collapse they just sort of said, "wow" and so they all just came in and offered instantly.* – UK [65] *In our community children and parents are very close. So if they can donate they will donate! This works both ways.* – The Netherlands [33] *She knows that if she had been the one in need I would have been there.* – UK [65]	17,33,37,65,70
Alleviating family burden	*I will be able to work and take care of my family.* – Mexico [31] *I just want to be a normal woman. I want to be a mother and a real wife, so that is why we are going through all this now, so that we can be a family.* – Mexico [31]	29,31,38,42
Reciprocal benefits for donors	*When potential donors are not allowed to donate, they feel sad.* – UK [38] There was also a very strong emphasis, particularly in spousal transplantation, of *"being in it together"*, with donors and recipients supporting each other through the process. – UK [28] *Ask her also, would you prefer to be a donor or a carer? Because her life may improve without you on dialysis, you can go on those holidays that you wanted to go on.* – Australia [42] *It seems to me it's important that you express the donor benefits to the recipients. If I take anything from this.. that's where we're not communicating very well, is to the recipients.* – US [15]	13,14,28,29,31,33,37,38,42-44,49,65,66,72-74,76,77,81
Religious approval	*I know Islam quite well and I know what the principles are. Islam is not against it.* – The Netherlands [40] *In Buddhism it's literally stated that you should save a life when you get the chance.* – The Netherlands [40] *No, religion wouldn't make a difference, people are people, and they help each other.* – The Netherlands [40] *I thought that because of religion it can only be someone from your own family, but isn't allowed from someone else, that's what I thought.* – The Netherlands [40]	33,40,41

Respecting donor autonomy	*If you were in her situation, would you want her to accept your kidney? Would you be happy?* – Australia [42] *They said, "your mother would do anything for you and by saying no, you're actually hurting her." So I suddenly realised, hang on, I'm almost selfish for saying no to such a gift, and it's for that reason I will accept...* – Australia [42] *It was up to my father [the donor] and I to make the decision, and it was not for her [doctor] to tell us what to do, it was not as if she knew me. I hate that soppy interference. I have seen other people coming out of her room crying. I wasn't going to have any of that.* – UK [65] *My mother was ready to donate before she was influenced by my sister.* – The Netherlands [33] They would feel more reassured that they were not at fault if the decision to donate had been made voluntarily by the donor. – The Netherlands [73]	14,33,42,65,79,81
External reassurance	*I want a great deal of certainty that my donor is going to be ok.* – The Netherlands [33] *I needed their (family) support.* – UK [72] *It would be really nice to discuss everything with your family. In this way they will get to know your miseries.* – The Netherlands [33]	33,72,79
	Needing social support	
Avoiding family conflict	*My sisters said that they do not want to have family problems in the future because of the donation.* – The Netherlands [44] *In many ways I would have liked to have refused but that would have caused so much conflict...* – UK [72] *I will not let this situation spoil my relationship with my family (I am really going to need them in the future), but I am disappointed.* – The Netherlands [17] *No one really asked me, it just happened and I never really liked him that much…* – UK [72] *We did not really discuss it. It is not something we talk about* – The Netherlands [17]	13,14,29,33,37,38,42-44,65,72-74,76,77,81
Unrelenting indebtedness	*You can keep your organ, I don't want you to run my life.* – US [13] Gina refused to accept the offer because her daughter "*kept talking about [me] covering her expenses while in the hospital and paying her wages*", which made Gina feel like her daughter was "*selling her kidney*". – US [13] [She] felt the offer was an act of manipulation by her sister so that she could "*become the martyr and take centre stage.*" – UK [72] *I was afraid that in case of an argument the kidney would be brought up, even just as a joke. I didn't want that.* – The Netherlands [74] *I knew what it would be like afterwards – eternal gratitude.* – UK [72] *May I still argue with the donor? I was afraid not* – The Netherlands [74]	13-15,27-29,33,37,42,43,65,68,72,74,75,77
Emotional isolation	*I'm disappointed with my brothers and sisters… Getting a kidney would solve lots of problems for me.* – Sweden [30] Most informants were reluctant to reveal their anxiety about the donation and the donor, and they seldom spoke with their doctors about this, only occasionally with the ward staff and the hospital chaplain. – Sweden [37] *I don't think there is any focus or not enough focus on the psychological things you go through.* – US [15] *I just go through it by myself.* – US [13] *I don't really want a transplant right now. But I don't tell that to the doctors, I go along with the tests, just in case.* – Mexico [31]	13,15,17,30,31,35,37,42,49,82
	Cautious donor recruitment	
Self-advocacy	*You cannot just wait for someone to give his kidney away. You should promote yourself and get to the point!* – The Netherlands [33] *You should come up with a really good story, so that they cannot turn down your request.* – The Netherlands [33] *If a doctor asks it, it would be seen as a legitimate request.* – The Netherlands [33] *I would make a joke about it: if I for example pick your name you will lose a kidney!* – The Netherlands [33] *I said to a young acquaintance that if he would donate his kidney to me, I would arrange a marriage and buy a house for him in Turkey* – The Netherlands [33]	15,33,76
Lacking self-	*The whole thing about asking….It's not like just saying, you know, "Can I borrow your car?" or "Will you lend me fifty bucks?" It's a whole life thing that*	13-15,17,30,33,36-

confidence	*can effect someone forever.* – US [15] *I also think it's easier to talk to people about it and ask these things when there's a sense of urgency…* – US [57] *I talked to them about it. Most of the family has kidney problems. So when I asked them about donating, then they had problems too.* – US [67] *They didn't cover approaching [others about LDKT] even of your family members. They said it could be done* - US [79] *It's hard to ask somebody. If you don't have family and real close friends, how do you come up to somebody and say, are you willing to be my donor?* - US [79] *Any the funny thing about it is my whole life, I've always had my driver's licence checked, even before I ever got sick, that I wanted to be a donor. And I would step up like that to give anybody else a kidney, but for me to ask somebody, I couldn't do that.* - US [79]	38,40,41,44,49,57,61,65,67,68,73,74,76,77,79,80
Avoiding donor coercion	*It's a totally voluntary thing. It's a gift. It's not something to ask someone.* – US [13] *We live the whole time with the hope that one of our siblings will offer to provide us a kidney sooner or later.* – Sweden [30] *Everyone that knew me, knew I was very sick… People knew this and if they weren't volunteering then they must not want to donate.* – US [15] *They all know I'm here. They all know I'm going to have a transplant. If they were going to donate, wouldn't they have called by now?* – US [78] *You would feel guilty, they would not dare to say no, and then, if something happens, you would feel even more guilty*. – The Netherlands [17] *If somebody wants to do that, they'll offer. I wouldn't want to put somebody in that position if they didn't really want it.* – US [13] *The social worker can act as an arbitrator … and lay out all of the costs on the table and the benefits, so that everybody knows what they're getting into* – US [49]	13-15,17,27,28,30-33,35-38,41-44,49,57,65,66,72-74,76,78,80
Emotional vulnerability	*I do not want to bother my family with this; it would feel like I want to bring them together to show them how sad I am.* – The Netherlands [44] *If I ask they may get angry, or try to avoid me. I do not want that, I really need them*. – The Netherlands [73] *Rather than ask and get my feelings hurt, I didn't even ask.* – US [15] *I was alarmed by my daughter's reaction. [After that] I have not asked anyone else. I might lose them.* – The Netherlands [17]	14,15,17,31-33,41,49,73,80
Respecting cultural and religious taboos	*I would not expect someone else to ask me such a question, so I would not ask anybody either.* – The Netherlands [33] *It is still a taboo to talk about your illness in the Antillean community.* – The Netherlands [33] *It would be unseemly for them to get to know about my illness through an intermediary like the doctor.* – Norway [41]	13,17,33,35,40,41,49,65,66

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Chapter 4: The lived experience of 'being evaluated' for organ donation: focus groups with living kidney donors

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4.1 Abstract

Background and objectives: Comprehensive evaluations are required to safeguard voluntarism and minimise harm to living kidney donors. This process is lengthy, invasive, and emotionally challenging, with up to one-fifth of potential donors opting-out. We aimed to describe donors' experiences of the evaluation process.

Design, setting and participants: We conducted 14 focus groups involving 123 kidney donors, who completed donation, from three transplant centres (Australia and Canada). Transcripts were analysed thematically.

Results: We identified six themes reflecting donors' experiences of evaluation. The themes that related to perseverance included emotional investment (prioritising the recipient's health, desperation for a normal life, protecting eligibility, shame of disappointing others, overcoming opposition); undeterred by low-risks (medical confidence and protection, worthwhile gamble, inherent invincibility, normalising risks); and mental preparation (avoiding regret, resolving decisional ambivalence, managing expectations of recovery). The challenges included underlying fears for health (processing alarming information, unsettling uncertainty, pre-operative panic); system shortfalls (self-advocacy in driving the process, stressful urgency, inconsistent framing of safety, unnerving bodily scrutiny, questioning risk information, draining finances); and lifestyle interference (living in limbo, onerous lifestyle disruption, valuing flexibility).

Conclusions: Previous donors described an emotional investment in donating and determination to protect their eligibility, despite having concerns for their health, financial and lifestyle disruption, and opposition from their family or community. Our findings suggest the need to prepare donors for surgery and recovery, minimise anxiety and lifestyle burdens, ensure donors feel comfortable expressing their fears and concerns, reduce

unnecessary delays, and make explicit the responsibilities of donors in their assessment process.

4.2 Introduction

Living kidney donor transplantation offers the best outcomes for many patients with end-stage kidney disease (ESKD), but their donors must accept potential risks and uncertainty regarding long-term outcomes.[1-3] Informed consent and comprehensive evaluations are necessary to safeguard donor voluntarism, exclude unsuitable donors, minimise harm and risk factors, and organise support for living donors.[1,4,5] The evaluation can be lengthy, invasive and anxiety-provoking[6-9], and it is estimated that up to 22% of potential donors opt-out of evaluation.[10]

Donors undergo rigorous assessment of their mental and physical health, their relationship with the recipient, motivations, expectations, lifestyle, finances, social support and their understanding of risks.[11,12] Difficulty navigating an unfamiliar healthcare system can cause considerable stress.[6-8] Many donors report anxiety and ambivalence about undergoing surgery.[13-15] Some donors are very intent on donating and therefore unable to fully comprehend the risks, or conceal their concerns in order to protect their eligibility.[16]

There are sparse data on the reasons why donors accept health risks, their experiences of being assessed, and how they persevere with evaluation. We aimed to describe kidney donors' experiences of the evaluation process to inform strategies to prepare donors for the donation and possible outcomes.

4.3 Methods

This is study is part of a larger study examining donors' priorities for outcomes.[17] We reported our study according to the consolidated criteria for reporting qualitative studies (COREQ) framework.[18]

Participant selection

Participants were recruited from three transplant units in Australia (Westmead Hospital, and Monash Medical Centre) and Canada (St Paul's Hospital). A researcher phoned donors to invite them to participate. Purposive sampling was used, whereby donors were selected to include diverse demographic and donation characteristics. All adult kidney donors, from the past 20 years, who were English-speaking, and able to provide informed consent, were eligible to participate. Participants were reimbursed AUD/CAD $50. Ethics approval was obtained from the Western Sydney Local Health District, Monash Health, and the University of British Columbia and Providence Health Care Research Ethics Board.

Data collection

The question guide (Appendix B.1) was based on a systematic review of donors' experiences[19], and discussion among the research team. The two-hour focus groups were conducted in a hotel meeting room. One facilitator (CSH/AT/AFR) moderated the groups and a co-facilitator recorded notes. Each group was audio-recorded and transcribed verbatim. Focus groups were ceased when saturation was achieved (no new information was elicited in subsequent groups) within each country.[20]

Analysis

Grounded theory and thematic analysis were used to analyse the data.[21] CSH initially read through the transcripts to inductively identify preliminary concepts. The transcripts were coded using HyperRESEARCH (ResearchWare Inc. version 3.5.2) software, in which CSH reviewed the transcripts line-by-line and assigned themes to each segment. The themes were iterated by comparing within and across groups and with feedback from AFR, KM and AT, who ensured all data were captured.

4.4 Results

We convened fourteen focus groups with 123 donors from July 2015 to July 2016 (median = 9 participants per group, IQR = 8-10, min = 5, max = 12). The demographic and donation characteristics are provided in Tables 4.1-4.2. The participants were aged from 27-78 years (mean 55 years, SD = 11.5), including 78 (63%) women. The time since donation ranged from two months to sixteen years (mean 3.6 years, SD = 3.1). One hundred and one (82%) participants donated to a family member, nine (7%) to an unrelated recipient, six (5%) were non-directed (anonymous) donors, and nineteen (15%) donated through a paired-exchange.

Six themes were identified. The relationships among themes are depicted in Figure 4.1. Quotations are provided in Table 4.3.

Emotional investment

Desperation for a normal life: Donation was seen as a "privilege" that provided the chance to "fix" their recipients health and family life. Even if they had risk factors, they believed there was "no other choice". Incompatible donors were relieved to find "a plan B" through paired exchange.

Shame of disappointing others: Directed donors felt a responsibility to "pass" their assessments to avoid disappointing the recipient and the recipient's family. At the final psychosocial evaluation, participants felt it was too late to let the recipient down. Non-directed donors became "emotionally connected" to being a donor.

Prioritising the recipient's health: Participants felt "blind[ed]" to information about risks - "I didn't care if I lived or died, because it was my daughter". Some were willing to "live with" short-lived and "manageable" consequences, like pain. Some were so "focused" on the recipient, that post-donation outcomes were "an afterthought".

Protecting eligibility: The possibility of being ineligible caused anxiety. Some maintained a strict diet and exercise regimen to ensure they were accepted. Donors were careful to say “all the right words” to “pass” the evaluation. Non-directed and unrelated donors were frustrated by repetitive questioning of their comprehension of risks and having to “convince” the hospital to accept them. Some related donors were not worried about being questioned because they felt their motives were straightforward.

Overcoming opposition: “The hardest things” were family opposition or the recipient’s reluctance for them to donate. Unrelated donors believed their family preferred someone closer to the recipient to donate. Some faced disapproval from their religious community, regarding the violation of bodily integrity. This left them feeling isolated - “people could not relate to me, so I couldn’t talk to them”.

Undeterred by low-risks

Worthwhile gamble: Participants, irrespective of time since-donation, felt “comforted” by statistics showing “very minimal” risks of morbidity and mortality that were no higher than “somebody living with two kidneys”. The “very positive” data conveyed that their safety was a “non-issue”. Participants felt guilty for prioritising their own safety.

Inherent invincibility: Unrelated and non-directed donors, in particular, felt confident in their safety. They believed they were the “rule, not the exception” when considering low-risks of harm - “[if] it’s 1/2000 or 1/500, that’s not going to be me”.

Normalising risks: Participants viewed surgery as a common risk to take, equating it to – “the chance you take every time you drive”. Nephrectomy was considered a “benign” procedure as they were aware of others who had donated safely or were born with one kidney.

Medical confidence and protection: The “stringent” medical evaluations convinced participants that they were unlikely to face complications. The surgeon was “the calming person before the storm” due to their positive and authoritative tone. Participants trusted their clinicians to protect them from harm – “the [doctors] don’t want to make another patient”. For Canadian donors, receiving wait-list priority helped to justify taking the risk.

Mental preparation

Avoiding regret: Participants were uncertain how they would cope if the transplant failed and many expected to feel “devastated”. They relinquished control over the ‘gift’ – “It’s like any gift you give. You give and you hope for the best”. Others avoided thinking about rejection. Some women feared recipient non-adherence would “change the dynamic of their relationship”.

Resolving decisional ambivalence: Some participants were undecided about donating, but continued with evaluation while “getting positive results”. They appreciated receiving reassurance from the psychosocial team, and support from family created a sense that they were not alone. They psychological evaluation gave them some “closure”.

Managing expectations of recovery: Donors sought practical advice to prepare for their recovery. Some preferred to hear previous donors’ experience of recovery “rather than the aggregate” outcome. Some watched videos of surgery and felt reassured by the “simplicity” of the process. Websites were used to find statistics about surgical outcomes, but some wanted local statistics relevant to their unit.

Underlying fears for health

Processing alarming information: It was challenging for participants to process information about complications, as this conflicted with their determination to donate. They were confronted by graphic details of surgery and had fears “at the back of their minds” about mortality and ESKD.

Unsettling uncertainty: Even small possibilities of harm were troubling for some participants, because “you could be an anomaly”. Some participants described fears relating to their awareness of gaps in current knowledge of living donor outcomes.

Pre-operative panic: Some participants were overcome with fear just prior to surgery, and worried about the consequences for their family, if they died. Men believed they had avoided their fears.

System shortfalls

Self-advocacy in driving the process: Some participants were surprised that they had to drive the evaluation. They had to “do [their] own research” to learn their eligibility status, and arrange further tests – “we were prompting them every step of the way for dates, times, any scope of information”. Some felt they discovered financial support too late, or had to “ask for it”.

Stressful urgency: The “long and exhausting” evaluation, “devastating” delays, and “unnecessary” duplication of tests, caused donors to fear their recipient would deteriorate on dialysis. Some believed they had to pressure the transplant team to progress, and felt they should have been “fast track[ed]” through the system.

Inconsistent framing of safety: Participants were confused by the “highly inconsistent” messages from different transplant professionals– “My surgeon [will] say, high-five we’re in…you see another surgeon and they say, you could die”. The reiteration of dangers and questioning of their commitment to donate by the surgeon, and psychosocial team felt like they “were trying to convince you not to do it”.

Questioning risk information: For some participants, information sessions were seen as unrealistically positive regarding post-donation outcomes – "everyone's up there saying this is wonderful". They were concerned when the transplant team could not provide more details about mortality statistics, such as the study population. They felt they had no way of "checking", information. Some believed that risk estimates were "overinflated" so "you can't complain later".

*Unnerving bodily scrutin*y: Some participants felt uneasy about becoming a "patient", and exposing their body and lifestyle to examination. Abnormal test results and delays in receiving results, caused them to fear the worst – "I had myself halfway into palliative care". Some were shocked by their surgeon's apparent lack of "bedside manner", and were upset by being labelled overweight. They felt they were treated like "just a number", diminishing the "massive thing you are going through".

Draining finances: Costs for transport, accommodation and lost income accumulated throughout evaluation. Some found the financial assistance "wasn't worth pursuing". One participant reported being fired due to the leave required for recovery. Some Canadian donors had concerns about increased costs for health, life and travel insurance post-donation.

<u>Lifestyle interference</u>

Living in limbo: Participants felt their "whole life was on hold", while waiting for their surgery date and had to be "ultra-careful with [their] body". Some non-directed donors questioned their commitment to the donation with increasing delays. They wanted to be given realistic estimates of the work-up timeframe.

Valuing flexibility: Donors valued the flexibility of the transplant team, in organising tests around their work schedule. Workplace flexibility, reimbursement of travel expenses and income support alleviated financial anxieties, and some felt this made it possible for them to donate.

Onerous lifestyle disruption: The evaluation was disruptive to their work and lifestyle. Participants travelling long distances to the transplant centre would have preferred to undergo tests closer to their home. Preparing for the surgery took a lot of organisation, particularly for donors with young children. Many had family members to "back [them] up" financially, or practically.

4.5 Discussion

The emotional investment in giving their organs sustained donors' commitment throughout the evaluation process, despite having underlying fears about their health, encountering opposition from others, and managing lifestyle disruptions and financial hardship. They were determined to improve the recipient's health and their family life. Although information about post-donation outcomes were concerning to donors, they trusted their clinicians to protect them from harm. They strived to protect their eligibility by adhering to a healthy lifestyle, and some concealed their concerns to demonstrate confidence in their decision. They also faced expenses and disruptions to their lifestyle in order to attend appointments and discovered their need to drive the evaluation forward, and find information. Increasing delays and uncertainty left donors in a state of limbo, and anxiety, as they feared their intended recipient would deteriorate on dialysis, or wanted to avoid the commencement of dialysis.

Some differences in the donors' perspectives were apparent, particularly by donor type, age, gender, and ethnicity. For related donors, the chance to improve the recipient's wellbeing outweighed concerns about their own risks, which they regarded as negligible and unjustifiable as a reason to not donate. Unrelated and younger donors gave more consideration to long-term health outcomes, feeling more vulnerable or distanced from the recipient. Non-directed donors had confidence in their safety as they believed they were in optimal health. Most donors feared failing their evaluations. Unrelated and non-directed donors described more intense questioning of their motivations, suitability and understanding of risks, likely reflective of different approaches for evaluating these donors. Women described concerns about tensions in their relationship with the recipient. Ethnic minority donors faced opposition from their family, and religious community, due to beliefs about bodily integrity, which has been described previously.[22]

Donors were undeterred by low-risks of complications and long-term health problems. Some donors recalled ignoring information that contradicted their decision to donate. This reflects an analysis of the dialogue between potential donors and transplant professionals, which found that donors express disinterest in risk information, as their decision is 'entrenched'[23]. This accords with cognitive dissonance theory, the tendency to minimise inconsistency between our thoughts and actions.[24] Clinicians have also expressed scepticism that donors understand risks.[25]

Psychosocial support enabled donors to resolve issues causing ambivalence or anxiety, for example the possibility of the graft rejection. The need to protect their eligibility left some donors unwilling to disclose their concerns. Other studies have also found that directed and non-directed donors feel anxious about undergoing psychosocial assessment due to their determination to donate, and attempt to manage how they are perceived, and some conceal experiences that might exclude them.[16,23,26] We found that some male donors were overcome with anxiety before their operation, which supports findings from a study that used self-administered anxiety scales.[27]

Our multinational study included a large sample of donors with a range of demographic and donation characteristics. However, we only included English-speaking participants. The applicability of the findings may be uncertain in healthcare systems outside of Australia and Canada, particularly those without universal access to healthcare and reimbursement programs. In the United States many donors are uninsured[28], and eligibility for reimbursement is means-tested[29]. Differences are also likely to exist within programs in Australia and Canada. However, we achieved saturation within each country, and found similar findings to other studies, suggesting the broader relevance of our findings.[6-8] We also relied on the donor's recall of their experience. However, donors discussed sensitive issues such as ambivalence, which they had not expressed prior to donation. Variability in perspectives on risks may reflect changes to the messages provided by clinicians. We only included participants who had completed donation, and the barriers experienced by those who opt-out might be different. Non-donors have reported some similar barriers (e.g. financial issues, concerns about risks and family opposition).[10,30]

Guidelines focus on ensuring psychological suitability, motivation and voluntariness, and informing donors of possible outcomes.[5,31] Conflicts between the goals of clinicians and those of donors may not be addressed in guidelines. Comprehensive risk information can be confronting or irrelevant to donors. A 'cooling-off' period and requiring donors to drive the evaluation ensures donors make a considered decision.[12,32] These practices can exacerbate stress for donors and prolong lifestyle intrusion. Caution to detect coercion and assess risk comprehension can cause donors to feel scrutinised and reluctant to express their anxieties. We suggest framing a component of the psychosocial evaluation as an opportunity to communicate and resolve concerns without feeling under threat of jeopardising their eligibility.

We also suggest the need to provide donors with support to cope with anxiety, lifestyle disruption and cultural barriers during evaluation. Some donors did not understand that they must drive the evaluation, as the transplant team is unwilling to push potential donors to complete the testing. Making explicit the expectations and responsibilities of potential donors, providing better information about the process, and expected timing-frame, can prepare donors for the commitment of undergoing assessment. Transplant centres should also strive to improve efficiencies in the evaluation process.[11] An independent live donor advocate, social worker or patient navigator, could facilitate comprehensive support by addressing donors' needs and concerns as they emerge, assess risk comprehension, and provide culturally-sensitive interventions to address family conflict.

Psychosocial interventions are needed to address donors' fears of surgery, mitigate the anxiety of testing, facilitate social and family support and prepare them for changes to their relationship, and the possibility of graft failure or being ruled out as a donor. For emotional preparation, some donors found it useful to discuss their concerns about graft failure and relationship problems with psychologists or social workers, and coped by relinquishing control over their 'gift'. Information about surgery, complications and recovery needs to be individualised to donors' preferences (e.g. statistics or narratives of previous donor's experiences).

Future studies should include donors from diverse cultural and linguistic backgrounds to better understand the challenges of evaluation in these groups, particularly given the low rates of kidney donation among ethnic minorities.[33] The experiences of non-directed donors should be studied further. While our study identifies some challenges that may influence the retention of donors, there is a need to understand the barriers for donors who opt-out.[10] Our findings may inform strategies for improving the process of evaluation, which would warrant further studies to evaluate effective practices (e.g. timing of the psychosocial assessment).

For potential donors, their emotional investment in the donation intensifies during evaluation and drives their perseverance and determination to protect their eligibility despite having concerns for their health, financial and lifestyle disruption, and facing family and community opposition. Their determination to donate can also limit their comprehension of risk information, disclosure of their fears and concerns, and thus lead to inadequate mental preparation for donation. Increased attention to the psychosocial challenges of evaluation are needed, which may include addressing donors' concerns, preparing for surgery and recovery, mitigating lifestyle burdens and anxiety, clarifying donor's responsibilities, and reducing delays in the evaluation.

4.6 Acknowledgments

We are grateful to all the living kidney donors who generously gave their time to share their insights and perspectives.

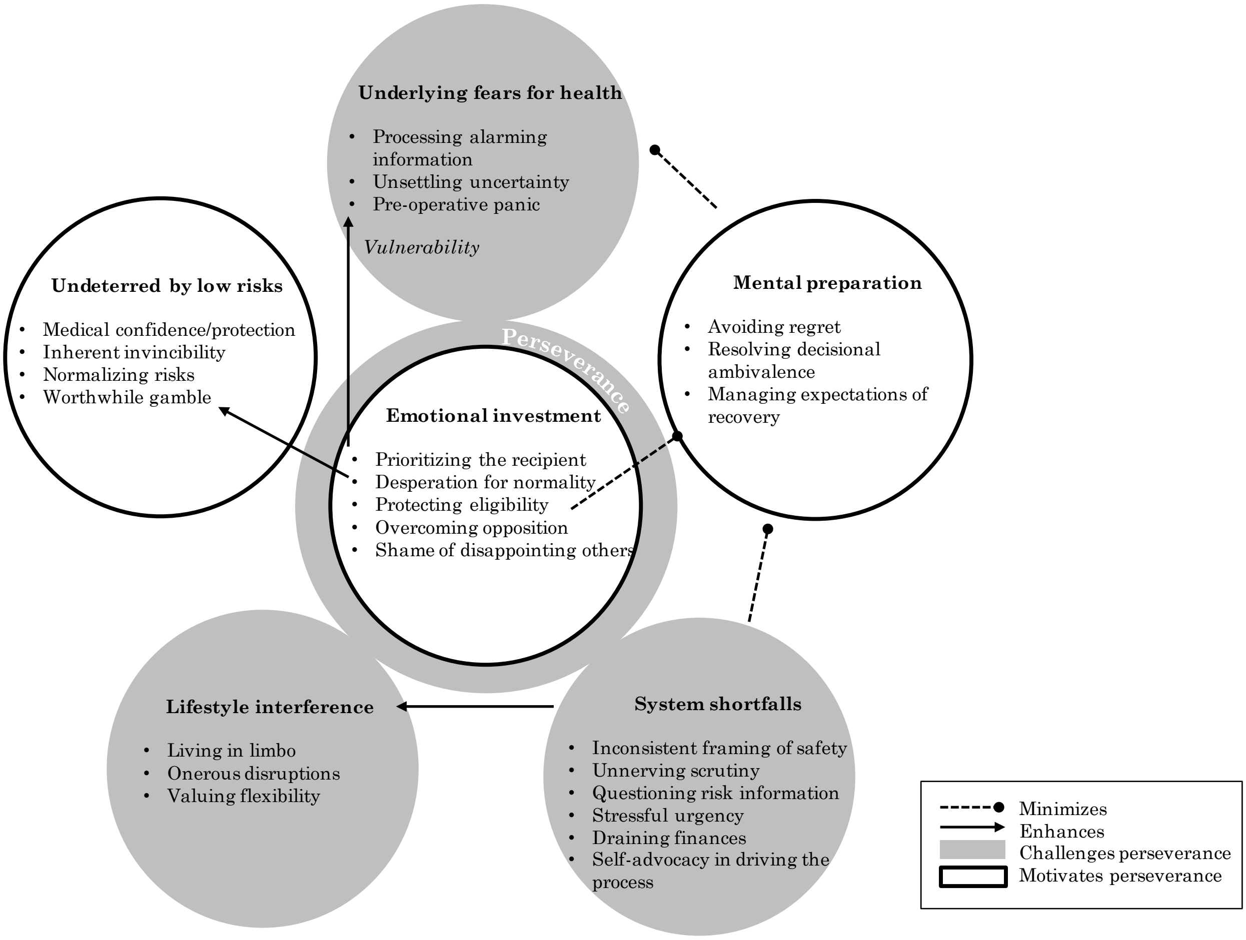

Figure 4.1. Thematic schema

Living kidney donors were emotionally invested in the donation, which sustained their commitment throughout the evaluation process, despite underlying fears and uncertainty about their health, difficulty navigating the transplant process, and increasing interference into their work and lifestyle. Their desire to help the recipient and improve their own lifestyle also led them to view low risks as a worthwhile gamble. Emotional support and medical confidence reassured donors of their safety, helped them resolve ambivalence, and prepare for their recovery and possible disappointment. Difficulties navigating the hospital system to access information, psychosocial services and speed up the process left some participants feeling unprepared, with unaddressed concerns. Their desperation to protect their eligibility prevented donors from seeking support and disclosing their apprehensions.

Table 4.1. Demographic characteristics of the participants (N=123)

Characteristics	n (%)
Gender	
Female	78 (63)
Male	45 (37)
Country	
Australia	67 (54)
Canada	56 (46)
Age (years) ^	
20-29	1 (1)
30-39	11 (9)
40-49	27 (22)
50-59	36 (29)
60-69	34 (28)
70-79	13 (11)
Ethnicity^	
White	100 (81)
Asian/South Asian	12 (10)
Middle Eastern	5 (4)
Other*	6 (5)
Highest level of education^	
University degree	59 (48)
Diploma/certificate	25 (20)
Secondary school: grade 12	24 (17)
Secondary school: grade 10	17 (14)
Total household income per year (AUD) ^ †	
$0 - $24,079	16 (13)
$24,080 - $50,169	29 (24)
$50,170 - $80,271	30 (24)
> $80,271	42 (34)
Employment status^	
Full time	68 (55)
Part time/casual	22 (18)
Retired/Pensioner	24 (20)
Not employed	7 (6)
Marital status^	
Married/De-facto relationship	96 (78)
Divorced	7 (6)
Widowed	6 (5)
Separated	6 (5)
Single	5 (4)
Partner (not living with)	2 (2)

+Age at time of participating in focus group; ^Total $N \neq 123$ due to non-response.; *Includes South American, African, Pacific Islander and First Nation (Canada); †As defined by Australian Bureau of Statistics 2011 Census Survey (Converted to USD)

Table 4.2. Donation characteristics (N=123)

Characteristics		**n (%)**
Time since donation (years)^		
	<1	13 (11)
	1-3	59 (48)
	4-6	35 (29)
	7-10	9 (7)
	>10	6 (5)
Relationship to recipient		
	Spouse	39 (32)
	Parent	33 (27)
	Sibling	23 (19)
	Friend/colleague	9 (7)
	Child	6 (5)
	Other relative (aunt, grandparent, in-law, cousin)	7 (6)
	Non-directed	6 (5)
Kidney exchange		
	Yes	19 (15)
	No	104 (85)
Post-donation complications		
	Mental health	8 (7)
	Hypertension	7 (6)
	Chronic pain	3 (2)
	Hydrocele	2 (2)
	Other[c]	11 (9)
Recipient outcome		
	Alive and functioning graft	113 (92)
	Graft failure or death	10 (8)

^Total N ≠ 123 due to non-response; [c] Includes hyperthyroidism, low blood pressure, kidney stones, gall stones, hernia, blood clots, endometriosis, gout, high cholesterol, scleritis and osteoporosis.

Table 4.3. Illustrative quotations

Theme	Illustrative quotations
Emotional investment	
Shame of disappointing others	“One thing I thought was wrong…We’re ready to go in virtually the next day and I’m having a psychiatric test. That should have been the first thing I had and I’ve now found out all these things that you didn’t know but someone’s waiting for me and if I was starting to get frightened, I wouldn’t be game at that stage to say, ‘No’. Whereas at the start…you can go back home with your head held high and say, ‘It didn’t work out.’ (Female, related donor, Australia, 70s)
Desperation for a normal life	“I’m glad you say selfish because that’s what drove me, and I can only kind of admit it now. He got admitted into hospital, six times one year. We said our goodbyes so many times. It was just so draining…And then this came up. I put hand my up faster than anybody in this room. I was like, “Right, a solution, let’s go and fix it,”. (Female, related donor, Australia, 60s). “Basically, my doctor told me…because I have a really high case of diabetes in my family, so he was like. I really would prefer not to use you, because more likely than not you are going to have diabetes when you are old, but I mean for us there was no choice.” (Female, related donor, Canada, 30s).
Prioritising the recipient ‘s health	“I went in there blind, mean…I didn’t ask questions…I didn’t care. I’d do anything for my family.” (Female, related donor, Australia, 50s) “But that was a big barrier, like the unknown for myself …because they say when you donate, there’s a risk that something could happen to you, but in the end, I said to myself my brother needs it more than yourself. Because you do have that fear regardless. Once I put him first everything just pretty much went away. (Male, related donor, Australia, 30s) “So, if I were to continue as a donor I had to take treatment [for an infection]…But they didn’t tell me that till, about four months on. But by that time I was emotionally connected to being a donor, an anonymous donor. I had very personal reasons for doing it. So, it was hard for me to just back out, and kind of give up.” (Female, unrelated donor, Canada, 50s)
Protecting eligibility	“When I was going through the test one of my great fears was that I wouldn’t be able to donate a kidney. I don’t know how that would have affected me because I was so committed to wanting to do it. I was sort of nervous right up until they said, you are a match.” (Male, non-directed donor, Canada, 60s). “That's a scary one actually, seeing a psych. It would be awful if I got so far.” (Female, spousal donor, Australia, 50s). “They took away my surgery date…I really wanted [this specific person] to get my kidney. So, I basically had to beg to get my surgery date back…it was really hard to convince the doctors that I was going to be okay” (Female, non-directed donor, Canada, 40s)
Overcoming opposition	“Well [my family], honestly, mine weren’t with me but it didn’t make me think twice about it…I’d have put them to the side and thought about my own family. So, it’ a hard choice; but in the end you think it’s my choice and my choice only. That’s what I thought.” (Female, related donor, Australia, 50s). “Because of customs of race and religion, people frown upon you…but it didn’t deter me from doing it. I didn’t put race, religion or anything into it… they say it’s God that brought you into the world so that you should go to him. But you’re helping, you’re going into the ground anyway, so why not?” (Female, related donor, Australia, 40s) “My best friend reacted much like your family. Was probably the only big fight we’ve ever had in about 25 years. At the end of it, I just said, you know what, you don’t get a vote. The only one who got a vote was my husband, nobody else got a vote” (Female, unrelated donor, Canada, 50s).
Undeterred by low risks	
Worthwhile gamble	“They didn't give you any guarantees; they did throw statistics at you. But you could be an anomaly and for whatever reason it doesn't work. But all of us, got to that place, where it doesn't matter. If it’s a year, it’s a year. But we have to do something, so we have to try.” (Male, related donor, Canada, 40s). “They couldn’t guarantee, even though I ticked all the boxes, that I wouldn’t develop renal failure. But I could have developed it with two kidneys.” (Female, related donor, Australia, 60s).
Inherent invincibility	“I wasn’t really worried about any of the outcomes. I knew I was a healthy individual. I didn’t really have any concerns”. (Female, non-directed donor, Canada, 40s) “I mean I haven’t won the lottery yet so I’m the rule, not the exception”. (Female, unrelated donor, Canada, 30s).
Normalising risks	“The information was that taking my kidney away is not likely to cause any problem. People live very healthy and long, and active lives with one kidney”. (Male, related donor, Australia, 60s). “She was my inspiration. I went home and I said to everybody, “I met this lady and son and if that lady can do it. I can do it.” (Female, related donor, Australia, 50s).

Medical confidence and protection	“They put you through such a stringent testing process…We don’t go into it thinking ‘Oh my god, am I going to make it?” (Female, related donor Canada, 50s) “The surgeon was very reassuring…I think it was more the confidence of how he spoke about the procedures he’d undertaken in his career.” (Male, related donor, Australia, 20s). “I did ask about life expectancy…He was very careful to tell me the data isn’t really there…So the answer he gave me is basically you have gone through all these tests. If something is going to show up it would show up. I guess in my mind I was okay with that answer. (Male, non-directed donor, Canada, 60s). “I was paying attention to post-kidney op pregnancy studies…once you’ve passed the two year mark it makes zero difference.” (Female, unrelated donor, Canada, 30s)
Underlying fears for health	
Processing alarming information	“You can’t help but look behind the curtain and start poking around, like, will it hurt?... don’t start trolling the internet looking for these things because you are going to find bad stories and they are going to freak you out”. (Male, unrelated donor, Canada, 40s). “Well I guess it does give you twinges of qualm as you are told the risks. And it does make you catch your breath maybe.” (Female, spousal donor, Australia, 50s). “Your primary motive is that you want to help your person. But simultaneously you’re weighing your own risks.” (Female, unrelated donor, Canada, 30s). “They were going to take my mum’s …and my mum’s pretty old, and I said ‘No. Take mine’. That made it easier for me.” (Male, related donor, Australia, 30s).
Pre-operative panic	“I don’t think it hit me until five minutes before when I was lying on the stretcher going into the operating room.” (Male, related donor, Canada, 70s). “A week before the operation, for final check-up, I sat in the park. I suddenly realised ‘I got a family’, what happens if? I don't think I got the support or counselling.” (Male, related donor, Australia, 50s).
Unsettling uncertainty	“They didn’t follow up with donors for like the last decade really. So, this is all pretty knew”. (Male, related donor, Canada, 50s). “He was very careful to tell me the data isn’t really there.” (Male, non-directed donor, Canada, 60s) “One of my biggest concerns afterwards was what would be the long-term repercussions because back at the time we did our transplant (10+ years ago), there was no ruling data on long term impacts.” (Male, 50s, Sydney).
Mental preparation	
Resolving decisional ambivalence	“I was a little bit anxious. I didn’t really want to donate at the beginning because I’d met my partner later on, so we hadn’t been really together that long and I kind of felt a bit of guilt if my daughter actually got sick…but then after a while, I thought well, she’s healthy. It’s really an unreasonable fear and yeah.” (Female, spousal donor, Australia, 40s) “Also going to get all the testing done by myself, I knew that was going to be one of the hard days for me and I did it and I broke down in tears, that was a real moment for me to say, ‘Hey can I do it? Do I want to do it?’ That was kind of one of my hard days.” (Male, related donor, Australia, 40s).
Avoiding regret	“I very selfishly was worried about how it would affect my marriage. Am I going to feel like he owes me a debt? Is it going to make things weird between us? What if he doesn’t treat it properly?…They got me a social worker to talk through this issue…they said, you really need to think of it as a gift. And you know that, but I think articulating it out loud made a difference.” (Female, spousal donor Canada, 40s).
Managing expectations of recovery	“They say about risks, maybe they do they generalise it. But they don’t tell you specifically what can happen. So, it doesn’t mean anything.” (Male, related donor, Canada, 50s) “I would like those statistics but later on when you've already said I’ll do it and then you have your tests and you're into it.” (Male, related donor, Australia, 40s). “There’s a Facebook page for kidney donors. I would ask the questions there and it was more helpful than the actual hospital. Because it was life experience, so it was people that went through it so they knew exactly what it was like. So, I found it very helpful.” (Female, spousal donor, Australia, 50s)
System shortfalls	
Unnerving bodily scrutiny	“He didn’t actually use the word ‘fat’, but ‘we won’t take because you’re too overweight’. He was totally unprofessional...My weight has been a sore point” (Female, Australia, 50s) “I wasn’t even a family member, and it wasn’t even someone I knew very well, they went through it [the risks] so many times…I almost started pulling out the worlds tiniest violin.” (Female, non-directed donors, 30s, Canada)
Self-advocacy in	“The amount of information we got was pretty much nil, we were prompting them every step of the way for dates, times, any scope of information we could get. We were

driving the process	pushing for it the whole time. It was never given freely. It was never given clearly. It was just a mess...” (Male, unrelated donor, Australia, 30s) “I got to speak to my surgeon, he said, ‘This whole process is like buying a car. You have to do the research. You have to look deeper because you can’t rely on people to spoon-feed you the information’…As soon as he said that, every bit of grey just went to black and white…that made everything heaps better for me. (Male, related donor, Australia, 20s)
Stressful urgency	“I do think they could’ve showed a little more zip to the process. I know it’s expensive to do all the screening but, when your loved one is not well and you just see them going downhill, and being with them through their dialysis is the most frightening thing I’ve ever seen.” (Male, related donor, Canada, 60s).
Inconsistent framing of safety	“The psychiatrist. It’s like they were trying to convince you not to do it. It’s like, ‘You don’t have to do it if you don’t want to. You could possibly die. This could possibly happen.’ And I’m like, ‘No. It’s all right. My brother’s sick. He needs it.’ But they kept strumming in your ear, “Are you sure?”. I don’t know if that’s part of the process. (Male, related donor, Australia, 30s) “I didn’t know if he was trying to scare me to make sure I was going to go ahead with the operation or going to chicken out”. (Male, spousal donor, Australia, 60s).
Questioning risk information	“Maybe even a resource sheet of valid references…Because a lot of the time I was told information but I didn’t have a way of checking it or validating it …” (Male, unrelated donor, Canada, 60s). “I think it’s a grey area. I mean, if you start listing complications, no one’s going to donate. I also think, you know, they don’t all tell you the truth. You know, coz they all say well people have it nothing happens everything’s okay. But I think that’s also not true.” (Male, spousal donor, Canada, 50s)
Draining finances	“It was a dent in the career a little bit…I think the financial assistance offered isn’t adequate. That’s just it wasn’t worth pursuing really.” (Male, unrelated donor, Australia, 30s) “I did research on life insurance. And how it would impact getting life insurance because of course I hadn’t had kidney yet. So, that was in the back of my mind, and that’s one of the things that I was researching, looking for studies on” (Female, unrelated donor, Canada, 30s).
Lifestyle interference	
Living in limbo	“My whole life was on hold. I had work and training to do, and I couldn’t do any of that until this was behind us. So, I thought it could have been a quicker. (Male, unrelated donor, Canada, 50s) “So it was, it was very difficult to stick with it. Because I had other things I wanted to do that I couldn’t get started on because of this whole process and not knowing anything about what the date would be…So it was really difficult. I eventually had to tell them “If you don’t tell me a date, like soon, despite all this time, I’m going to have to back out”. Because what I wanted to do, what else I want to do was important to me…(Female, non-directed donor, Canada, 60s)
Onerous lifestyle disruption	“It was more about organising everything around it…organising work, organising kids, organising people. So, it wouldn’t have stopped us but it obviously took a lot of planning…They rang me and said, “Well, we can do it next week,” and, “No, I’m not ready for next week”. (Female, related donor, Australia, 40s) “I work casually and I got told one test, allow an hour. When I got there, “Sorry. Didn’t you get told, it’s A, B, C.” And that happened quite a lot…So, that was one of the annoying things I could have changed that shift and not missed financial benefit. (Female, unrelated donor, Australia, 50s) “If there was potential to group all the tests together in a consecutive day, it would be beneficial to a lot people, I think.” (Male, related donor, Australia, 20s)
Valuing flexibility	“I was fortunate I could use my sick leave and be away from work. But I think for anyone else who didn’t have that, that might be tough.” (Female, related donor, Canada, 50s)

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Chapter 5: Nephrologists' perspectives on recipient eligibility and access to living kidney donor transplantation

Hanson CS, Chadban SJ, Chapman JR, Craig JC, Wong G, Tong A. Nephrologists' perspectives on patient eligibility and access to living donor kidney transplantation. Transplantation 2014; 199 (4): 943-953.

The chapter is structured as per the journal article.

5.1 Abstract

Background: Wide variations in access to living kidney donation are apparent across transplant centres. Such disparities may be in part explained by nephrologists' beliefs and decisions about recipient eligibility. This study aims to describe nephrologists' attitudes towards recipient eligibility and access to living kidney donor transplantation.

Methods: Face-to-face semi-structured interviews were conducted from June to October 2013 with 41 nephrologists from Australia and New Zealand. Transcripts were analysed thematically.

Results: We identified five major themes: *championing optimal recipient outcomes* (maximising recipient survival, increasing opportunity, accepting justified risks, needing control and certainty of outcomes, safeguarding psychological wellbeing); *justifying donor sacrifice* (confidence in reasonable utility, sparing the donor, ensuring reciprocal donor benefit); *advocating for patients* (being proactive and encouraging, addressing ambivalence, depending on supportive infrastructure, avoiding selective recommendations); *maintaining professional boundaries* (minimising conflict of interest, respecting shared decision-making, emphasising patient accountability, restricted decisional power, protecting unit interests) and *entrenched inequities* (exclusivity of living donors, inherently advantaging self-advocates, navigating language barriers, increasing centre transparency, inevitable geographical disadvantage, understanding cultural barriers).

Conclusions: Nephrologists' decisions about recipient suitability for living donor transplantation aimed to achieve optimal recipient outcomes, but were constrained by competing priorities to ensure reasonable utility derived from the donor kidney, and protect the integrity of the transplant program. Comprehensive guidelines that provide explicit recommendations for complex medical and psychosocial risk factors might

promote more equitable and transparent decision-making. Psychosocial support and culturally sensitive educational resources are needed to help nephrologists advocate for disadvantaged patients and address disparities in access to living kidney donor transplantation.

5.2 Introduction

Living donor transplant programs have been established in more than 80 countries[1] in response to the unresolved shortage of organs from deceased donors[2]. Kidney transplants from living donors now comprise between 28-36% of all transplants in high-income countries including the United States, United Kingdom and Australia.[3-5] However, there is concern about the significant disparities in access to the living donor pool, particularly for patients from ethnic minorities, or who are socio-economically disadvantaged, less educated and older.[6-13]

Nephrologists play a central role in providing access to kidney transplantation, through education, referral to a transplant program, completing transplant evaluations, and participating in recipient acceptance meetings.[14-16] Clinical care and decision-making may be more complex in disadvantaged populations who are more likely to present with medical and psychosocial risk factors.[16-21] Previous research suggests that clinician's interactions with disadvantaged patients may reflect their inherent biases regarding patient preferences, their likelihood of finding a donor, completing evaluations or adhering to treatment, and the expected survival benefit of transplantation compared to dialysis.[19,20] Clinicians also report difficulties in communicating and establishing trust with ethnic minorities, and completing their referral and evaluation processes[19,22].

Nephrologists are also uniquely placed to provide insight into the factors preventing patients from receiving a living donor transplant that are not referred or assessed. The beliefs, attitudes and priorities underpinning nephrologist's decisions about recipient eligibility for living donor transplantation have not been explored in-depth. Further, nephrologists' perspectives regarding the challenges in navigating the complex pathway to living kidney donor transplantation are unknown, particularly regarding their interactions with disadvantaged patients. Our study aims to describe nephrologists' perspectives on recipient eligibility and access to living kidney donor transplantation to inform strategies to mitigate disparities and improve equity.

5.3 Methods

We followed the Consolidated Criteria for Reporting Qualitative Research (COREQ) framework.[23]

Participant selection and practice setting

Nephrologists involved in referral and assessment for living donor transplantation in Australia and New Zealand were purposively selected to capture a range of years of clinical experience, age, gender and practice locations. Nephrologists were chosen because of their ongoing involvement across the continuum of recipient care, from education and referral through to evaluation and assessment for transplantation. The practice of living kidney donor transplantation in Australia and New Zealand is similar, as demonstrated by the joint data registries and professional societies. In both countries, general and transplant nephrologists assess potential recipients for kidney transplantation. While quantitative research aims to achieve statistical generalisability with a random and representative sample, qualitative research seeks to explore a range of diverse viewpoints within a small and diverse sample until reaching the saturation of concepts.[24-28] Invitations were sent via email and the interviews were conducted in clinic offices, meeting rooms or at conference venues. A snowballing technique was also employed, whereby participants could nominate other nephrologists who they believed might offer a unique or important perspective on this topic. The University of Sydney provided ethics approval for the study.

Data collection

The interview guide was based on a systematic literature review of disparities in kidney transplantation[17], and discussion among the research team (Appendix C.1). The interview questions focused explicitly on recipient eligibility and assessment, and data pertaining to donor eligibility and assessment were excluded from analyses. CSH conducted a face-to-face semi-structured interview with each participant from June to October 2013. Participant recruitment ceased when theoretical saturation (i.e. when little or no new information was being obtained from subsequent interviews) was reached. All interviews were digitally audio-recorded and transcribed verbatim.

Analysis

The transcripts were entered into HyperRESEARCH software (ResearchWare Inc, United States, Version 3.5.2,), software for qualitative data management and coding. Based on adapted grounded theory methodology[26] and thematic analysis[29], CSH coded the transcripts line-by-line, and translated common and divergent concepts into existing or new codes, respectively, as they emerged in the data. Similar concepts were then grouped into themes and subthemes. We identified relationships and patterns between themes to develop a thematic schema (Figure 5.1). To enhance the comprehensiveness and validity of the thematic framework, the preliminary findings were discussed among the research team (investigator triangulation) and emailed to all participants who were asked to provide feedback and any additional opinions (member checking).

5.4 Results

Study participants

Of the 46 invited nephrologists, 41 (89%) participated in the study from 22 centres in Australia and New Zealand (11 centres had a transplant program). Twenty-three (56%) participants were transplant nephrologists and 18 (44%) were general nephrologists. Non-participation was due to travel, clinical commitments or non-response. Participant characteristics are provided in Table 5.1. On average, each interview lasted 30 minutes and was conducted in a hospital office or meeting room, or at a conference venue. Participants were from New South Wales (n = 17), Queensland (n = 4), South Australia (n = 5), Tasmania (n = 1), Victoria (n = 11), Western Australia (n = 1), and New Zealand (n = 2).

Themes

Five major themes reflecting nephrologists' perspectives on patient eligibility and access to living donor transplantation were identified: championing for optimal recipient outcomes, responsibility for patient advocacy, justifying donor sacrifice, maintaining professional boundaries, and entrenched inequities. Illustrative quotations are provided in Table 5.2.

The relationships between themes are depicted in Figure 5.1. Decisions about recipient eligibility for living kidney donor transplantation involved complex negotiations between achieving optimal recipient outcomes and ensuring that the sacrifice to the donor was justified and worthwhile. A willingness to accept justifiable risks was validated by acknowledging reciprocal benefits to the donor, but nephrologists were often restricted by conservative centre policies or were cautious to protect their professional reputation and ensure patients were informed and accepting of possible consequences. Nephrologists' felt powerless to address inequities faced by their patients of ethnic minority and low socio-economic backgrounds due to entrenched barriers including poor self-advocacy, the limited availability of suitable donors, and uncertainties in facilitating shared decision-making. Arguments for making eligibility decisions and centre performance outcomes explicit to patients were met with concerns about reinforcing the gatekeeping of high-risk patients by transplant centres.

Championing for optimal recipient outcomes

Maximising recipient survival: Living kidney donor transplantation, particularly pre-emptive transplantation, was considered the "first line" treatment for eligible patients as it offered the best survival and graft outcomes and could reduce or avoid time on dialysis. Organs from deceased donors were perceived to be of poorer quality due to a longer cold ischemic time and an aging donor population.

Increasing opportunity: Kidney transplantation from a living donor was regarded as the "only way to make up for the short-fall of deceased donation", and reduce the burden on the waiting list. Living donation was viewed as "the only feasible way of getting a transplant" for complex patients, because of the possibility of ABO incompatible transplantation, desensitisation therapy or paired exchange.

Accepting justified risks: A "relaxed" attitude towards recipients who were ineligible for wait listing, due to their age or comorbidities, was justified by the safer and more "controlled conditions" compared to deceased donor transplantation. Living donation could ensure optimal timing of the operation, adequate planning for immunosuppression and more predictable graft outcomes. A few participants encouraged leniency for young people with previous history of malignancy because of the burden of dialysis. Some were willing to accept high-risk recipients with a living donor because the "simple contract between the donor and recipient" would not unfairly "waste" a community resource.

Needing control and certainty of outcomes: Caution to minimise the risk of graft failure, patient sensitisation, and perioperative complications led to reluctance to pursue high-risk transplants due to fears of "do[ing] more harm than good" to the patient. Some argued that complex procedures like ABO incompatible transplantation should only be performed in centres with sufficient surgical expertise.

Safeguarding psychological wellbeing: Some participants believed it was necessary to exclude recipients who might not cope with the potential psychological challenges after transplantation, including guilt about graft failure and donor complications, or donor-recipient relationship problems. Others did not consider psychological factors to be contraindications to receiving a living donor transplant because the "medical benefit supersedes any psychological issues".

Justifying donor sacrifice

Confidence in reasonable utility: There was uncertainty about taking chances on recipients who were at risk of graft complications or had a less than five-year life expectancy because they needed assurance that the donor's sacrifice was justified by reasonable utility of the kidney. Younger patients were thought to gain the most from living donation, whereas some questioned the value of the gift to an older recipient. Some preferred to waitlist non-adherent patients who had a potential donor, and were wary of non-adherence for adolescents, or patients with depression or limited social support. However, some nephrologists believed that using estimates for patient or graft survival, especially non-adherence and donor specific antibodies were "unethical" because of the unreliability of these criteria.

Sparing the donor: To potentially avoid risk to the living donor, some kept their patients with "short-wait blood groups" on the waiting list whilst simultaneously evaluating their donor. However, others argued that it was unethical to "deprive" someone on the waiting list without a living donor available, especially if they were reserving their living donor for a subsequent transplant.

Ensuring reciprocal donor benefit: Some participants believed in respecting the autonomy of the donor-recipient dyad, particularly for older pairs. For example, they would accept a recipient-donor dyad aged over seventy, even when the expected patient survival was less than five years as this was justified by a collective improvement in quality of life.

Advocating for patients

Being proactive and encouraging: A primary responsibility of nephrologists was to proactively educate and facilitate assessment (particularly for pre-emptive transplantation). Some stressed the need to "sell" living donor transplantation as the ideal treatment, to build patient trust and confidence in the transplant team, and to encourage patients to "hunt around" for potential donors.

Addressing ambivalence: Participants acknowledged that the recipient's decision about accepting a living donation involved ethical and psychological considerations including guilt, difficulty asking someone to donate, family disagreement, concerns for donor safety, financial and occupational pressures, and relationship problems due to indebtedness. Strategies to address these barriers included identifying an "ally" in the patient's social network to help them find a donor, encouraging patients to consider the benefits of living donation from their donor's perspective or involving a multidisciplinary team to provide psychosocial support.

Depending on supportive infrastructure: Some participants observed that patients treated in smaller or private units had "someone in there batting for them" because of a stronger doctor-patient rapport, whereas patients in larger units often became "lost in the system" due to being seen by different consultants. Inefficiency in coordinating assessments was attributed to overloaded clinics, a lack of “streamlining” of evaluations, and poor communication between independent donor and recipient physicians. General nephrologists faced difficulty coordinating pre-emptive transplantation, and often delayed discussion about living donation because of competing clinical priorities, and limited access to resources including transplant education and coordinators. Transplant nephrologists felt responsible for improving referrals from non-transplant services by educating general nephrologists, to ensure their patients had equal opportunity.

Avoiding selective recommendations: Although it was important to participants to convey a consistent message and offer the same opportunity to all patients, this conflicted with their reluctance to encourage unrealistic expectations in patients who had significant comorbidities or were unlikely to have a suitable donor.

Maintaining professional boundaries

Minimising conflict of interest: Some transplant nephrologists believed they were more “passive” in promoting living donation to potential recipients because of their dual responsibility to protect the donor from coercion and ensure their long-term safety. The policy for independent donor assessment was considered crucial to avoid unwarranted pressure on donors. However, they found it difficult to manage competing interests in preliminary consultations where family members of the potential transplant candidate were present during discussions about living donation. Some were willing to provide initial information to potential donors, or “allude to the fact that they might be a donor”. Nephrologists felt powerless when their patients were unwilling to openly discuss living donation with their family, particularly when faced with a young person who had a seemingly large potential donor pool.

Respecting shared decision-making: Participants highlighted the importance of providing balanced information and addressing patients' misconceptions to ensure an understanding of the risks of graft failure, donor complications, and possible psychosocial challenges. They respected their patient's moral decision to refuse a living donor, arguing that "we shouldn't try too hard to change their mind" because their concerns were often valid and justified. For high-risk patients, transplant nephrologists needed to be convinced the patient was accepting of possible risks, to protect their professional integrity.

Emphasising patient accountability: It was difficult for participants to encourage patients who they felt were unable to accept their diagnosis of ESKD and the need for transplantation to attend education programs, undergo assessment, and discuss living donation with family members. They believed that patients held some responsibility to ensure they were eligible for transplantation, for example, by quitting smoking or making lifestyle modifications for weight management.

Restricted decisional power: Some general nephrologists felt powerless because patients they considered suitable could be deemed ineligible by the transplant assessment team – "they make their decisions and we need to live with them". Transplant nephrologists believed that democratic decision-making or conservative unit policies sometimes prevented them from accepting suitable recipients.

Protecting unit interests: There was a perceived obligation to protect the credibility and reputation of their transplant unit by refusing a high-risk patient because poor graft or patient survival outcomes "do not look good on the hospital statistics". General nephrologists thought this led to the "hyper vigilant" scrutiny and "unnecessary duplication" of the clinical assessments they had performed by transplant nephrologists. Some general nephrologists were frustrated by an apparent lack of trust in their competence. Simultaneously, a competitive drive among transplant units to justify their existence applied pressure on nephrologists to increase their rates of transplantation. Some voiced disappointment that this led to the unwillingness of transplant centres to relinquish the care of their patients to another unit with unique expertise, such as ABO incompatible transplantation. Some suspected that private physicians might not promote pre-emptive transplantation because "every time they lose a dialysis patient…they lose income".

Entrenched inequities

Exclusivity of living donors: Socio-economically disadvantaged and ethnic minority patients were deemed less likely to have a suitable donor because of a higher incidence of obesity, cardiovascular disease, diabetes, high blood pressure, end-stage kidney disease (ESKD) and smoking. Some believed that these patients were often "pre-judged" regarding their likelihood of finding a donor, and that socio-economically disadvantaged patients were likely to have a limited social network and thus a small potential donor pool or their potential donors could not afford to take time off work to donate.

Inherently advantaging self-advocates: Patients of higher socio-economic status were expected to be more likely to receive a living donor transplant because they were described as being typically "a good advocate for themselves" in terms of their motivation to find a living donor, seek information, and achieve weight loss or smoking cessation. Some believed that patients from ethnic minority and low socio-economic backgrounds were likely to smoke and present with comorbidities, predominantly obesity. Patients with lower education or health literacy were thought to be "hard to engage" due to often lacking an understanding of their diagnosis of ESKD and the benefits of living donor transplantation.

Navigating language barriers: There were distinct challenges in providing access for patients who did not speak English, or those with low health literacy, because of the difficulty in helping them to “understand what is quite a complex process”, and relay complicated information onto their families. Nephrologists expressed frustration with using interpreters, believing that the accuracy and emotional elements of their “delicate” dialogue needed to “convince” someone of the safety of living donation were not conveyed. Participants observed that some non-English speaking patients were not referred for transplantation or failed to complete assessments because “it’s more troublesome, more time consuming” due to difficulty communicating instructions.

Understanding cultural barriers: Some participants felt helpless to address ethnic disparities because they had a limited understanding of cultural barriers. They found it challenging to address patients concerns about the spiritual influence of the donor’s kidney, and cultural norms pertaining to receiving gifts, asking favours, and family hierarchies.

Increasing centre transparency: Participants believed that a patient could be disadvantaged if they were referred to a transplant unit that had a conservative live donor transplant policy or a lower volume program because of presumed lesser expertise. While variability across centres was deemed acceptable by some, they insisted that centres publicise their policies to prevent gatekeeping, so that high-risk patients could be advised to seek an opinion from other units. Some also advocated for making variations in centre performance known to patients by publicly reporting transplantation rates and outcomes, but expressed concerns that this might lead to risk aversion by transplant programs.

Inevitable geographic disadvantage: Delays in coordinating tissue typing and transplant evaluations, isolation from family and the financial costs associated with travel, accommodation and lost productivity, and a reluctance to travel were identified barriers to living donor transplantation for patients living outside of metropolitan areas. Rural nephrologists were frustrated as they felt these barriers could be reduced by using local tissue typing services, utilizing teleconferencing and streamlining and prioritizing assessments to minimize travel. Some transplant nephrologists also felt unable to provide the same opportunity to rural patients compared to local patients, and wished to increase outreach clinics and transplant education programs in rural areas.

5.5 Discussion

Central to decisions about recipient eligibility for living kidney donor transplantation was maximizing recipient survival and quality of life. Simultaneously, nephrologists want to ensure that the donor's sacrifice is worthwhile, and protect their centre's performance, as measured by recipient and graft survival. They struggle to resolve these competing responsibilities, particularly when faced with patients who have medical, psychosocial and/or behavioural risk factors, and might be ineligible for wait listing for deceased donor transplantation. Substantial variability in the recommendations of nephrologists may intensify inequity for vulnerable patients. Nephrologists also encounter difficulties addressing patient ambivalence, supporting patients with donor recruitment, achieving shared decision-making and navigating referrals and assessments, particularly for patients with limited language proficiency or health literacy barriers. However, they primarily attributed ethnic and socio-economic disparities to the limited availability of suitable donors, and regarded this inequity to be beyond their control.

Our findings describe the professional attitudes and unit policies that may explain the disparities of access to living kidney donor transplantation and variability among transplant centres.[12,13,30] Nephrologists were apparently polarized regarding whether to allow living donor transplantation for patients who were older, highly sensitized, non-adherent, and those with low social support, mental health issues, comorbidities, and recurrent disease. Academically affiliated nephrologists questioned the fairness of determining access based on estimates of graft survival including donor specific antibodies and non-adherence due to their poor predictive value. Mostly older and experienced nephrologists encouraged individualized judgments that valued quality of life over graft survival, particularly for young patients, and older donor-recipient pairs.

Inconsistent and inexplicit recommendations may intensify inequity for disadvantaged patients. Our findings support suggestions that nephrologists' decisions regarding disadvantaged patients may sometimes reflect their inherent biases or assumptions regarding a candidate's expected survival and chances of finding a donor, for example, due to expectations of low motivation and poor self-advocacy.[19] The hypothesis that ethnic and socio-economic disparities are largely caused by a limited donor pool due to the higher burden of disease is prevalent in the literature, but this evidence is based on single-centre studies.[10,11,31,32] Our findings also indicate that there may be some reluctance to unnecessarily raise patient's expectations, and uncertainties about communicating risk due to language and health literacy barriers. Moreover, nephrologists distanced themselves from assisting candidates with donor recruitment to avoid a conflict of interest, and this is an important barrier for ethnic minorities, uneducated, older and female populations.[32-37]

This is the first study to describe in-depth nephrologists' attitudes toward recipient eligibility for living donor transplantation and highlights the challenges they encountered in advocating for potential candidates. However, there are some limitations. The transferability of some of the concepts in our study to other settings is uncertain, particularly to low-income countries. Our findings are potentially limited by the underrepresentation of female participants, although previous research suggests that nephrologists' views regarding transplant eligible are not associated with gender, but rather with age, experience in transplantation, academic affiliation, and location of practice[17]; which are broadly captured among participants in our study.

Our study has important implications to address disparities in access to living kidney donor transplantation, primarily by making more explicit and informed decisions concerning recipient eligibility (Table 5.3). Implementation of an explicit pathway for patient education and referral to transplant services could promote consistent and equitable recommendations to patients. Clinical guidelines for transplant eligibility fail to address the real uncertainties faced by nephrologists in determining risks for older, sensitized, ethnic minority and socio-economically disadvantaged patients and emphasis on estimates of graft and patient survival inevitably introduce subjectivity.[38] Evidence-based recommendations to address psychosocial risk factors are needed, including non-adherence, depression, and low social support.[18,39,40] Training to improve interactions with interpreters might alleviate nephrologists' uncertainties during shared decision-making with non-English speaking patients.[41,42] There are also concerns that publicized centre reports evaluating centre performance based on recipient outcomes may encourage risk avoidance strategies among transplant centres, and these trends have been observed in the United States.[40,41] We support recommendations that both patient outcomes and transplant volume should be regarded as equally important in quality evaluations, to ensure that efforts to maximize outcomes are not maintained at the expense of expanding access to transplantation.[38]

The assignment of multidisciplinary staff to provide interventions targeted to disadvantaged populations may improve patient advocacy. Promising interventions include a social worker consultation to identify and address individual patient barriers[43], peer supporters' to navigate referral and assessment processes[44], and culturally-sensitive home education[45]. Strategies to support patients in engaging in discussions with potential donors are available[43], which should be directed by multidisciplinary staff to help minimize nephrologists' conflict of interest. Moreover, the responsibilities and boundaries of nephrologists representing the recipient, in supporting and facilitating donor education and recruitment require clarification, and should be restricted to the role of the donor advocate.[46] Educating patients with a limited donor pool about options such as ABO incompatible transplantation, paired exchange and unrelated donation might increase their chances of finding a donor.[8] Patients should also be informed about the considerable variability among kidney transplant centres in terms of patient outcomes, unit policy, expertise and resources such as ABO incompatible transplantation. In many countries, hospital performance reports are accessible to patients via websites such as Hospital Compare (http://www.medicare.gov/hospitalcompare/search.html). Importantly, efforts are needed to ensure that patients have the capacity to understand centre reports and to travel to an alternative unit[47-49], which are likely to be challenging for disadvantaged patients and could potentially reinforce disparities.

Nephrologists can offer important insights to address disparities in transplantation; therefore it would be beneficial to conduct similar research in 1) low-income countries, 2) countries like Japan where living donation accounts for the majority of all kidney transplants, and 3) jurisdictions where commercial transplantation prevails. Further research is needed to develop a broad understanding of cultural barriers, to inform educational interventions of potential candidates from diverse backgrounds. Our findings can also inform the development of a survey to investigate the frequency of opinion among nephrologists and enable comparison with other transplant professionals and nephrologists working in various settings. Our study did facilitate comparison among nephrologists working in rural and urban settings, transplant and general nephrologist and years of clinical practice. The perspectives of nephrologists in other countries as well as transplant clinicians involved in the multi-disciplinary care of transplant recipients, including surgeons and transplant coordinators, should be studied, because their attitudes might differ due to their unique professional responsibilities and settings in which they work.

Decision-making about patient eligibility for living kidney donor transplantation involves unique ethical, psychosocial and medical uncertainties. Nephrologists weigh opportunities to provide complex patients their only chance of avoiding dialysis against their moral and professional responsibility to ensure reasonable utility of the kidney transplant to justify the donors sacrifice. A preference for certainty of graft outcomes and difficulties facilitating shared decision-making may contribute to disparities for disadvantaged populations. Increased consensus and standardized practice regarding complex medical and psychosocial cases, transparency of centre performance and practice, and resources to provide culturally competent care might assist with reducing disparities in access to living kidney donor transplantation.

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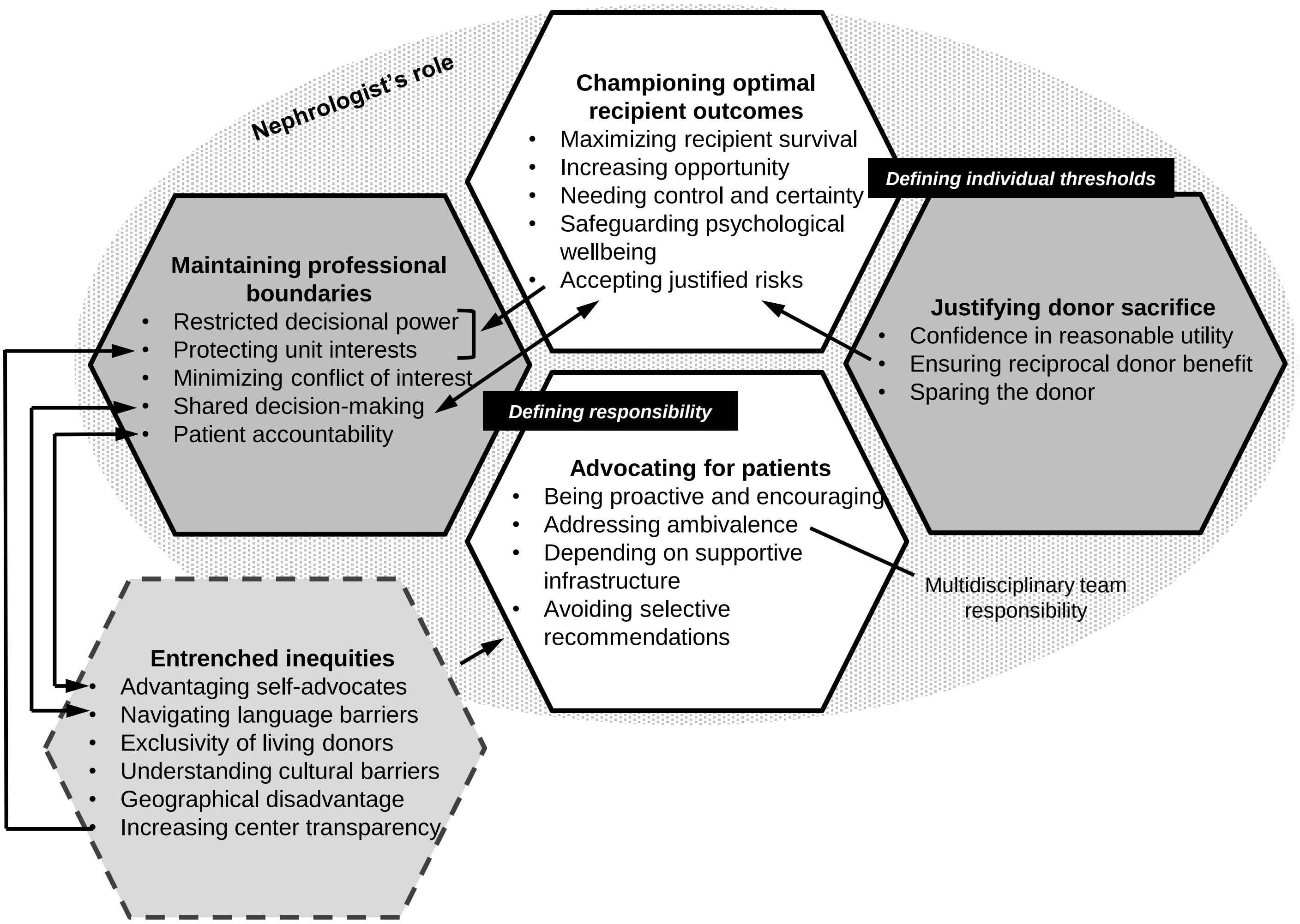

Figure 5.1. Thematic schema

Decisions about recipient eligibility for living kidney donor transplantation involved complex negotiations between achieving optimal recipient outcomes and ensuring that the sacrifice to the donor was justified and worthwhile. A willingness to accept justifiable risks was validated by acknowledging reciprocal benefits to the donor, but nephrologists were often restricted by conservative centre policies or were cautious to protect their professional reputation and ensure patients were informed and accepting of possible consequences. Nephrologists' felt powerless to address inequities faced by their patients of ethnic minority and low socio-economic backgrounds due to entrenched barriers including poor self-advocacy, the limited availability of suitable donors, and uncertainties in facilitating shared decision-making. Arguments for making eligibility decisions and centre performance outcomes explicit to patients were met with concerns about reinforcing the gatekeeping of high-risk patients by transplant centres.

Table 5.1: Participant characteristics

Characteristic (n = 41)	n (%)
Specialty	
Transplant nephrologist*	26 (56)
General nephrologist	15 (44)
Gender	
Male	33 (80)
Female	8 (20)
Age (years)	
30-39	6 (15)
40-49	15 (37)
50-59	13 (32)
60+	7 (17)
Clinical experience (years)	
≤ 10	9 (22)
11-20	12 (29)
21-30	13 (32)
> 30	7 (17)
Location of practice	
Australia	
New South Wales	17 (42)
Queensland	4 (10)
South Australia	5 (12)
Tasmania	1 (2)
Victoria	11 (27)
Western Australia	1 (2)
New Zealand	
Christchurch	1 (2)
Auckland	1 (2)
Location of interview	
Conference venue	10 (24)
Hospital office/ meeting room	31 (76)

*Transplant nephrologists were defined as nephrologists directly involved in the transplant assessment team and the immediate post-operative care of transplant recipients

Table 5.2. Illustrative quotations

Theme	Illustrative quotations
	Championing for optimal recipient outcomes
Maximizing recipient survival	From the selfish view of the recipient, it does give them a related transplant or less damaged transplant without a waiting time. (Male, general nephrologist, 50s) Every patient should be getting a living, related transplant, or organize one if they can. That would be very much our first line. It just doesn't happen very often. (Male, general nephrologist, 50s)
Increasing opportunity	We all need living donors to try and get our patients off dialysis and give them a half decent life, especially if they're young. (Male, general nephrologist, 50s) In our current environment when we have such a low deceased donation rate for a lot of people it's the only feasible way of getting a transplant and the best way. (Male, transplant nephrologist, 30s).
Needing control and certainty	We have people on our live donor recipient list who are transplanted who are older and sicker than the worst patients on the deceased donor list. And the argument we're putting in terms of the recipient is that the medical milieu in which you're doing a live donor transplant is somewhat safer than in which you're doing a deceased donor. You're doing it electively in perfect daylight prepared, so you can take an older and sicker patient on and believe that they'll survive. (Male, transplant nephrologist, 60s). We need to be mindful that we're good at living donation, but with the new ways we have to overcome immunological barriers, we may actually be doing quite high-risk transplants using living donors…You just wonder what the long-term outcomes of these really heightened risk transplants may be. (Female, transplant nephrologist, 40s)
Accepting justified risks	Some people are very regimented by guidelines, and not necessarily personal patient issues. Sometimes, the longer you've been practicing, the more likely you are to consider you can probably get across a problem as opposed to being more junior; you're less likely to take a risk. (Female, transplant nephrologist, 50s). I think most practitioners are more relaxed about recipient eligibility for living donor transplantation because it is a simple contract between the donor and recipient. The deceased donor list is the property of the community at large, and decisions made utilizing an organ from the deceased donor pool must benefit the community in a way that is completely equitable and transparent. With living donation, if the transplant doesn't work out, this disadvantages no one else. . (Male, general nephrologist, 40s) My only negative feeling about it is that everyone's got their own threshold... Physicians tend to be fairly confident and have very strong opinions that they hold quite vehemently. Sometimes we transmit our own ethical beliefs into the clinical situation quite strongly. (Female, general nephrologist, 50s)
Safeguarding psychological wellbeing	There can be some kind of psychological impact on relationships but, generally speaking, I probably, look at things more from a medical point of view. What's the alternative? I think the medical benefit supersedes any psychological issues, quite frankly. I wouldn't see that as a contraindication. (Male, transplant nephrologist, 30s). I think we often think about matching in terms of blood group, but I think in terms of the relationships and how that's going to impact. (Male, general nephrologist, 40s).
	Justifying donor sacrifice
Confidence in	If you think someone's going to be non-compliant but you're not really sure… with a deceased donor you might be a bit more likely to just give it a go. Whereas if it's a live donor, you think about the consequences for their relationship if they don't take the pills and they lose their kidneys. (Male, transplant nephrologist, 30s).

reasonable utility	
Sparing the donor	If you're waitlisted, you can keep both options open and perhaps in the next six months, if you do get a deceased donor, hoping that it's a good one, then obviously that will spare your friend or family member who was going to donate your kidney. (Male, transplant nephrologist, 30s)
Ensuring reciprocal donor benefit	What happens if the recipient's only going to live three years? Well that wouldn't be a good use of a community resource, a cadaveric kidney. But if the donor knows exactly what's going to happen and that person has three good years - that's a good result. (Male, transplant nephrologist, 50s).
Advocating for patients	
Being proactive and encouraging	You have to be proactive. It's actually about saying your GFR is 20, you are progressing towards renal failure. You need to find yourself a donor. It's the way that you phrase the conversation and the way that you drive things. Otherwise, a different clinician would just sit there saying you are GFR is 20, how are you feeling? I think it's personality and its bedside manner but I think it's also about attitude to transplant. (Male, transplant nephrologist, 30s).
Addressing ambivalence	Perhaps we need to ask a little bit more about when someone says, ‘no, I don't have a donor’, enquire as to…’ is there no-one or do you find it difficult asking?’ So maybe digging a little bit deeper. That might help us help our patients. (Female, transplant nephrologist, 40s). I try to motivate it away from just selfish concerns or selfish, in inverted commas; and more trying to say this is the family helping you at very little cost to themselves and you being healthy can be a better contributor and less of a burden to your family. I think we’ve got to sell the family side of things. (Male, general nephrologist, 40s).
Depending on supportive infrastructure	There are increasing numbers of units that only dialyze and no matter what you do that places a physical and intellectual barrier. From a mental point of view they are dialyzers. Every thought is about how to dialyze this person better. I know of a doctor who feels people shouldn’t be transplanted till they have been on dialysis for a period because when they get their transplant they’ll be more compliant. (Male, transplant nephrologist, 60s). It’s the responsibility of the transplanting hub to make sure that these people are getting the same opportunity as their own patients. So we have to get these messages out we need to educate the non-transplanting nephrologists about what's important. (Male, transplant nephrologist, 60s).
Avoiding selective recommendations	We tend to be a bit paternalistic, take away the decision-making processes a little bit from the patients. It's partly because we give them selective information along the way, and biased information. (Male, transplant nephrologist, 60s).
Maintaining professional boundaries	
Minimizing conflict of interest	I think you have to be careful to not be giving the potential recipient a whole sort of structure to go out there to solicit a kidney. (Female, transplant nephrologist, 40s). We feel that that these are not our patients. We have no right to be in medical contact with them. They have their own private lives and we, without being invited, would be invading their private life and we won’t do that and doctors don’t go out knocking on doors looking for work. It’s not what we do. (Male, transplant nephrologist, 60s). My policy has always been that we should get the potential donor to raise the question…I make sure it is one of my colleagues who hasn’t seen the potential recipient yet in the clinic” (Male, nephrologist, 30s).
Facilitating shared decision-making	But I think the important thing is that the risk is communicated, so you're all taking the risk, not just the doctor taking the risk on behalf of the patient, because that is a dangerous position to put yourself in. (Female, transplant nephrologist, 50s). I guess as I grow older I do realize that people have their own patient-centred outcomes and sometimes, although they might appear completely bizarre, if they're

	really competent to make that decision we shouldn't try too hard to change their mind. (Male, general nephrologist, 40s).
Emphasizing patient accountability	The area where it may fall down is that the recipient really has to be approaching potential living donors within their family group, don't they? If the recipient isn't keen to do that, the nephrologist has no role in being able to facilitate that. So if you don't have the recipient completely on board, then probably those conversations may not happen. (Female, transplant nephrologist, 40s).
Restricted decisional power	The transplant team have a meeting, we're not invited. They make their decisions and we need to live with them. If we disagree, we either live with it or take our business elsewhere. It usually spurs them on to think harder. A lot of the problems we have revolve around moderately obese patients. (Male, general nephrologist, 50s). Rather than have the member of the team who's quite uncomfortable about, we'd err on the side of not doing it rather than doing it. (Male, general nephrologist, 50s).
Protecting unit interests	We've had several episodes of threatened closure that influenced attitudes here. Nothing like hearing on the radio from the Minister of Health that he's been advised that your program should be shut down. (Male, general nephrologist, 60s). Many centres are not good at what they do, but they keep doing it, because they do it for the centre and not the patient. (Male, transplant nephrologist, 50s). There is a strong motivation for transplanting hospitals to protect their credibility and maintain their performance, and to some extent this leads to gatekeeping to avoid high-risk patients. The clinical assessments and clinical testing done at other hospitals is scrutinized, as it should be, but this can be, and is often, overdone so that there is unnecessary duplication… and can lead to a somewhat adversarial atmosphere for both the patient and referring doctor. (Male, general nephrologist, 40s)
Entrenched inequities	
Exclusivity of living donors	The barriers are probably different, just in different communities and different ethnicities. A big Tongan or Samoan family will have lots of potential donors. They all get on together and they'll all be willing, but they'll all be pre-diabetic and overweight. (Male, general nephrologist, 50s). More valued people in the community are more likely to get offers and that probably equates to higher socio-economic groups. (Male, transplant nephrologist, 60s).
Advantaging self-advocating patients	If they're a professional type person, a good advocate for themselves, then they'll go out and get a donor. Whereas if they haven't gone to university or haven't finished high school then they don't have a social network around them, then actually finding a donor is quite difficult. (Male, transplant nephrologist, 30s) There's a constellation of things that go with poverty. It can be a low IQ, a low education, low motivation, or a combination… Poor people smoke more. They don't exercise very much. They get more diabetes. There's a whole stack of things that go with poverty, but they're not all causal. They're all circular. Even when you do that multivariate analysis there's this big gap which doesn't explain why they do worse. So the gap is just the intrinsic drive, like conscientiousness. It's very, very hard to actually put a number on and factor in. But you can sense it. (Male, general nephrologist, 50s).
Navigating language barriers	I think language barriers do play a role as well. It's a lot easier to convince someone of the benefits of live donor transplants if you can have a full frame conversation with them. It's just not the same. If you're communicating with someone you do it not just at a verbal level. It can be very delicate. It's very hard to have a delicate conversation through an interpreter. (Male, transplant nephrologist, 30s). They're less likely to be referred on, probably because it's more troublesome, more time consuming. Doctor speaks, they don't understand. Or he gives them a piece of paper, it says, go and make an appointment, and they don't know where or how to go to make it happen. (Male, general nephrologist, 60s).
Increasing center transparency	I think the shame is the disparity between units. Both integrated and disintegrated renal services and different doctors have really quite different rates of promotion of live donor transplant and if they would voice them, publicize them, I'd be happy. You need to know to move on. Because I think everybody and every

	institution has the right to do things according to their moral judgment as long as they make it public, that they're not giving advice based on their own thing. I'm very for the concept that units' habits and outcomes be publicly available. (Male, transplant nephrologist, 60s). Different sites might have different policies, for example, about who they'll accept. What tends to happen is once a person gets referred to a particular unit, they'll tend to stay at that unit rather than looking around for different opinions. (Male, transplant nephrologist, 50s). So if they happened to be referred to a unit that has a very conservative live donor policy then they might be disadvantaged. (Male, general nephrologist, 50s)
Geographical disadvantage	We don't think we do as good a job with [the rural centres], and it's about communication with the teams down there. It's something that we're trying to work on now, because we don't think we're providing the same opportunity, and we don't think they're getting as good information. (Male, transplant nephrologist, 60s). There's no coordination as a one-stop shop, which there really should be if you're asking people to travel four, five, six hours down to the city to see them, which they do, and then make them come back repeatedly for different tests. I think they don't understand the challenges. They don't have a clue actually. To them, the patients turn up, everything's done, what's the problem? (Male, general nephrologist, 50s).
Understanding cultural barriers	We know there are barriers, but we're not the right people to ask, to get that information. They don't tell us. We don't know how to ask properly. We don't know how to ask them. (Female, transplant nephrologist, 50s). To be fair we probably ought to be targeting some of the groups who we've cast a fairly jaundiced eye on. (Male, general nephrologist, 30s).

Table 5.3. Implications for practice and policy to address barriers and inequity

Key issues	**Suggested research and policy priorities**
Unit variability and transparency	• Identify policies and practices associated with higher rates of living kidney donor transplantation • Develop national key performance indicators to benchmark and monitor rates of living kidney donor transplantation (including pre-emptive transplantation), the rates of referrals, and efficiency of evaluations • Develop a platform to publicize transplant centre characteristics (*e.g. policies, practices, resources, expertise, rates of transplantation)* to patients
Delayed referral to transplant services	• Promote a commitment to living donor transplantation in non-transplant services (*e.g. staff education*) • Provide resources to support the facilitation of referrals to the transplant centre (e.g. *transplant coordinators, web-based system to monitor patients estimated glomerular filtration rate*)
Inefficiency	• Adopt strategies to reduce delays in completing evaluations or operations *(e.g. negotiate a higher priority status for operations and assessments, utilize private physicians, surgeons and theatres, increase resources for assessment clinics, avoid unnecessary duplication of assessments)*
Donor recruitment	• Provide counselling to assist patients to engage in discussions about living donor transplantation with potential donors • Define the roles and responsibilities of nephrologists in supporting and facilitating donor recruitment and family education
Disadvantaged populations	• Reduce delays for rural patients *(e.g. prioritize and streamline appointments at the transplant centre, increase funding for out-reach clinics, utilize Telehealth services and local medical services for tissue typing and assessments).* • Identify strategies to counsel potential recipients with low health literacy or English proficiency about donor risks and "high-risk" living donor transplants (e.g. *family education*). • Engage with community members to develop strategies to address cultural barriers to living kidney donor transplantation • Provide multidisciplinary support to identify and address barriers to transplantation during early stages of renal care
Psychosocial barriers	• Identify strategies to provide psychosocial support to potential recipients to address fears and concerns, denial, non-adherence, weight-loss, smoking, alcohol and drug abuse, and promote self-advocacy
Eligibility criteria	• Develop explicit and shared policies regarding the eligibility of older donor-recipient dyads • Develop explicit and shared policies regarding the inclusion/exclusion of non-adherence in eligibility criteria • Develop explicit and shared policies regarding the interpretation of donor specific antibodies to determine patient eligibility
Evaluation procedures	• Develop explicit and shared policies regarding cardiovascular screening using coronary angiography and implications for pre-emptive transplantation

The suggested research and policy priorities were formulated by participants and discussion among the research team

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Chapter 6: Identifying outcomes that are important to living kidney donors: a nominal group technique study

Hanson CS, Chapman JR, Gill JS, Kanellis JK, Wong G, Craig JC, Teixeira-Pinto A, Chadban SJ, Garg AX, Ralph AF, Pinter J, Lewis JR, Tong A. Identifying outcomes that are important to living kidney donors: a nominal group technique study. (Submitted to the American Journal of Kidney Diseases, August 2017)

The chapter is structured as per the journal article.

6.1 Abstract

Background: Living kidney donor candidates accept a range of risks and benefits when they decide to proceed with nephrectomy. Informed consent around this decision assumes they receive reliable data about outcomes they regard as critical to their decision making. We identified the outcomes most important to living kidney donors and described the reasons for their choices.

Methods: Previous donors were purposively sampled from three transplant units in Australia (Sydney and Melbourne) and Canada (Vancouver). Using the nominal group technique, participants identified outcomes of donation, ranked them in order of importance, and discussed the reasons for their preferences. An importance score was calculated for each outcome. Qualitative data was analysed thematically.

Results: Across 14 groups, 123 donors aged 27-78 years identified 35 outcomes, with clear regional differences. The five most important donor outcomes for Australian participants were impact on family (importance score = 0.35, scale 0-1), followed by time to recovery (0.34), donor-recipient relationship (0.27), kidney function (0.26) and lifestyle restrictions (0.21). The five most important donor outcomes for Canadian participants were kidney function (0.57), followed by surgical complications (0.29), kidney failure (0.22), life satisfaction (0.20), and time to recovery (0.19). The themes identified included worthwhile sacrifice, downplaying risks and harms, confidence and empowerment, unfulfilled expectations and heightened susceptibility.

Conclusions: Living kidney donors prioritized a range of outcomes, with the most important being kidney health, and the surgical, lifestyle, functional and psychosocial impacts of donation. Donors also valued improvements to their family life and donor-recipient relationship. Kidney

function and kidney failure was more important to Canadian participants, compared to Australian donors, perhaps due to the inclusion of non-directed donors. The outcomes most relevant and meaningful to donors should be routinely addressed in research, informed consent, assessment, post-donation education, and follow-up care.

6.2 Introduction

In 2014, living kidney donor transplants comprised 42% of kidney transplants performed worldwide.[1] Living kidney donor transplantation has been widely advocated to address the global shortage of organs, and can offer transplant recipients superior graft and survival outcomes compared with a deceased donor transplant.[2,3] Whilst there are significant benefits for recipients, living kidney donors must accept various risks associated with nephrectomy.

Living donation is considered ethically justified on the proviso that donors undergo rigorous medical screening and assessment, provide informed and voluntary consent after education about the potential risks and uncertainty regarding long-term outcomes, and have access to long-term health care.[4-6] However, understanding of the risks to living kidney donors is evolving, with the progressive publication of more robust long-term data.[7-9] Recent evidence of small absolute increases in the risk of end-stage kidney disease (ESKD), hypertension, hypertension in pregnancy, and all-cause mortality in donors in the three decades following donation, compared to the general or healthy population[4,7,8,10-13] reinforces the need for ongoing research and follow-up of living kidney donors.

Living kidney donors experience a broad range of post-donation outcomes that span physical and mental aspects of their health, function, relationships, wellbeing, and livelihood.[14] Current guidelines for informed consent and follow up do not consistently or comprehensively address psychosocial outcomes and other donor-reported outcomes.[14-17] This study aims to identify the impacts of kidney donation that are deemed important by living kidney donors, and to understand the beliefs and attitudes underpinning the outcomes they value. This can help to ensure that research, informed consent and education and follow-up care address outcomes and provide information that is meaningful and relevant to kidney donors.

6.3 Methods

Participant recruitment and selection

We recruited living kidney donors from three transplant units in Australia (Sydney, Melbourne) and Canada (Vancouver). Participants were purposively sampled to include a range of demographic (gender, age), and donation characteristics (time since donation, relationship with the recipient, self-reported complications). All adult kidney donors from the past 20 years, at the participating units, who were English-speaking, and able to provide informed consent, were eligible to participate. Participants were reimbursed AUD/CAD $50 for their travel expenses. Ethics approval was obtained from the Western Sydney Local Health District, Monash Health and the University of British Columbia/Providence Health Care.

Data collection

We conducted focus groups using the nominal group technique. The nominal group technique involves structured 'brainstorming' to develop ideas, followed by individual voting on the list of ideas.[18] Group discussion was used to identify reasons for individual preferences, as well as divergent and similar opinions within the group.[19-21]

The two-hour meetings were convened between July 2015 and July 2016 and included four phases: 1) discussion about the experience of kidney donation; 2) identification of outcomes as a group (which were augmented with outcomes from previous groups and research studies[7,8,11,14,22-28]; 3) independent ranking of the relative importance of each outcome (on a printed list); and 4) group discussion of the reasons for their rankings (See Appendix D.3). Three researchers (CSH, AFR or AT) facilitated the groups in a centrally located venue external to the participating hospitals. Outcomes were included as distinct options according to the participant's preferences, and there was an effort to maintain consistently in subsequent groups. An observer (CSH, AFR, AT, JP) recorded field notes during the discussion. Each session was audio-recorded and transcribed verbatim. Recruitment was stopped upon reaching data saturation i.e. when no new outcomes or concepts were raised in subsequent groups.

Data analysis

Quantitative analysis: The ranking from the nominal groups produced ordinal data. Some groups did not raise a particular outcome, and some participants within a group did not rank all the outcomes on the groups list. Therefore, it was not appropriate to calculate means. A measure of importance (i.e. importance score) of each outcome was used to prioritize the outcomes, based on the rankings attributed by participants. To calculate this measure, the distribution of the ranking for each outcome was obtained, by calculating the probability of each rank for each outcome [$P(O_j\ in\ rank\ i)$, i.e., the probability of the outcome O_j being assigned the rank first place, second place and so on]. By the total law of probabilities:

$$
\begin{aligned}
&P(O_j\ in\ rank\ i) = \\
&\qquad = P(O_j\ in\ rank\ i\ |O_j\ is\ nominated) \times P(O_j\ is\ nominated) \\
&\qquad + P(O_j\ in\ rank\ i\ |O_j\ not\ nominated) \times P(O_j\ not\ nominated)
\end{aligned}
$$

where “nominated” means that the outcome was considered (and given a rank) by the participant. We assumed that the $P\left(O_j \ in\ rank\ i\ \middle|O_j\ not\ nominated\right)$ is 0, because if the participant did not rank the outcome O_j, then the probability of any rank is 0. Therefore, the equation is simplified t:

$$P\left(O_j\ in\ rank\ i\right) = P\left(O_j\ in\ rank\ i\ \middle|O_j\ is\ nominated\right) \times P\left(O_j\ is\ nominated\right)$$

The probability therefore has two components: 1) the importance given to the outcome by the ranking and 2) the consistency of being nominated by the participants. We computed the weighted sum of the inverted ranking $\left(\frac{1}{i}\right)$ to obtain the importance score.

$$IS = \sum_{i=1}^{\substack{nr\ of \\ outcomes}} P\left(O_j\ in\ rank\ i\right) \times \frac{1}{i}$$

The importance score can be interpreted as a summary measure of importance of the outcome that incorporates the consistency of being nominated and the rankings given by the participants. The ranks are inverted so that more weight is given to top ranks and less to lower ranks. Higher scores identify outcomes that are more valued by the participants. The score can range between zero and one. This measure has a similar motivation to the Expected Reciprocal Rank Evaluation Metric that was proposed in a different context.[29] The analysis was conducted using the software package R version 3.2.3 (*R Foundation for Statistical Computing, Vienna, Austria*). Importance scores for all identified outcomes are presented in Appendix Table D.1.

Qualitative analysis: We entered the transcripts into HyperRESEARCH (ResearchWare Inc. www.researchware.com, Version 3.5.2), and used an adapted grounded theory approach[30] to inductively identify preliminary concepts and themes. Accordingly, CSH conducted line-by-line coding, assigning a code to meaningful segments of text. Comparisons were made within and across groups, identifying similar and divergent concepts in the data to develop preliminary themes. These preliminary findings were discussed among the research team (investigator triangulation) to consolidate the list of themes and sub-themes, and ensure they captured the range and breadth of the participants' reasons for their rankings.

6.4 Results

Participant characteristics

In total, 123 people aged 27-78 years (mean 55 years) participated across 14 groups (median = 9 participants per group, IQR = 8-10, min = 5, max = 12). Sixty-seven participants were recruited in Australia, and fifty-six from Canada (Appendix Table D.2). The time since donation ranged from two months to sixteen years (mean 3.6 years, standard deviation =3.1). Demographic and donation characteristics are provided in Table 6.1 and Table 6.2, respectively. Seventy-eight (63%) participants were female, and 100 (81%) were white. The sample included 101 (82%) related donors (spouse, child, sibling, parent), 9 (7%) unrelated donors (colleague, friend), and six (4%) non-directed donors, from Canada. Nineteen (15%) donated through a kidney paired donation. Thirty-one participants (25%) reported mental or physical outcomes which they attributed to the donation (Table 6.2). No participants reported ESKD.

Nominal group ranking

The participants identified a combined total of 35 post-donation outcomes and the mean number of outcomes identified by each group was 22 (range 19-28). The importance scores for donor outcomes across all participants, stratified by country, are shown in Figure 6.1. Across all participants, the ten highest ranked outcomes were kidney function (i.e. glomerular filtration rate and creatinine levels) (importance = 0.40), time to recovery (0.27), surgical complications (0.24), impact on family (0.22), donor-recipient relationship (0.21), life satisfaction (0.18), lifestyle restrictions (0.18), kidney failure (defined as the need for dialysis or transplant) (0.14), mortality (0.13) and acute pain/discomfort (0.12) (Appendix Table D.1). Differences in ranking between Canadian and Australian participants are shown in Figure 6.1.

Qualitative analysis

We identified five main themes that explained participants' ranking of outcomes. Quotations to illustrate each theme are provided in Table 6.3. A schema depicting the relationship between the themes and participants' ranking of outcomes is provided in Figure 6.2.

Worthwhile sacrifice

Primacy of recipient outcome: Participants' satisfaction with the donation depended primarily on the outcome for the recipient. Recipient graft failure was expected to feel "similar to a stillbirth", accompanied by guilt, and "helplessness" because "you've got no kidney left to give". Surgical complications and lifestyle restrictions were considered "totally worth it", given the observable improvements in their recipient's health. Donors declared they concealed their complications to avoid being "selfish" or making the recipient feel guilty.

Deriving personal and familial benefits: Related donors valued the improvement to their own wellbeing, impact on family and relationship with the recipient, as this had been a primary motivator to donate. For some participants, these positive outcomes were the only impacts they had experienced. However, other participants ranked these outcomes lower because they felt these psychosocial benefits were “implicit” or difficult to measure - “I think it’s important. But it’s very subjective…I’m answering the questions myself, I could be lying to myself.”

Downplaying risks and harms

Tolerable burdens and sacrifices: Some participants were less concerned with short-term or non-life-threatening outcomes like pain because these were expected or they could “tough out those ones”. The ease of their recovery surprised some participants, and they wanted these outcomes recorded to let potential donors know that “it was not as bad as having a broken toe”.

Irrelevance to self: After full recovery, participants experienced no perceptible physical impacts of donating a kidney (“it’s like it never happened”) and some believed their health had improved due to their adoption of a healthy lifestyle. Therefore, long-term health outcomes seemed irrelevant.

Denying causation: Some participants questioned whether conditions they had developed after donation, such as gout, fatigue and hypertension, were caused by their lifestyle, pre-existing circumstances or age, rather than the donation. Some participants did not believe the nephrectomy would increase their risk of developing ESKD, and instead attributed these outcomes to a “bad” lifestyle.

Accepting fate and bad luck: Participants were reluctant to consider hypothetical repercussions of their nephrectomy because “there’s no going back from [donation]”. Older participants believed that they would inevitably develop health complications due to age (“after a certain age…stuff’s going to happen”). Surgical complications were viewed as “bad luck” and some ranked this low to avoid “put[ting] people off” from becoming a donor.

Confidence and empowerment

Power to prevent morbidity: Participants believed that they could actively prevent kidney disease, cardiovascular disease and diabetes by managing their diet and weight, and medication could keep their cholesterol or blood pressure under control. Similarly, some ranked psychological outcomes lower because these were “within [their] own control” – “whereas for medical outcomes, you need science and technology”.

Medical reassurance and protection: The “stringent” pre-donation assessment gave participants confidence that their health was “not an issue” – “I’m not going to second guess medicine”. They recalled “very positive” statistics about mortality and long-term outcomes. Participants believed that outcomes such as kidney function, fatigue, blood pressure and depression were already on the “radar” because they were being monitored in follow-up or in the research studies that they participated in. The promise of transplant wait-listing priority in Canada somewhat reduced participants concerns about ESKD.

Financial safety net: Many participants had a financial buffer or assistance to help them absorb out-of-pocket expenses and replace lost income as a result of donation, thus they ranked this lower.

Unfulfilled expectations

Misled and unprepared: Some participants ranked time to post-operative recovery, surgical complications, and pain highly because they felt “deeply disappointed” and “resentful” about enduring a more debilitating and protracted recovery than they had been “led to expect”. They considered a full recovery to mean “to be back to your life”, and to encompass their mental and physical health. Participants had vivid memories of “excruciating” pain. Younger participants had considered themselves “bulletproof” and were frustrated by being unable to resume physical activity. Younger participants noticed that their self-esteem and sex drive diminished, whilst their wound healed.

Unrecognized anguish: Persistent complications (e.g. chronic pain, fatigue, hydrocele and seromas) were considered overlooked by their clinicians. Some experienced an unexpectedly difficult emotional recovery due to their physical incapacitation, or a sense of loss – “I was surprised by how low I felt for a while”. Participants also described anxiety about their recipient’s graft function, the devastation of recipient death or graft failure, their discomfort with their “hero status” amongst their social network, lack of support from some family members, and complexities in their relationship with the recipient. Donor psychosocial wellbeing was considered a “missing part of the research”.

Financial loss: Other participants ranked financial impact highly because they believed that lost income and out-of-pocket expenses contributed a significant barrier to potential donors, and represented an unfair burden given their altruistic act. For younger participants, single parents, and the donor who was not a resident and therefore uninsured, the costs were “a big hit”, and for some, “an absolute destruction”. The time off work for recovery caused some donors to lose their jobs.

Heightened susceptibility

Avoiding catastrophic consequences: Surgical mortality, life-expectancy and morbidity were important, particularly during decision-making, because they considered these to be the “most serious” outcomes which would also impact their family. Some were focused on their kidney function due to a fear of kidney failure and the impact of reduced kidney function on cardiovascular disease. This was concerning for younger donors – “I’m thirty-one, I’ve got a lot of years to come”. However, these hypothetical long-term outcomes were “not necessarily the things that impacted them the most”, and so sometimes ranked relatively lower. Non-directed donors explained that “[their] own health was most important” as they “didn’t know anything about [the] recipient”.

Protecting the remaining kidney: In the short-term period after donation, some participants felt “paranoid” about their kidney function, and were concerned whether their glomerular filtration rate (GFR) was “normal”. ‘Lifestyle restrictions’ were important because they wanted greater understanding on protective and harmful activities, diets and medicines, and travel restrictions related to dangerous infectious diseases, so they could protect their long-term kidney function. Diabetes and hypertension were of concern because they were perceived precursors to kidney failure.

Disconcerting uncertainty: A few participants, from both countries, expressed concern regarding the lack of clear long-term data on ESKD and mortality. They considered further research imperative to gain a “longer statistical window”, to “confirm” the safety of donation. Participants also wanted answers to their unexplained complications, like chronic pain, and therefore felt these outcomes were important for research.

6.5 Discussion

Post-donation outcomes that were most important to kidney donors included long-term health outcomes (kidney function and kidney failure), short-term surgical and functional outcomes (post-operative recovery, surgical complications, pain, and physical function) and psychosocial impacts (impact on family, donor-recipient relationship and life satisfaction). Donors are concerned about their health and some were disappointed by unmet expectations regarding their recovery, physical function, relationships, and psychological wellbeing. While their priorities were largely based on their experience of donation, some donors downplayed short-lived problems in light of the improvements to their family life, relationship and their recipient's health. The hypothetical long-term risks associated with nephrectomy, including mortality and cardiovascular disease was of relatively lower importance. While some donors worried about their heightened susceptibility to morbidity and mortality, most donors believed their clinicians had ruled out long-term risks through screening, and believed they were able to prevent disease through a healthy lifestyle and maintaining their kidney function.

There were some differences observed in the importance of outcomes between donors recruited from the Australia and Canada. Canadian participants ranked kidney function and kidney failure higher than Australian participants, who ranked time to recovery, physical function, impact on family, donor-recipient relationship, and financial impact higher. A few participants in both countries expressed concerns about their heightened susceptibility to kidney failure. This may have been ranked higher among the Canadian sample, because of the inclusion of non-directed donors, and more unrelated donors, who focus more on their own health as they are unaware of the recipient's outcome, or lack a close relationship with the recipient. There may also be an era effect, as most Canadian participants were more recent donors, after literature on ESKD risk had been published. The transplant clinicians in Vancouver may emphasize these outcomes differently to donors. The Canadian cohort also had a higher proportion of tertiary educated people. The percentage of participants who reported complications was higher for Australian participants than Canadian participants (Table 6.2), perhaps explaining the higher ranking of physical function and time to recovery. Financial impact may have been more important to Australian donors because 60%

donated prior to the introduction of the Support for Living Organ Donors Program, in 2013. Canadian participants donated after a reimbursement program was available in British Columbia.

Kidney function was the highest ranked outcome, closely linked to donors underlying fears of developing kidney failure. Monitoring their kidney function gave donors reassurance that they could prevent the onset of kidney failure. However, many participants were uncertain whether their GFR after donation was 'normal' and how to modify their lifestyle and diet to protect their long-term kidney function. On the one hand, many donors' felt that they had ruled out any risks of developing kidney failure during donor assessment, and were focused on the outcomes they experienced rather than hypothetical long-term outcomes. However, some also expressed underlying fears about their susceptibility to kidney failure, particularly younger and more recent donors. A recent study found that concerns for long-term outcomes motivate ongoing health monitoring and participation in follow-up among donors.[31] Mild anxiety about kidney failure has been found to be common among donors within ten years of donation.[32]

Psychosocial and physical functioning was also highly important to donors. Previous studies suggest that only a minority of donors (5-25%) report negative psychosocial and physical outcomes.[24,33-35] However, we found that donors prioritized these outcomes (e.g. relationship problems, emotional distress, diminished body image and libido, pain, fatigue, and financial hardship) because they were often unexpected and unaddressed in follow- up, causing donors to feel unprepared, misled and unsupported.

We recruited donors from two countries with various donation characteristics. A combined quantitative and qualitative methodology provided comprehensive data about donors' priorities, attitudes and beliefs regarding donation outcomes. While surveys with donors are often susceptible to social desirability bias, inhibiting discussion of negative outcomes[24], the focus group enabled open-communication due to the shared experiences among participants. However, there are limitations of our study. Our sample was limited to English-speaking participants who were 81% white and attained a high level of education. Importantly, donors from Australia and Canada have access to universal health coverage. Therefore, the transferability of our findings may be limited in other countries. Due to the semis-structured nature of the nominal group technique, each group did not generate the same list of outcomes. Our quantitative analysis incorporated both the ranking and the consideration of the outcome, but comparisons among participants were not possible. The outcomes that are important to donors are also likely to change over time for example surgical mortality may be more important prior to donation. We included donors, who were 2 months to sixteen years post-donation, but we were unable to assess how donors' priorities might change over time. Furthermore, donors who are thirty or more years post-donation may have different perspectives on lifetime risks.

Our findings suggest there is a need to improve donors understanding of long-term outcomes, but also improve education, follow-up care and standardized information around the outcomes that are important to each individual donor. The recent Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend informing donors of individualized risks, benefits including medical, surgical psychosocial and economic outcomes during the perioperative period and the remaining lifespan of the donor.[6] They suggest communicating absolute risks, and disclosing uncertainty in long-term outcomes.[6] An online risk calculator tool to assess the lifetime ESKD risk has been developed to help transplant centres evaluate, counsel and accept living donors, which may improve donor comprehension of their lifetime risk of ESKD.[36] However, donor's strong motivations and the confidence in their safety pose additional barriers to comprehending risk information prior to donation.[37-39] Continued education about donor outcomes and emerging evidence is therefore critical after donation.

The assessment of donor-reported outcomes can provide information to help prepare donors for a range of outcomes they may experience and care about, and enable follow-up care to be individualized to the donor's needs.[40] The Organ Procurement Transplant Network (OPTN) mandates the collection of data on a range of post-donation outcomes for two years after donation, including two psychosocial outcomes – employment status and loss of insurance. A broader scope of psychosocial and functional outcomes should be assessed in follow-up. For example, a validated longer-term measure of recovery is needed, that captures donors' full recovery.

Living kidney donors were concerned about their kidney health and the surgical, lifestyle and psychosocial impacts of donation that were unexpected, debilitating, or unaddressed in post-donation follow-up care. They also valued improvements to their emotional wellbeing, impact on family and donor-recipient relationship. These findings emphasize the importance of identifying donors' priorities and concerns during the informed consent process, and being cognizant of the donor's confidence in the transplant process such that they may readily accept or disregard long-term health risks. The assessment of donor-important outcomes during follow-up, the collection of more robust data on long-term outcomes, and efforts to keep donors updated on emerging evidence on donor outcomes and protective lifestyle behaviours could improve donor satisfaction and wellbeing after donation, and reduce their anxieties about their vulnerability to kidney disease. Our findings can provide a framework to ensure that the outcomes most relevant to donors are consistently included research, education, assessment, and follow-up care.

6.6 Acknowledgments

We are grateful to all the living kidney donors who generously gave their time to share their insights and perspectives.

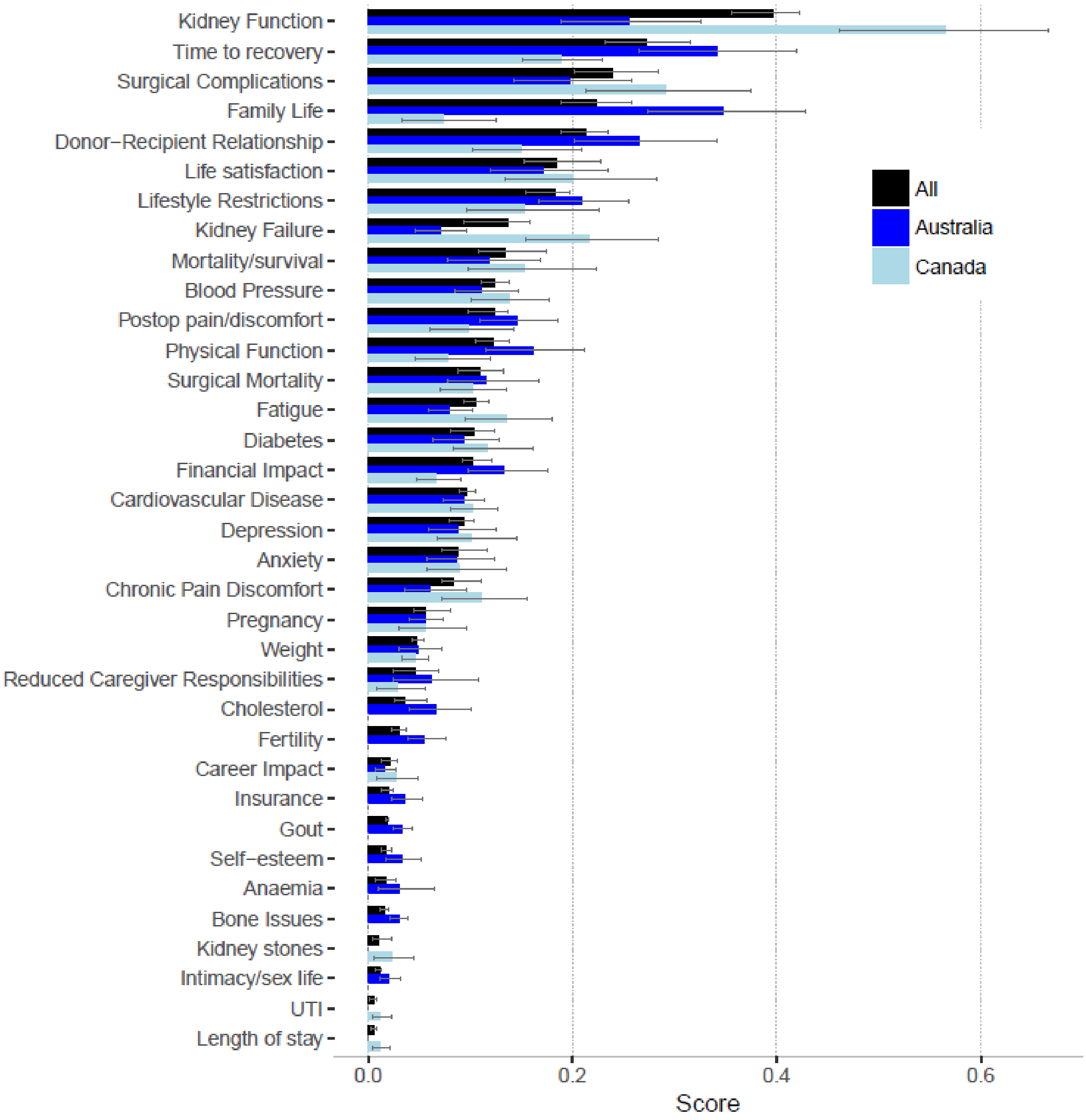

Figure 6.1. Importance scores for donor outcomes by country (confidence intervals)

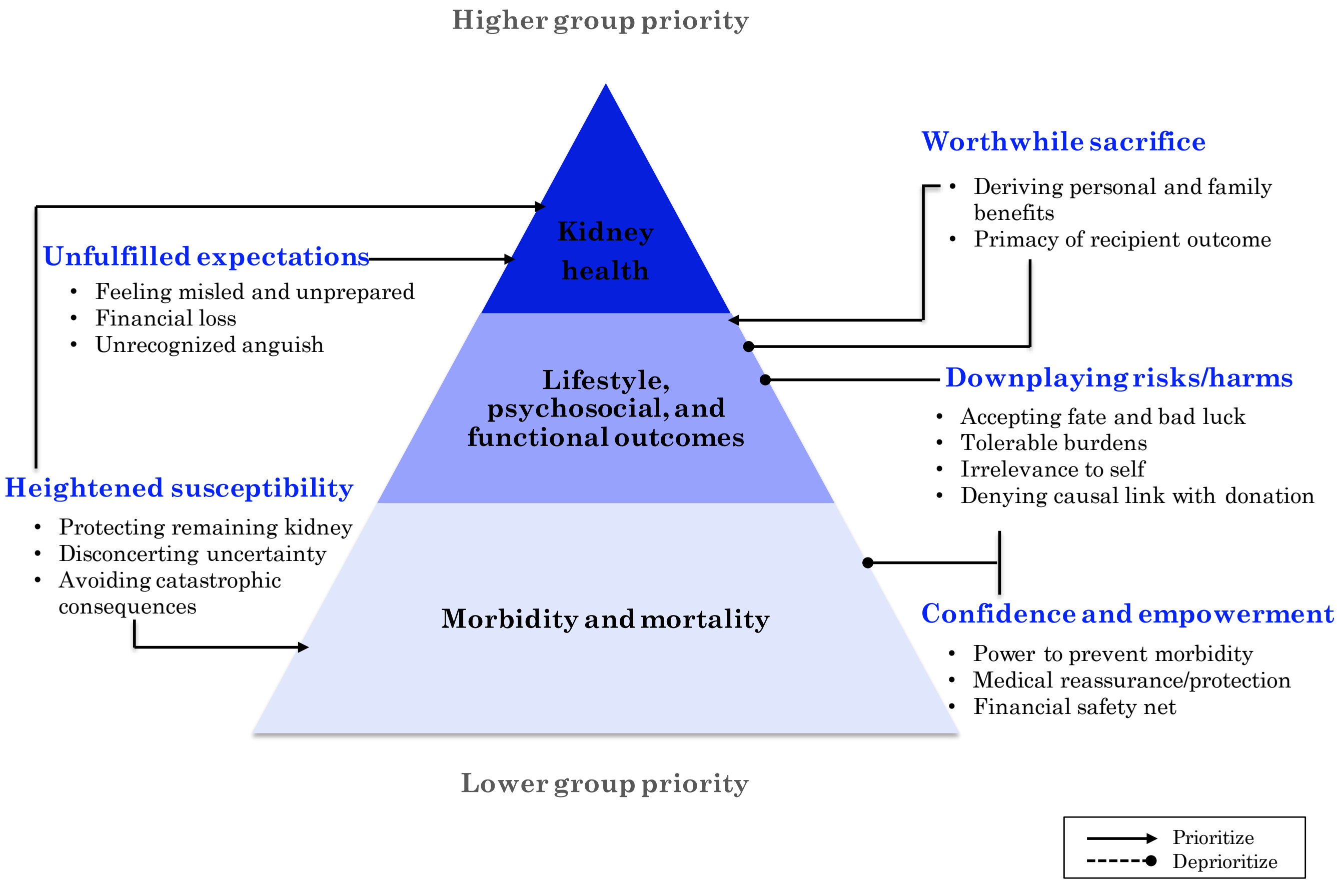

Figure 6.2. Thematic schema depicting themes underpinning ranking of outcomes

Table 6.1. Demographic characteristics of the participants (N=123)

Characteristics	Australia, n = 67 (%)	Canada, n = 56 (%)	All, n = 123 (%)
Gender			
Female	41 (61)	37 (66)	78 (63)
Male	26 (39)	19 (34)	45 (37)
Age (years) ^			
20-29	1 (1)	0 (0)	1 (1)
30-39	6 (9)	5 (9)	11 (9)
40-49	15 (22)	12 (21)	27 (22)
50-59	22 (33)	14 (25)	36 (29)
60-69	15 (22)	19 (34)	34 (28)
70-79	8 (12)	5 (9)	13 (11)
Ethnicity^			
Caucasian	56 (84)	44 (79)	100 (81)
Asian	5 (7)	7 (13)	12 (10)
Middle Eastern	5 (7)	0 (0)	5 (4)
Other*	1 (1)	5 (9)	6 (5)
Highest level of education ^			
University degree	25 (37)	34 (61)	59 (48)
Diploma/certificate	15 (22)	10 (18)	25 (20)
Secondary school: year 12	9 (13)	15 (27)	24 (17)
Secondary school: year 10	17 (25)	0 (0)	17 (14)
Total household income per year (USD)^ †			
$0 - $32, 135	15 (22)	1 (2)	16 (13)
$32,136 - $66, 949	16 (24)	13 (23)	29 (24)
$66, 950 - $107,120	15 (22)	15 (27)	30 (24)
> $107,120	16 (24)	26 (46)	42 (34)
Employment status^			
Full time	35 (52)	33 (59)	68 (55)
Part time/Casual	15 (22)	7 (13)	22 (18)
Retired/Pensioner	12 (18)	12 (21)	24 (20)
Not employed	4 (6)	3 (5)	7 (6)
Marital status^			
Married/De-facto relationship	57 (85)	39 (70)	96 (78)
Divorced	0 (0)	7 (13)	7 (6)
Widowed	5 (7)	1 (2)	6 (5)
Separated	1 (1)	5 (9)	6 (5)
Single	2 (3)	3 (5)	5 (4)
Partner (not living with)	2 (3)	0 (0)	2 (2)

^Total N ≠ 123 due to non-response. *Includes South American, African, Pacific Islander and First Nation (Canada) †As defined by Australian Bureau of Statistics 2011 Census Survey, converted to United States Dollars (USD) using average 2011 exchange rate

Table 6.2. Donation and health characteristics of the participants (N=123)

Characteristics	Australia (n = 67)	Canada (n = 56)	All n (%)
Time since donation^			
<1 year	3 (4)	10 (18)	13 (11)
1-3 years	26 (39)	33 (59)	59 (48)
4-6 years	16 (24)	19 (34)	35 (28.7)
7– 10 years	7 (10)	2 (4)	9 (7.4)
>10 years	6 (9)	0 (0)	6 (4.9)
Relationship to recipient			
Spouse	28 (42)	11 (20)	39 (32)
Parent	17 (25)	16 (29)	33 (27)
Sibling	15 (22)	8 (14)	23 (19)
Friend/Colleague	2 (3)	7 (13)	9 (7)
Child	2 (3)	4 (7)	6 (5)
Other relative	3(4)	4 (7)	7 (6)
Non-directed (anonymous)	0 (0)	6 (11)	6 (5)
Kidney paired donation			
Yes	9 (13)	10 (18)	19 (15)
No	58 (87)	46 (82)	104 (85)
Recipient outcome*			
Alive and functioning graft	52 (78)	61 (109)	113 (92)
Graft failure or death	6 (9)	4 (7)	10 (8)
Self-reported post-donation complications			
Any	19 (28)	12 (21)	31 (25)
Mental health	5 (7)	3 (5)	8 (7)
Hypertension	5 (7)	2 (4)	7 (6)
Chronic pain	1 (1)	2 (4)	3 (2)
Hydrocele	2 (3)	0 (0)	2 (2)
Other†	7 (10)	4 (7)	11 (9)

^Total N ≠ 123 due to non-response.

*The timing of the recipient outcome was not captured

†Includes hyperthyroidism, low blood pressure, kidney stones, gall stones, hernia, blood clots, endometriosis, gout, high cholesterol, scleritis and osteoporosis. Note that acute pain and fatigue were not reported as complications, despite being indicated in qualitative data.

Table 6.3. Illustrative quotations

Theme	Illustrative quotations
Worthwhile sacrifice	
Primacy of recipient outcome	"One of the key ones for me is the success of the donation for the [recipient]. Had it been negative or there had been problems it would have been very emotional." (Female, Canada, 40s) "They're all important it's just hard to pick one as long as whoever is getting the kidney is okay…but as we all said we'll do it again no matter what the outcome was." (Female, Australia , 50s) "Even now I still don't get any feeling in my arm when I wake up. It is disturbing. I don't make a big deal of it because I donated my kidney to my sister and I don't want her to think that my lifestyle has changed. I just want for future reference." (Female, Canada, 40s) "When that fails, you're no longer in control of that person's health, and therefore you would feel a sense of blame, maybe? And helplessness, yeah." (Female, Australia, 50s)
Deriving personal and familial benefits	"My top one was family life, as long as all that's fine everything else will be fine." (Female, Australia, 70s) "Ever since then we have been travelling all over the world. So freedom! The freedom is amazing so that is really important to us." (Female, Canada, 50s)
Downplaying risks and harms	
Tolerable burdens and sacrifices	"I mean, I am now never going to be a professional kick-boxer. There are some things that you're taking out of your life as options." (Female, Canada, 30s) "But I'd like the media, or the general public to know that it's not hard… just the recovery period." (Male, Canada, 60s) "Yeah, just a little bit of the recovery but, you forget about that after a while." (Male, Canada, 70s)
Irrelevance to self	"You can feel the points; they were six months, twelve months, and then the two years. And after that it's like it never happened." (Male, Australia, 60s) "I wasn't really worried about any of the outcomes. I knew I was a healthy individual. I didn't really have any concerns." (Female, Canada, 40s) "I haven't lived with [chronic pain]. So it's hard for me to say because you don't know what that is until you experience it. So beforehand, I don't think it would've made a difference to me". (Female, Australia, 60s)
Denying causation	"But quite a lot of those things, I've got, but it's nothing to do with my kidney I would think. I think it's because of my age. Post-menopausal." (Female, Australia, 70s) "But I mean like you could develop it later in life, like type 2 diabetes, if you have like a poor diet or whatever. If you're going to make poor choices in your life, are you going to have a worse outcome if you have one kidney or two kidneys, right?" (Male, Canada, 50s)
Accepting fate and bad luck	"I got a massive hernia, so I had to go back in for another five days and have that repaired and [I've got another one]...But they just said I was just one of the unluckiest ones they'd had, so but it wouldn't have changed my decision to do it. It's just that it was damn unlucky. Very unexpected. They got fright too." (Female, Australia, 60s) "If it is your time it is your time and you cannot stop it right? You can die crossing the street…When it is your time, it is your time, never thought about it…"

	(Male, Canada, 40s) "Because I read that [risk of kidney failure] in the literature before I had the operation, you know, but at the end of day, you just can't afford to think about that." (Male, Australia, 70s)
Confidence and empowerment	
Power to prevent morbidity	"Weighted risk compared to other things like smoking and high blood pressure seems to like, far outweigh the kidney thing, so I wouldn't be concerned about it." (Male, Canada, 60s) "I am actually healthier now just because I have had this on my mind. So I eat healthier, exercise more and so I feel like health wise it has been beneficial." (Female, Canada, 50s) "I was of the impression that if you kept your blood pressure down, you didn't have diabetes and you didn't have high cholesterol and you have average weight that there'd be no problems with kidney function." (Female, Australia, 50s)
Medical reassurance and protection	"For the rest, they already screened us, so I think if I was going to be worried about all of these, I'm not because they screened me for it. Like I have enough faith in the pre-work that I'm not going to sweat it now. So it's done, I'm not going to worry about it or second guess medicine." (Male, Canada, 50s) "The longer the years go on, the longer statistical window they have, but the statistics they brought up to me were all very positive. So it was, again, another non-issue." (Male, Canada, 60s) "Well I remember the surgeon told me there's no proof at all that says somebody with two kidneys lives any longer than someone with one." (Male, Canada, 50s)
Financial safety net	"Through the organ donation program, they reimbursed all that which was really good. I didn't lose any of my long service leave... some people can't have that eight weeks off or they might depend on that one income coming in. Even though it's important to donate, there are other things as well…" (Female, Australia, 50s) "I guess I had the luxury of all I had to worry about was getting better, work was paid, I had sick leave and if I was allowed that time off work without issues." (Male, Australia, 50s)
Unfulfilled expectations	
Misled and unprepared	"I don't regret my decision at all. But I did not have an easy recovery…but I wish I had known it wasn't as super easy as some people will lead you to believe. And that is why the donor blogs were super helpful because there are some people on there who have had truly awful experiences. And I knew that wasn't going to be my experience. There were some people on there who had truly amazing experiences and mine ended up somewhere in the middle." (Female, Canada, 40s) "What would been interesting if there was some sort of follow up as to how long you're in hospital for, what was your recovery like? At what report did you return to full health? All that seems like valuable information. I didn't really fee that captured at all. If it was recorded in a way that it could be used to better inform people or perhaps maybe target different things for different people. And maybe complications… Information that no one bothers to record." (Male, Australia, 40s) "It was really awful and I've never had that in my life, and they didn't warn me about all the digestive stuff. From the nausea to the constipation." (Female,

	Canada, 60s) “Well lifestyle restrictions. I’ve been healthy all my life, I didn’t have to worry about what I ate or drank or whatever. Now I’m worrying about what medications I can take.” (Female, Canada, 50s) “I must admit I feel bad sometimes but you would do it again if you had to, I’m so glad I can’t really. I found it pretty horrible to be honest. I had partial lung collapse and the only way to fix that was to cough.” (Male, Australia, 40s) “The main thing for me was my sex drive went completely out the window…It was more just the fact that every time I looked down, my guts were smiling back up at me and, it was again, a vanity thing, psychological like, ‘Oh, my God! Look at that. It’s horrific.’” (Male, Australia, 30s)
Unrecognized anguish	“What I’m saying it as a point of study. Not that I have regret. But it would definitely be interesting to see if people have regret after.” (Female, Canada, 50s) “It actually surprised me how long it took me to recover. It wasn’t just the physical part of it. It was the emotional and the mental part of it.” (Female, Canada, 50s) “I focused on the other ones for the entire opposite reason. It’s easier to manage your scientific stuff. It’s really difficult to quantify emotional and relationship things, and I think that’s a missing part of the research.” (Female, Canada, 30s) “It was like, you know how you get the baby blues? On the fourth day, I just lost it…I don’t know whether it’s because I lost this thing and I just fell to pieces.” (Female, Australia, 50s) “I think for me after I donated a kidney, I got depression for a few months. It took me probably a year to feel better, and I started gaining a lot of weight and I didn’t have any energy. I wasn’t feeling happy. I mean I was feeling happy for my daughter but no, inside me I wasn’t happy.” (Female, Canada, 30s) “I was surprised to hear that you suffered depression. I wasn’t told that that could be an impact and I think that’s really crucial. People really need to know that that’s a possibility. I don’t remember them saying anything about it… But if it does happen it can be quite, I would imagine, very discombobulating.” (Female, Canada, 50s) “It seemed to me that stuff like kidney function, cardiovascular disease, end stage kidney disease, diabetes, all those things with a disease on them will probably be studied or come up in other studies. It seemed to me that I was choosing stuff that probably wouldn’t necessarily be studied.” (Male, Canada, 60s) “If my husband's kidney failed, I'm not sure how I'd react to that. Right now he's doing extremely well. But if something should happen to him, would I be exposed to this depression and anxiety? That would worry me.” (Female, Canada, 50s) “I had a lot of bloating. I had a lot of pain and that went on years. I think they now know that [the surgeon] cut a nerve. But all this has really gotten me down a lot.” (Female, Australia, 50s) “I don’t regret it. But I’m not fine. I’m not 100%. It’s a frustrating position to be in because I don’t fit what the ranges are….I definitely felt there was an expectation that I wouldn’t have any needs past 6 weeks. It was a magical number.” (Female, Canada, 40s) “Number two would be chronic pain/numbness because I’m still suffering from the after effects of that complication, every day. It’s not serious right now but I’m afraid it might get worse. I don’t know what to expect.” (Female, Canada, 50s) “I mean I don’t feel good about it, having a medical condition. You know I’m happy to help somebody but I was a healthy person, and now I’m stuck with this…Probably not. I wouldn’t have done it…if I’m harming my health and I have to live the rest of my life like this… It’s really quite intense”. (Male, Canada, 50s)

	“For me, what I’d like to know. They are very good at the beginning at telling you this should happen. This should happen. Afterwards, my feeling on it, was they didn’t really follow up with you and say did that happen? Did that happen in your case? They said the percentages of whatever, but am I one of those percentages?” (Female, Canada, 30s)
Financial loss	“For me it was absolute destruction. Bankruptcy. I was off for a year…But you know, it is embarrassing to tell the family that ...” (Male, Canada, 60s) “That had a bit of an impact, we didn’t get any money back for the medication because I had to get medication and whatnot, I had to pay for all that.” (Male, Australia, 30s) “I was actually fired for the amount of time that I was about to take off…apart from the actual firing itself, I found it very hard after the recovery of about two months to get another job. People just didn’t want to look at me. It was the weirdest thing ever.” (Male, Australia, 30s)
Heightened susceptibility	
Protecting the remaining kidney	“‘Because there seems to be, just in my mind anyway, some sort of connection between kidneys and particularly diabetes and blood pressure. And I'm not sure which is the chicken and which is the egg?” (Male, Australia, 70s) “It’s not so much function. It’s, can you preserve or enhance your kidney health as a result of diet… I just got told to keep doing what I was doing, whatever that is…” (Male, Canada, 40s)
Avoiding catastrophic consequences	“Your mortality is not just about yourself, it's about your family or the family that you're going to have.” (Male, Australia, 40s) “So, they’re, I suppose, the most serious things… They’re not necessarily the things that impacted me the most but they would be the things that if I was looking to donate a kidney, I would want to know that those things are going to be okay.” (Female, Australia, 40s) “I mean it was top ten because I have kids…I worry about diabetes because I don’t want both of us going for dialysis. That’s the only reason why I worry, it’s not my self-preservation but more for family worry.” (Female, Canada, 30s)
Disconcerting uncertainty	“We’re all adding to the data pool with our annual lab requisitions, but we don’t hear back as a group on the overall experience. You’ve got a mass of data there, it’s easy enough to manipulate, and an incoming donor should have access to that information. Like on average, your GFR will go down to whatever, and you can rank that based on the demographic… you’ve got a pool of information that should be mined.” (Male, Canada, 60s) “Now that I think on it, one of my biggest concerns afterwards was what would be the long-term repercussions because back at the time we did our transplant, there was no ruling data on long term impacts…” (Male, Australia, 50s) “Is there any study, is there any data the impact of donation on the life expectancy of donors? Is there any statistic? Do we know anything about that? Is that one of the things that could be kind of explored so there’s information? It helps towards making an informed decision if people are assessing all sorts of things.” (Female, Canada, 70s)

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Chapter 7: Living kidney donor outcomes reported in randomised trials and observational studies

Hanson CS, Sautenet B, Craig JC, Chapman JR, Knoll G, Reese, PP, Tong A. Informative for decision-making? The spectrum and consistency of outcomes following living kidney donation reported in trials and observational studies. (Submitted to the Journal of the American Association)

This chapter is structured as per the journal article.

7.1 Abstract

Background: Evidence about outcomes following living kidney donation is needed both to inform donor acceptance criteria, and to guide the decisions of potential donors and their healthcare providers about donation. However, the scope and consistency of outcomes reported in research and their relevance to decision-making is uncertain.

Aim: To determine the spectrum and consistency of outcomes reported in randomised trials and observational studies in living kidney donors aged 18 years or over.

Methods: Electronic databases were searched for randomised trials and observational studies reporting outcomes in adult living kidney donors published from January 2011 to May 2017. All outcome domains and measurements were extracted, and their frequency and characteristics were evaluated and reported.

Results: Of the 268 eligible studies, 14 (5%) were randomised and 254 (95%) observational. Overall, 136 studies (51%) were short-term (≤1 year follow up) and reported 109 outcome domains, of which 51 (47%) were classified as clinical, 35 (32%) were surrogate and 23 (21%) were donor-reported. The five most commonly reported domains were kidney function (154, 58%), time to discharge (96, 36%), blood loss (85, 32%), operative time (79, 30%) and blood pressure (74, 28%). Quality of life (13%), mortality (16%), end-stage kidney disease (ESKD) (10%) and cardiovascular events (9%) were reported infrequently. Kidney function and pain had 116 and 75 different outcome measures, respectively.

Conclusions: The outcomes of living kidney donation reported in contemporary trials and observational studies are numerous, heterogeneous, and often focussed on short-term surgical complications. Kidney function was the most frequently reported outcome, but multiple measures were used making comparisons across studies problematic.

Mortality, ESKD, cardiovascular disease, and donor-reported outcomes including recovery, physical function and psychological impact were uncommonly reported. Consistent reporting of outcomes relevant to decision making is needed to better inform and prepare donors for outcomes after donation.

7.2 Introduction

Living kidney donor transplantation is the preferred option for most kidney transplant candidates due to superior graft and survival outcomes, and reduced waiting times.[1-3] Living donors now provide more than 40% of kidney transplants performed globally.[4] As donors voluntarily undergo a medical procedure that primarily benefits another person, ensuring the safety, wellbeing and informed decision-making of donors is of primary concern. Surgical complications, mortality and major morbidity have been considered rare following kidney donation.[5] However, recent evidence of small but important increases in the risks of end-stage kidney disease (ESKD), hypertension, and all-cause mortality in donors, compared to the general population, have reinforced the need for ongoing, robust research of long-term donor outcomes.[6-11]

Progressive publications that comprise long-term data may change assessment policies, and will likely also change the information provided to donors about post-donation outcomes.[12] Donors experience and value a broad range of outcomes that span their health, physical function, psychosocial wellbeing and livelihood (8-10), but outcomes measured and reported in studies of living donor outcomes have had minimal or no input from donors.[13] Additionally, inconsistencies in outcome measurement diminish the ability to combine and compare data on donor outcomes across studies, and thus limit the reliability and certainty of available evidence.[14-21]

We aimed to determine the spectrum and consistency of outcomes for living kidney donors reported in recent randomised trials and observational studies. The ultimate goal of the work is to improve the relevance and heterogeneity of outcome reporting, and so to better understand the outcomes experienced by living kidney donors.

7.3 Methods

Selection Criteria

We searched MEDLINE, Embase, CINAHL and PsychINFO for all randomised trials of any intervention (e.g. surgical techniques, analgesia, pain control, infection control, psychosocial interventions) and observational studies (cohort, cross-sectional, case series) reporting biomedical and psychosocial outcomes in living kidney donors aged 18 years or over. We included articles published from January 2011 to May 2017 to ensure contemporary relevance (Appendix Table E.1). We excluded studies with fewer than 10 kidney donors, or if outcomes of donation were not the primary focus (for example, studies that used donors as ‘healthy controls’ and diagnostic validation studies).

Data extraction

We extracted the following characteristics from each study: first author, year of publication, study design, participating countries, sample size, follow up period, mean age of participants, year of donation, and all outcomes/outcome measures. For randomised controlled trials and observational studies evaluating the effects of an intervention, we also identified the type of intervention. An outcome measure was defined as any measurement or event reported in the results of the study. For each outcome measure, we extracted the type of measure (e.g. pain on a visual analogue scale), method of aggregation (e.g. mean), specific metric (e.g. change) and time frame (from the time of the intervention or donation).[13]

Analysis

The first author (CSH) categorised all similar outcome measures into outcome domains. This was cross-checked by three reviewers and revised until a consensus was reached (BS, AT, JCC). All outcome domains were categorised as clinical (medical event or comorbidity diagnosed by a clinician)[22], surrogate (biochemical, imaging, or other markers used as a substitute for a clinical outcome)[23] or donor-reported (outcomes reported by donors that reflect how they feel or function e.g. pain, anxiety)[22,24]. Some domains included measures that could fit into multiple categories, and were categorised as clinical, surrogate or donor-reported based on the largest proportion of outcomes measures. For example, physical function can be measured via self-report or clinical assessment (e.g. gait analysis), but was most frequently measured by self-report and thus classified as a donor-reported outcome in this study. We calculated the number of studies that reported each outcome domain. This analysis was cross-checked by three reviewers (BS, AT, JCC). Any differences in opinion were resolved through discussion. The dataset was stratified by type of research question into treatment and prognosis studies, according to Cunningham's classification of research questions.[25] Therapy studies include questions of the outcomes of a treatment or exposure (e.g. drugs, surgical intervention, psychological intervention).[25] A prognosis question assesses the progression of a disease or the likelihood of a disease occurring.[25] We did not stratify by study design because there were a very small number of randomised controlled trials. Because of the very large number of outcomes, we conducted a detailed analysis of outcome measures (type of measure, definition, method aggregation, metric and time point) for the three most frequently reported surrogate and donor-reported outcome domains.[13] Of the clinical outcomes mortality, ESKD and cardiovascular disease were chosen for detailed analysis. Statistical analyses (including frequencies) were conducted using R version 3.2.3 (R Foundation for Statistical Computing, Vienna, Australia, URL http://www.R-project.org/).

7.4 Results

Study characteristics

We included 268 studies that involved 556,102 (not unique) living kidney donors from 35 countries (Figure E1). The study characteristics are outlined in Table 7.1. Overall, most studies were conducted in Asia (33%), North America (31%) and Europe (29%). Most studies were prognosis studies (n=177, 66%) and 91 (34%) were classified as therapy studies. Of these 91 therapy studies, 14 were randomised controlled trials and the rest were cohort studies or case series. Interventions included surgical techniques (78, 86%), intra-operative analgesia (7, 8%), post-operative pain control (3, 3%), infection control (1, 1%), psychosocial support (1, 1%) and a haemostatic agent (1, 1%). Of the 177 prognosis studies, 56 (32%) were prospective studies. Four (4%) therapy studies included more than 1000 donors (median 83, interquartile range 43.5-189), compared with 37 (21%) prognosis studies (median 143, interquartile range 57-588). Of the therapy studies, 107 (60%) of studies followed donors up for a maximum of 12 months. One hundred and thirty-seven (77%) prognosis studies had follow up exceeding 12 months, and 37 (21%) exceeding 10 years follow up (maximum 32 years).

Outcome measures and domains

Across all studies, there were 4513 outcome measures reported which were categorised into 109 outcome domains. Overall, 51 outcome domains (47%) were clinical, 35 (32%) were surrogate and 23 (21%) were donor-reported outcome domains (Appendix E.12-E.14). The five most commonly reported domains included kidney function (154, 58%), time to discharge (96, 36%), blood loss (85 ,32%), operative time (79, 30%) and blood pressure (74, 28%) (Table 7.2). Quality of life (13%), mortality (16%), ESKD (10%) and cardiovascular event (9%) were reported infrequently.

The number of outcome measures per study (including time points of measurement) ranged from 1 to 151, with a median of 12 (IQR 7-19). The number of unique outcome measures per study (excluding time points) ranged from 1 to 78 with a median of 9 (IQR 6-16). The number of studies that reported a minimum of one clinical outcome domain was 184 (72%), and 172 (64%) and 109 (41%) reported at least one surrogate and donor-reported domain, respectively.

Frequency of outcome domains reported in therapy studies

Across the 91 therapy studies, 1385 outcome measures were reported and categorised into 70 outcome domains. Figure 7.1 depicts the proportion of therapy studies that reported each of the outcome domains, of which 38 (54%) domains were clinical, 17 (24%) were surrogate, and 15 (21%) were donor-reported (Appendix E.15). The five most frequently reported outcome domains were: time to discharge (72, 79% studies), blood loss (66, 73%), operative time (62, 68%), unspecified donor complications (45, 50%) and kidney function (45, 50%) (Table 7.2; Appendix E.15). Recovery and mortality were infrequent, reported in 10 (11%) and 9 (10%) of studies, respectively.

Frequency of outcome domains reported in prognosis studies

Across the 177 prognosis studies, 3128 outcome measures were reported and categorised into 100 outcome domains. Figure 7.2 depicts the proportion of the prognosis studies that reported each of the outcome domains, of which 46 (46%) were clinical, 32 (32%) were surrogate, and 22 (22%) were donor-reported (Appendix Table E.16). The most frequently reported outcome domains were: kidney function (109, 62% studies), blood pressure (69, 39%), proteinuria/albuminuria (61, 35%), BMI/weight/composition (36, 20%), mortality (33, 19%), pain (33, 19%), mental health (31, 18%), physical function (31, 18%) and psychological impact (31, 18%) (Table 7.2; Appendix Table E.16). Quality of life (28, 16%), ESKD (24, 14%), and cardiovascular events (18, 10%) were reported infrequently.

Outcome measures and time points

The number of unique outcome measures and time points of measurement reported for ten outcome domains (three surrogate domains, four clinical domains, and three donor-reported domains) are shown in Figure 7.3. These examples were selected based on frequency and to include a range of surrogate, clinical, and donor-reported outcomes.

The clinical outcome ESKD had 18 different outcome measures (34 including time points), mortality had 23 (27 including time points), and cardiovascular event had 21 (25 including time points) (Appendix E.2-E.4). The three most frequently reported surrogate outcomes were kidney function with 116 different outcome measures (264 including different time points); blood pressure with 88 (172 including time points); and proteinuria/albuminuria with 29 (93 including time points) (Figure 7.3 and Appendix E.5-E.7). For the most frequent donor-reported outcomes, pain had 75 outcome measures (181 including different time points); physical function had 33 outcome measures (67 including different time points) and psychological impact had 44 (58 including time points) (Appendix E.8-E.10).

7.5 Discussion

Recent studies in living kidney donors report an extensive range of outcomes, which are mostly short-term clinical or surrogate endpoints, with large heterogeneity in the measures used to assess the same outcomes. Interventions were predominantly of surgical procedures related to nephrectomy, and most frequently reported perioperative outcomes with time to discharge, blood loss and operative time each reported in more than half of the studies. For prognosis studies, there were more outcome domains, of which most were clinical outcomes.

However, the most frequently reported domains were surrogate outcomes, including kidney function, blood pressure, proteinuria/albuminuria and body mass/weight. Across all studies, relevant clinical and donor-reported outcomes such as mortality, quality of life and physical function were reported in less than twenty percent of studies.

Feasibility and resource limitations could partly explain the relatively high frequency of short-term clinical and surrogate outcomes in therapy studies. Time to discharge, blood loss and operative time were the three most frequently reported outcomes in therapy studies, and are quality indicators that are easily obtained from administrative data. However, these outcomes provide limited information to inform donors' expectations of surgical recovery – which, donors have defined as the return to "normal" health in terms of their physical and emotional functioning, and resumption of their regular roles and activities.[26] Surveys and qualitative studies suggest that some donors experience an unexpectedly prolonged recovery, and report fatigue and pain, up to twelve months after donation .[20,27] "Unspecified" complications are commonly reported, but these are not informative to potential donors or clinicians, without elaboration.

In prognosis studies, there is a dominance of surrogate outcomes (e.g. kidney function, blood pressure and proteinuria/albuminuria) which is probably also driven by concerns regarding burden of data collection. Surrogate outcomes are routinely collected in follow-up, and changes can be detected in short-term assessment.[28] Mortality, ESKD and cardiovascular events were not measured beyond twenty-five years after donation, therefore lifetime risks, particularly for younger donors, are uncertain. Most transplant centres have been unable to systematically follow up kidney donors.[29,30] Some studies suggest donors are emotionally invested in donating to the recipient, and thus not focused on long-term outcomes of donation during decision-making.[31] However, a mild fear of kidney failure was found to be common among donors, and concerns for long-term outcomes motivates ongoing health monitoring and participation in follow-up.[26,32]

While a wide-range of outcomes was reported across studies, donor-reported outcomes were reported less frequently in both therapy and prognosis studies. Donor-reported measures can help donors understand and prepare for their recovery, return to work, the financial impact after donation and possible changes to their physical and psychological functioning after donation.[33] It is increasingly argued that clinical trials should include patient-centred outcomes and standard measures for global, physical, mental and social health are being developed.[34] However, generic psychosocial assessments may not capture donation-specific experiences, particularly interpersonal and emotional benefits, for which validated, donation-specific measures may be warranted.[15,35] Recent guidelines recommend discussing anticipated psychosocial outcomes with potential donors including both benefits and risks. Most studies have found a minority of donors (5-25%) experience negative psychosocial outcomes but it has been difficult to pool data across studies due to heterogeneity in outcome measurement.[15,36-38] We found that psychological impact was reported in 15% of studies, measured in 44 different ways, most frequently by the SF-36 instrument. Other psychosocial outcomes including mental health, satisfaction with the donation, depression, anxiety, donor-recipient relationship, and life satisfaction were also reported infrequently.

A reliance on surrogate outcomes, such as proteinuria, can be problematic, as they may not be valid predictors of clinically meaningful outcomes.[28] Equations for estimating glomerular filtration rate (GFR) underestimate kidney function in living kidney donors, and are less precise than measured GFR.[22,39,40] Current guidelines recommend assessing serum creatinine measurements and GFR estimation.[12] We found that kidney function was most frequently measured by estimated GFR and serum creatinine. Blood pressure was the second most frequently reported surrogate outcome in prognosis studies. Recent qualitative studies suggest that kidney function and blood pressure, despite being surrogate endpoints, may be important to donors, as they allow donors to monitor their health after donation.[26] However, donors were uncertain what their absolute level of estimated GFR meant. Their change in kidney function over time may also provide meaningful information to donors. The importance of other frequently measured surrogates to donors, including proteinuria, albuminuria and body mass or composition is uncertain.

We have also demonstrated heterogeneity in outcome domains and measures across studies on living donor outcomes, with 4513 outcome measures and time points reported across 109 different outcome domains. Surrogate and donor-reported outcome measures have greater heterogeneity than clinical measures, because the data routinely collected vary across units, and many investigator-developed surveys are used for donor-reported outcomes which often lack clear definitions of their outcomes.[15] Clinical outcomes such as mortality, cardiovascular disease and ESKD were reported in using 23, 21, 18 different outcome measures, respectively, as they were sometimes reported as composite outcomes or identified based on treatment codes. This heterogeneity hampers efforts to compare the effectiveness of trials or synthesise data across studies, and clinicians' ability to provide evidence-based recommendations in response to donor's concerns, with certainty. Our findings support the need to identify standardised outcomes measures.[41,42] To facilitate routine collection by transplant centres, researchers, and registries, outcomes must also be feasible to measure in large prospective studies and registries, which may be particularly challenging for self-reported outcomes.[43] Identifying the outcomes of critical importance of donors could help identify suitable measures.

We have provided a detailed examination of the scope and consistency of outcome domains and measures reported in recent research on living kidney donor outcomes. This analysis has identified problems specific to research on living donor outcomes. We did not appraise the risk of bias or quality of the included studies, as our analysis was concerned with outcome reporting in studies that may inform donor practice and policy. Non-English articles were excluded from our search, and most articles that were included examined donors from high-income countries. Brazil, India, Mexico and Iran do high numbers of living kidney donor transplants each year, but publish very little data on donor outcomes[1]. Seventeen (6%) of the studies in our review were from Brazil, India, Mexico or Iran. Our search was limited to the past five years, as it was not feasible to include all existing studies. This enabled us to comment on recent research conduct, and minimise heterogeneity due to changing definitions/thresholds for outcomes over time (e.g. hypertension).[18]

Among recent studies on outcomes for living donors, surrogates and short-term clinical outcomes are more frequently reported, while donor-reported and long-term clinical outcomes are relatively uncommon. While flexibility and creativity in outcome measurement is important for progress and innovation, the varied and inconsistent definition and measurement of similar outcomes across studies can stifle efforts to synthesise evidence, and generate higher quality evidence on living donor outcomes. As strategies to collect long-term data on donor outcomes are improved, involving donor registries, researchers should seek to include the addition of outcomes in their study that are meaningful and relevant to all stakeholders, including donors. Improved outcome reporting and measurement could ultimately lead to better informed consent practices and evidence-based decision-making in living kidney donation

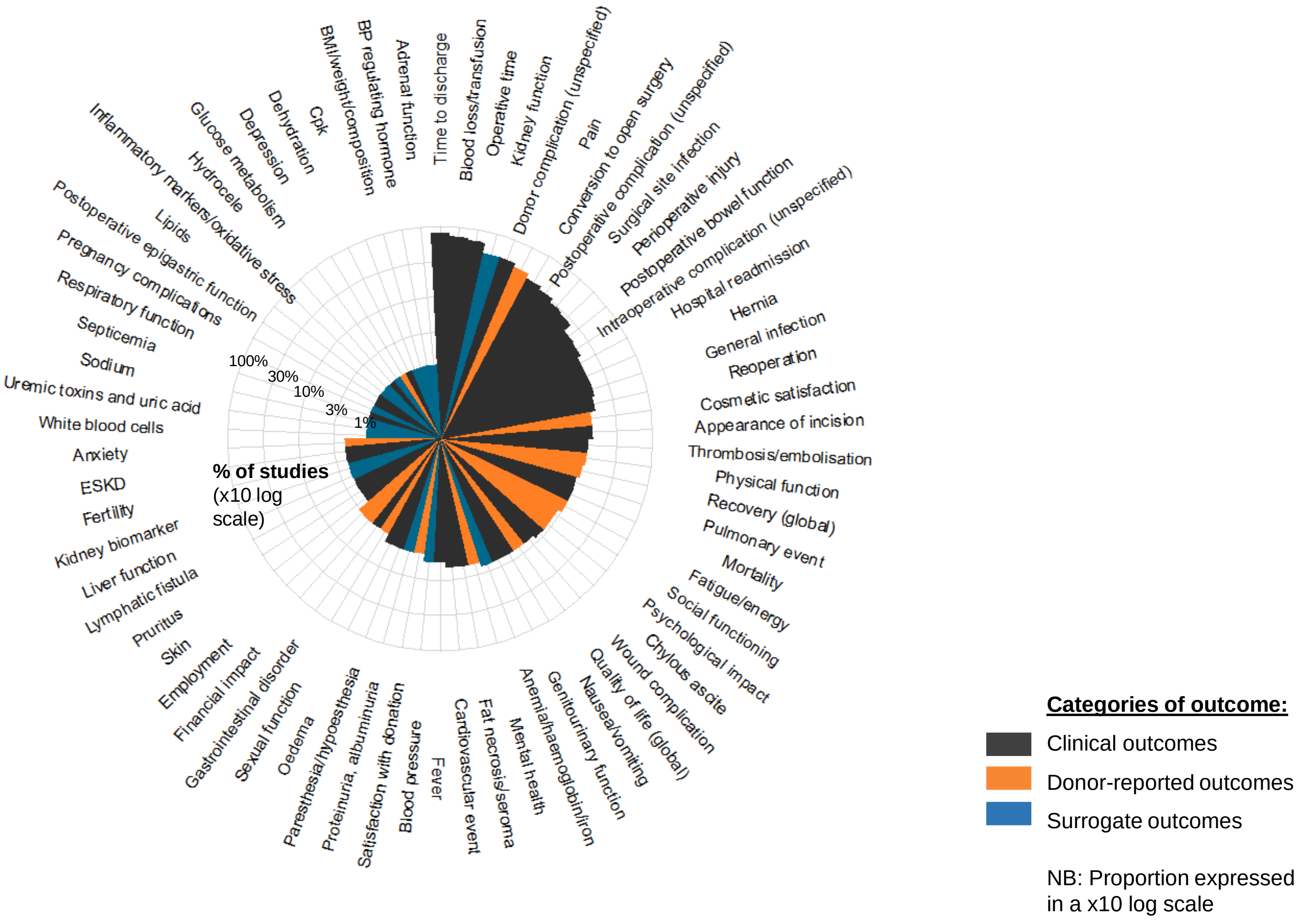

Figure 7.1. Proportion of therapy studies reporting each outcome domain (total 91 studies, 70 outcome domains)

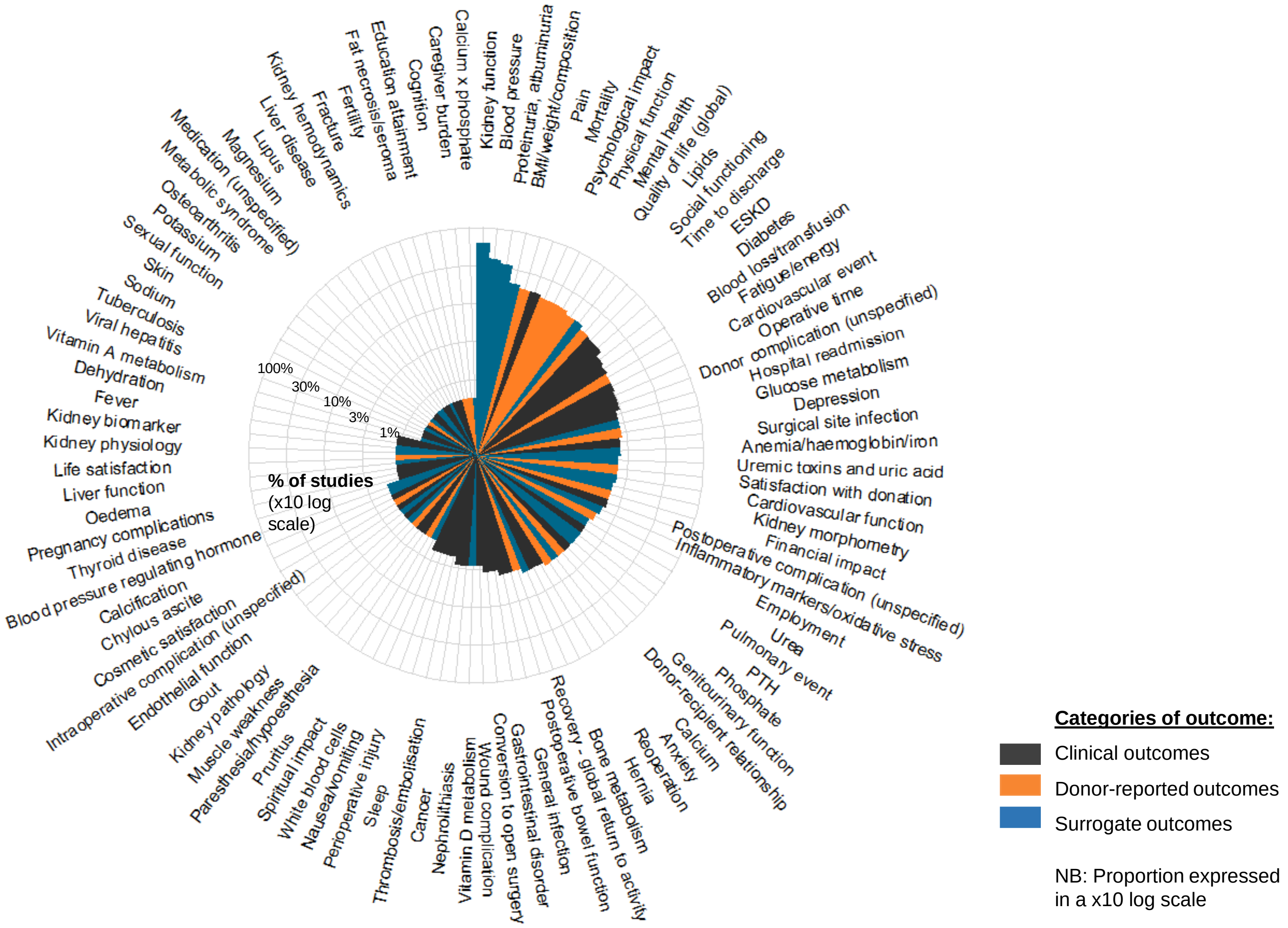

Figure 7.2. Proportion of prognosis studies reporting each outcome domain (total 177 studies, 100 outcome domains)

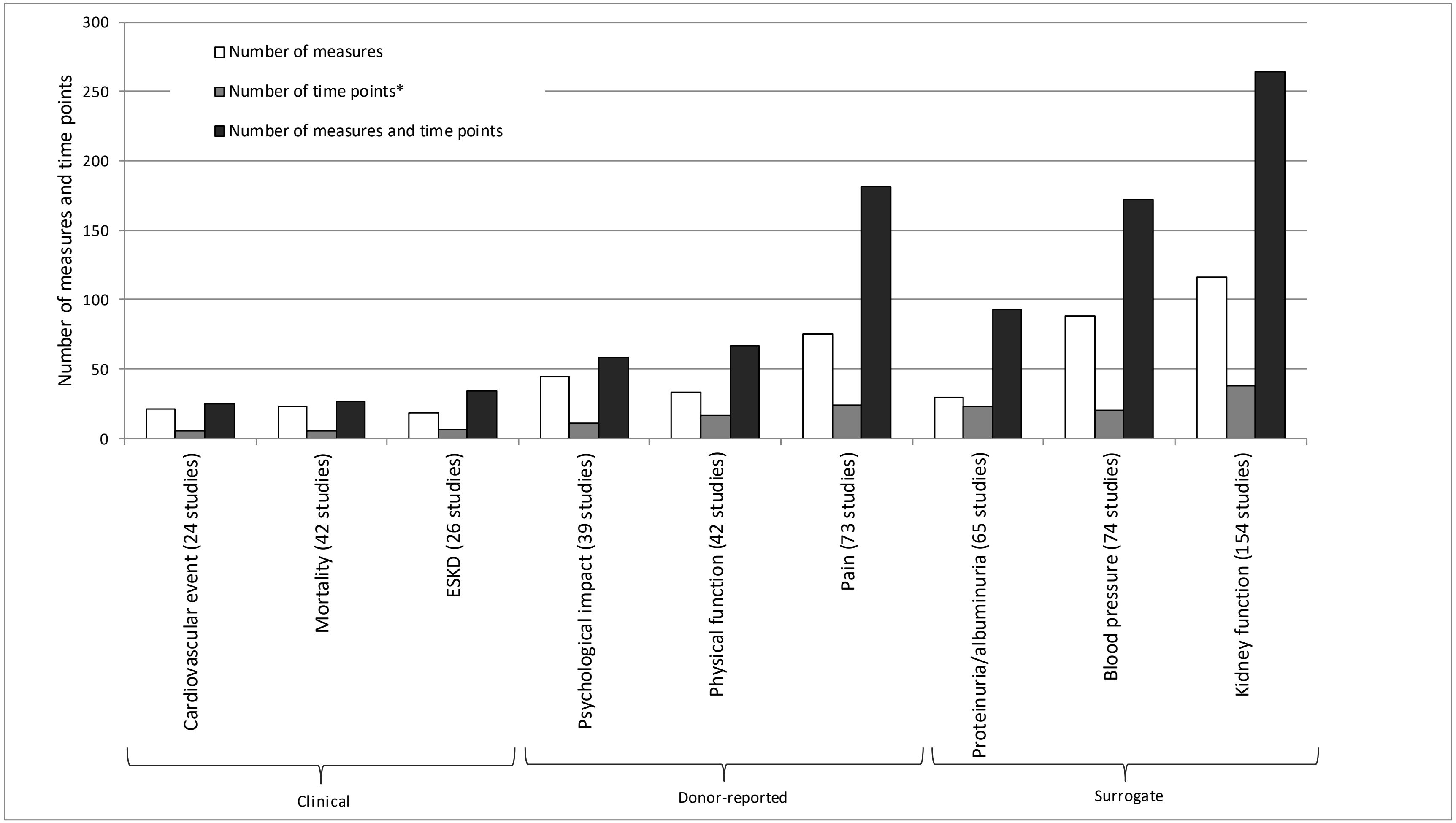

Figure 7.3. Number of outcome measures (definitions and time points) for selected outcome domains among studies *Number of unique time points per measure

Table 7.1. Characteristics of included studies (n = 268)

	Number of studies (%)		
Study characteristics	Therapy studies[1] (n =91)	Prognosis[1] studies (n =177)	All (n = 268)
Study design			
Observational studies[2]	77 (85)	177 (100)	254 (95)
Randomised Trials	14 (15)	0 (0)	14 (5)
Location			
Asia	34 (37)	53 (30)	87 (33)
North America	21 (23)	62 (35)	83 (31)
Europe	28 (31)	49 (28)	77 (29)
South America	4 (4)	4 (2)	8 (3)
Africa	2 (2)	5 (3)	7 (2)
Oceania[3]	2 (2)	3 (2)	5 (2)
Multinational	0 (0)	1 (1)	1 (0)
Year of publication			
2011	20 (22)	26 (15)	46 (17)
2012	13 (14)	25 (14)	38 (14)
2013	16 (18)	20 (11)	36 (13)
2014	11 (12)	29 (16)	40 (15)
2015	18 (20)	41 (23)	59 (22)
2016	9 (10)	27 (15)	36 (13)
2017	4 (4)	9 (5)	13 (5)
Number of participants[4]			
0-50	33 (36)	39 (22)	72 (27)
51-100	19 (21)	32 (18)	51 (19)
101-1000	35 (38)	68 (38)	103 (38)
1000-100,000	4 (4)	37 (21)	41 (15)
Follow up period (years)[5]			
≤1	81 (89)	61 (34)	136 (51)
1.1-5	7 (8)	43 (24)	50 (19)
5.1-10	2 (2)	44 (25)	46 (17)
>10	1 (1)	20 (11)	21 (8)
Year of earliest donation[6]			
1950-1969	1 (1)	11 (6)	12 (4)
1970-1989	0 (0)	23 (13)	23 (9)
1990-2009	66 (73)	93 (53)	159 (59)
2010+	14 (15)	24 (14)	38 (14)

[1] Therapy studies include questions of the outcomes of a treatment or exposure. Prognosis questions assess the progression of a disease or the likelihood of a disease occurring.[25]

[2] Includes cohort, cross-sectional and case series

[3] Includes Australasia (Australia/New Zealand and neighboring islands in Pacific Ocean, Melanesia, Micronesia and Polynesia

[4] One study did not report number of participants

[5] Fifteen studies did not report follow up. Categories based on mean/median for most studies.

[6] The year of earliest donation was not reported in 36 studies

Table 7.2. Ten most frequently reported outcome domains

Domains	**Therapy[1] n = 91 (%)**	**Prognosis[1] n = 177 (%)**	**All n = 268 (%)**
Kidney function	45 (49.5)	109 (61.6)	154 (57.5)
Time to discharge	72 (79.1)	24 (13.6)	96 (35.8)
Blood loss	66 (72.5)	19 (10.7)	85 (31.7)
Operative time	62 (68.1)	17 (9.6)	79 (29.5)
Blood pressure	5 (5.5)	69 (39.0)	74 (27.6)
Pain	40 (44.0)	33 (18.6)	73 (27.2)
Proteinuria, albuminuria	4 (4.4)	61 (34.5)	65 (24.3)
Complication (ns)	45 (49.5)	17 (9.6)	62 (23.1)
Postoperative complication (ns)	31 (34.1)	12 (6.8)	43 (16.0)
Mortality	9 (9.1)	33 (18.6)	42 (15.7)

NS = not specified

[1] Therapy studies include questions of the outcomes of a treatment or exposure. Prognosis questions assess the progression of a disease or the likelihood of a disease occurring.[25]

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Chapter 8: Discussion and Conclusions

8.1 Summary of findings

This thesis examined two aspects of living kidney donor transplantation – a) patients', donors' and nephrologists' perspectives on different aspects of the pathway to living kidney donor transplantation; and b) outcomes for living kidney donors, with the overall aim of improving access and outcomes in living kidney donor transplantation.

Specifically, this thesis addressed the following aims:

1. to identify and describe the beliefs, attitudes and expectations of patients with CKD (stages 1-5) regarding living kidney donor transplantation (Chapter 3)
2. to describe living kidney donors' experiences of the evaluation process (Chapter 4)
3. to ascertain nephrologists' perspectives on barriers and disparities in living kidney donor transplantation (Chapter 5)
4. to identify living kidney donors' priorities for outcomes and describe the reasons for their choices (Chapter 6), and
5. to determine the scope and heterogeneity of outcomes reported in randomised trials and observational studies in adult living kidney donors (Chapter 7).

Both qualitative and quantitative methods were used to address these aims. A systematic review of qualitative studies, focus groups, and semi-structured interviews was used in Chapters 3 to 5 to describe patients', donors' and nephrologists' perspectives on different aspects of the donation pathway. In Chapter 6, a mixed-methods approach was used to identify and rank a range of outcomes important to donors (nominal group technique) and describe the reasons for their priorities (focus groups). Chapter 7 is a quantitative systematic review that assessed the scope, consistency, and relevance of outcomes of living donation in recent trials and observational studies.

The findings in the first part of this thesis identified a range of barriers and facilitators to receiving a living kidney donor transplantation, which may help to explain some of the disparities in access to living kidney donation. Several challenges experienced by donors throughout the evaluation process were also described. The second part of this thesis was focussed on understanding the range of outcomes that are important and relevant to living kidney donors, and determining the consistency and range of outcomes reported in recent studies. These two studies demonstrated some mismatch between the outcomes prioritised by donors, and those that are frequently reported in research. The findings from each study are integrated and discussed in this final chapter.

The pathway to living kidney donor transplantation

The socio-ecological model[1], adapted from Bronfenbrenner's ecological systems theory (1998) informed the aims of this thesis. This model examines the influence of personal values, family, extended social network, health care system, and cultural or societal values on health care decision-making and behaviour. The studies in this thesis predominately focused on the views of key stakeholders involved in living kidney donor transplantation – donors, recipients and clinicians. Other factors within this model have also been considered including the health care system and family and cultural values.

Chapter 3: Patient perspectives

The systematic review and thematic synthesis of qualitative studies (Chapter 3) described the perspectives of patients with CKD towards receiving a living kidney donation. Three facilitators were identified, including prioritising their own health, receiving validation of their decision and needing social support. Four themes described barriers including guilt and responsibility, ambivalence and uncertainty, and a fear of directly asking someone to donate. Patients' decisions about pursuing or accepting a donation involved a conflict between their desperation for improved health and quality of life, and their concerns about the donor's vulnerability to physical harm, coercion and financial hardship. While living kidney donor transplantation offered them the best health outcomes, they expected to face difficult emotional consequences, including guilt, indebtedness to the donor and family conflict.

Concerns about jeopardising the donor's health, shortening their life and causing burdens and inconvenience, were insurmountable barriers for some patients, particularly older patients with younger potential donors. Patients were concerned about the risks of perioperative death, shortened life-expectancy, kidney failure and fertility and pregnancy complications for their donor. Other patients were able to overcome their ambivalence and found decisional validation through their confidence and trust in their transplant team to protect their donor from harm. Patients also felt they could justify accepting a donation from a family member, as they believed this would reduce the burdens on their family. Some felt they should respect their donor's desire to donate.

However, many patients felt unable to communicate and resolve their concerns due to receiving insufficient information and lacking emotional support. Discomfort and a lack of confidence with asking people to donate, and being unable to accept or understand their CKD diagnosis and need for transplantation, were also significant barriers to actively pursuing living kidney donation.

Chapter 4: Donor perspectives

The focus group study conducted in Australia and Canada (Chapter 4) identified six themes reflecting donors' experiences of the evaluation process and donation pathway: emotional investment, undeterred by low risks, mental preparation for the surgery and recovery, underlying fears for their health, system shortfalls and lifestyle intrusion.

The emotional investment in giving their organs sustained donors' commitment throughout the evaluation process, despite experiencing fears about health risks, encountering opposition from significant others, managing lifestyle disruptions and financial hardship, and difficulty accessing information and support. They were determined to improve the recipient's health and their family life. However, their commitment to donating also prevented potential donors from disclosing their concerns and seeking support, for a fear of being deemed ineligible.

Although post-donation risks were concerning to donors, they trusted their clinicians to protect them from harm. This view was also expressed by potential recipients in Chapter 3. However, some felt that their determination to donate had limited their ability to comprehend and process information about risks prior to donation. They described themselves as going into donation "blind", ignoring information that contradicted with their decision to donate. This was particularly evident among non-directed donors, who felt confident they were in good health, and therefore deemed the risks of donation and complications of surgery to be overstated or irrelevant to them.

Chapter 5: Clinician perspectives

Nephrologists provided insight into the barriers and disparities that impact recipient eligibility and access to living kidney donor transplantation. The semi-structured interview study with clinicians (Chapter 5) identified five major themes. These included championing optimal recipient outcomes, justifying the donors sacrifice, advocating for their patients, maintaining professional boundaries, and entrenched inequities. Nephrologists' decisions about recipient suitability for living kidney donor transplantation aimed to achieve optimal recipient outcomes, but they felt constrained by competing priorities of ensuring reasonable utility of the transplant to justify the donors sacrifice, and protecting the integrity and reputation of the transplant program.

Nephrologists struggled to resolve these conflicting priorities when faced with patients with medical, psychosocial and/or behavioural risk factors, but who might not be eligible for deceased donation due to the strict eligibility criteria for waitlisting. Specifically, variable views were expressed among nephrologists regarding whether to allow living donor transplants for patients who were older, highly sensitised, non-adherent, and those with low social support, mental health issues, comorbidities, and recurrent disease, because they were uncertain of achieving reasonable graft outcomes and being able to justify the donor’s sacrifice.

Nephrologists described needing to be proactive in encouraging potential recipients to search for a donor, providing education and counselling, and facilitating assessments and referrals early, particularly to enable pre-emptive transplantation (prior to dialysis). The clinicians recognised many of the concerns raised by patients in Chapter 3. However, they found it difficult to advocate for their patients because of limited psychosocial and educational resources available to them, and their perceived conflict of interest in actively helping their patients find a donor. They also emphasised that patients were accountable for ensuring that they were eligible for transplant (e.g. by demonstrating adherence).

Chapters 3-5: Ethnic and socio-economic disparities

The triangulation of donor, recipient and nephrologist perspectives provided greater understanding of disparities in living kidney donor transplantation. Nephrologists largely viewed inequities as entrenched, and felt powerless to facilitate access for their patients of ethnic minority backgrounds due to a lack of culturally-sensitive resources. These patients were deemed less likely to have a suitable donor because of a higher incidence of obesity, cardiovascular disease, diabetes, high blood pressure, ESKD and smoking. Some believed that patients from ethnic minority groups were often “pre-judged” regarding their likelihood of finding a donor, and that socio-economically disadvantaged patients were likely to have a limited social network and thus a small potential donor pool, or their potential donors could not afford to take time off work to donate. Nephrologists also believed that the living donor transplant pathway inherently advantaged patients with the resources and skills to advocate for themselves, due to the difficulty of coordinating work up and referrals.

In Chapter 5, nephrologists practising in Australia described their ethical responsibility to distance themselves from assisting potential recipients with donor recruitment to avoid a conflict of interest. However, this was found to be an important barrier for patients from ethnic minority groups, in Chapter 3. Patients described cultural values that created a reluctance to discuss donation with their family and social network, including the impropriety of discussing illness, rules of family hierarchy in identifying a potential donor, and unfamiliarity with living kidney donation among their community. Patients also mentioned some potential religious barriers; for example, the notion of bodily integrity (i.e. being buried whole), or concerns that interfaith or unrelated donation might be condemned by their religious community. Some patients described their culture as passive information seekers, and believed their family members would be unwilling to attend information sessions with them. In chapter 4, donors of ethnic minority background described opposition from their family and community regarding their decision to donate, also mentioning bodily integrity.

Financial considerations were a barrier for donors and recipients (Chapters 3 and 4). Patients were reluctant to pursue living kidney donor transplantation because they did not want to cause financial burdens to the donor, including out-of-pocket expenses and career disruption. During evaluation, donors described the significant and accumulating costs for transport, accommodation, and lost income, and struggled to access adequate financial assistance.

Outcomes important to living donors and the relevance of outcomes reported in trials and observational studies

The nominal groups held with donors from Australia and Canada identified the outcomes of donation that are most important to donors and their perspectives on a range of possible outcomes (Chapter 6). The ten highest ranked donor outcomes were their kidney function (i.e. glomerular filtration rate or creatinine levels), followed by time to post-operative recovery, surgical complications, impact on family, donor-recipient relationship, life satisfaction, lifestyle restrictions, kidney failure, mortality and acute pain/discomfort. The themes underpinning their priorities included: unfulfilled expectations; heightened susceptibility; confidence and empowerment; downplaying risks and harms; and worthwhile sacrifice.

From a range of possible and experienced outcomes associated with kidney donation, the outcomes that were most important to donors included kidney health, short-term surgical and functional outcomes, and psychosocial impacts. The long-term risks associated with nephrectomy, for example, mortality and cardiovascular disease, were of relatively lower priority. While some donors were concerned about their heightened susceptibility to kidney disease or a shortened life expectancy, most believed their clinicians had minimised long-term risks through the screening process, and they could prevent disease through a healthy lifestyle and maintaining their kidney function. Kidney function was the highest ranked outcome, because of underlying fears of developing kidney failure in their remaining kidney, uncertainty regarding a ‘normal’ post-nephrectomy glomerular filtration rate, and worry about avoiding nephrotoxic products.

Recent observational studies and trials (Chapter 7) in living kidney donors reported an extensive range of outcomes, which were mostly surrogate or biochemical parameters, and short-term clinical endpoints, with large heterogeneity in measures used to assess the outcomes. Therapy studies (i.e. RCTs and observational studies testing the effects of surgical and post-operative interventions) frequently reported short-term surgical outcomes (e.g. time to discharge, blood loss and operative time), and non-specific complications. The three most frequently reported outcome domains in prognosis studies were all surrogate end-points (including kidney function, blood pressure and proteinuria/albuminuria). Important clinical and donor-reported outcomes including mortality, quality of life, cardiovascular events, and ESKD, were reported in less than 20% of prognosis studies. The review also demonstrated heterogeneity in outcome domains and measures across studies, with the 268 studies reporting 109 different outcome domains. Surrogate and donor-reported outcome measures had greater heterogeneity of measures than clinical outcomes. ESKD, a clinical outcome, was reported in 18 different ways.

There was a mismatch between the outcomes frequently studied, and those described as relevant and important to donors, in Chapter 6. Donor-reported outcomes were included infrequently, limiting the relevance of these studies to help donors understand and prepare for their recovery, return to work, deal with the financial impact after donation and possible changes to their physical and psychological functioning after donation. Time to post-operative recovery was the most important outcome to donors; however, this is typically reported as time to discharge from the hospital. In the focus group study (Chapter 6), donors defined their recovery as their return to normal health in terms of their physical and emotional functioning, and resumption of their regular roles and activities. Also, some donors described experiencing fatigue, pain, and psychosocial problems for a few years after donation, and they believed they were not informed or adequately prepared for these outcomes, and they were not addressed in follow-up care. These outcomes were rarely reported and only followed up in the short-term (for a maximum of twelve months in most studies). The positive psychosocial impacts of donation that donors experienced and valued (Chapter 6), which motivated their decision to donate (Chapter 4) were rarely reported. An awareness of these positive impacts also provided decisional-validation to potential recipients (Chapter 5), and nephrologists (Chapter 5).

Mortality, ESKD and cardiovascular events were not measured beyond 25 years after donation. Most donors did not expect to be at an increased risk of long-term health outcomes, and they believed that these risks had little influence on their decision to donate (Chapter 4). However, kidney failure and mortality were still of interest to some donors, particularly after donation, and motivated their participation in life-long self-care, including monitoring their kidney function (Chapter 6). Surrogate end-points such as kidney function and blood pressure were important and relevant to donors as they used these to monitor their health after donation (Chapter 6). Other frequently measured surrogates, including proteinuria, albuminuria and body mass or composition, were also frequently measured but were not identified as highly important to donors in Chapter 6.

8.2 Strengths and limitations

The strengths and limitations of the studies are provided in more detail in the relevant chapters. This section will focus on the overall strengths and limitations of the thesis.

This thesis is comprised of a systematic review of qualitative studies, a focus group study, a semi-structured interview study, a nominal group technique study, and a review of the scope and consistency of outcomes reported in recent research. The qualitative and quantitative methods used were complementary, and the qualitative methodologies enabled stakeholders' beliefs, attitudes, and priorities to be elicited. The systematic review and synthesis of qualitative studies on patients' perspectives of living kidney donation pooled together existing evidence from different health care contexts and populations, and enabled the identification of knowledge gaps and the development of a new analytical framework to understand recipient perspectives on living kidney donor transplantation. The triangulation of different stakeholders' perspectives generated a more comprehensive understanding of different aspects of the transplant pathway[2]. The studies sought to understand both barriers and facilitators to living kidney donor transplantation, and contextual understandings to develop implications for policy and practice.

A multi-centre perspective was gained by recruiting donors from three centres cross Australia and Canada, and nephrologists from twenty-two centres in Australia and New Zealand. The quantitative component of the nominal group technique provided an understanding of donors' relative priorities. The systematic review of trials and observational studies on donor outcomes enabled a comparison between donors' priorities and the outcomes that are frequently reported.

Across all the qualitative studies in this thesis there were limitations regarding the selection and inclusion of specific subgroups. Participating donors were all English-speaking, and mostly Anglo-Saxon, and had achieved a high level of education; although, this reflects the majority donor population in the included countries. Despite providing reimbursement to participants for travel costs, rural and remote donors are typically more difficult to recruit to focus group studies. All interviews and groups were conducted face-to-face, due to the difficulty of establishing rapport and managing the interview dynamic over telephone or Skype interviews. A purposive sampling strategy was used in each study to achieve a diverse sample. Data saturation was achieved in each study. The transferability of these findings to other settings beyond the participating sites is uncertain. However, some complementary and similar findings to other studies conducted in other regions have been demonstrated, which suggest broader transferability of the results.

Brazil, India, Mexico and Iran do high numbers of living kidney donor transplants, but publish very little data on donor outcomes.[3] There were very few studies from these countries in our qualitative and quantitative systematic reviews.

Qualitative methods were used to elicit a range and depth of beliefs, attitudes and perspectives. Across these studies, steps were taken to demonstrate rigour. The author was trained to conduct interviews, focus groups and nominal groups by an experienced qualitative researcher and supervisor. Across the fourteen groups there was a learning curve, such that the author's skills with prompting elaboration and facilitating the direction of the discussion improved with experience. For example, donors were often focused on the recipient and would discuss their concern for recipient wellbeing more readily than their own outcomes. A range of techniques was used (e.g. directing questions to individuals or shifting attention using eye contact and body language) to keep the discussion on topic and minimise undue individual dominance of the discussion and to encourage all members to contribute.[4] Being present at all the focus groups, the author used the knowledge gained from previous groups to prompt wider or more detailed discussion in subsequent groups. Living kidney donors have been found to be reluctant to reflect negatively on their experience[5], and may not feel comfortable expressing this to researchers. To encourage open discussion, time was spent building rapport with participants, and it was emphasised that the discussion was confidential and would be de-identified. The group format enabled participants to feel comfortable discussing the difficult and challenging experiences of donation, due to their shared experience. Donors whose recipient had died or experienced graft loss have been found to be difficult to recruit to research, and only a few such donors were included in the studies.[5] As for the clinician interviews, it was also challenging to ensure clinicians felt comfortable disclosing their personal attitudes and beliefs, particularly if they differed from the status quo or from the principles and approach of their unit.

Qualitative researchers need to demonstrate the confirmability of their findings; i.e., that their interpretations reflect the participant's perspective rather than the researcher's predetermined ideas. Reflexivity is one such way that researchers can recognise any undue influences on their interpretations of the data.

I was not involved in the assessment and clinical care of living kidney donors or recipients. However, the insights I had gained through my research, and my personal background may have influenced the information elicited during data collection and my interpretations adopted during analysis. To minimise this, multiple researchers were involved in the analysis (investigator triangulation) to ensure the findings and conclusions were directly linked to a participant's data and captured the full range and depth of the data. Member checking was conducted for the clinician study, whereby participants were provided with feedback on the preliminary findings to ensure the range of opinions was captured. Inductive coding also ensured that the themes were developed from the data.

8.3 Comparison with other studies

The studies in this thesis provided new insights and addressed knowledge gaps in living kidney donor transplantation.

Pathway to living kidney donor transplantation

Patient perspectives

Surveys of transplant candidates' attitudes towards living kidney donor transplantation have consistently found that concerns about graft failure, and about the future health of the donors are the most common barriers for patients.[6-8] The qualitative systematic review reported in Chapter 3 described recipients' beliefs and attitudes that help explain these concerns. It is noted that potential recipients understood the risks to the donor to be low, but felt they were potentially catastrophic and therefore patients may prefer to wait for a deceased donor transplant. The possibility of graft failure or donor harm was expected to cause unbearable guilt, and patients expected that the donor may regret their decision. The conceptual schema depicts how recipients persevere with living kidney donor transplantation, despite their fears and concerns, through receiving emotional support, education and decisional validation.

Reticence to initiate discussions with potential donors is one of the most frequently reported barriers among patients waitlisted for transplantation.[6,9] Insufficient information about living donor outcomes, uncertainty about donor eligibility criteria, and doubt and discomfort about asking someone to donate prevented patients from considering living kidney donation further. The reluctance among potential recipients to ask someone to donate was multilayered, underpinned by a determination to avoid coercion, a preference for a donor to initiate the discussion, and a need to avoid the disappointment of rejection. Patients also lacked confidence in how to ask someone to donate.

Previous studies have found that patients from minority ethnic backgrounds are less likely to initiate discussions with potential living donors than non-minority patients.[9,10] In the systematic review in Chapter 5, patients emphasised various cultural values which underpinned their reluctance to seek potential donors, including the impropriety of discussing illness, rules of family hierarchy, and suspected community unfamiliarity with living donation, perceiving it as "strange". A sense of medical urgency and desperation mobilised patients to initiate discussions with potential donors, but some did not accept or understand their diagnosis of CKD, or need for transplant. Previous studies suggest this may be more common among patients of ethnic minority backgrounds.[9-13] Patients may also feel uneasy about incorporating a living person's kidney into their own body. This may be due to concerns about how transplanted organs can influence their recipients' personality and thoughts.[14]

Donor perspectives

In previous studies, donors have described being highly motivated to donate, and attempted to manage how they are perceived during the psychosocial evaluation, to protect their eligibility.[15] Other studies have reported that both directed and non-directed donors feel anxious about undergoing psychosocial assessment due to their determination to donate, and some are reluctant to disclose experiences that might exclude them from donating.[15-17] Uncertainty about their eligibility status whilst waiting for test results, long delays, and navigating an unfamiliar healthcare system, has been identified as a considerable source of emotional strain during evaluation.[18-20] In addition to confirming these previous findings, the focus group study in Chapter 4 illuminated this concept of emotional investment that underpins donor perseverance despite the challenges of assessment, and an intense need to protect their eligibility.

Surveys have shown that donors have a higher acceptance of risks of mortality, kidney disease, hypertension, cardiovascular disease and hypertension, compared to transplant recipients and transplant professionals.[21,22] This study provides some potential explanations for the higher acceptance of risk among donors. Donors felt invincible, trusted transplant professionals to protect them from harm, normalised surgical risks, and believed that it would be reprehensible to deny the recipient the opportunity for live-saving and life-improving transplant based on a minimal and theoretical risk to the donor. While donors have previously been found to be accepting of risks to themselves[23], some donors conveyed concern for health risks and uncertainty regarding long-term outcomes (Chapter 4). The findings in Chapter 6 suggest that, for many donors, concerns about health risks may arise or become more prominent after donation. Underlying concerns about long-term health risks have been found to be a strong motivator for donor participation in follow-up care with their general practitioner or transplant unit.[24] Mild anxiety about developing kidney failure was found to be common among people who have donated a kidney.[25] However, many donors continue to be unconcerned by health risks and lack a patient or 'sick' identity after donation, and regard follow-up care as unnecessary.[24]

Nephrologist perspectives

Nephrologists' perspectives on recipient eligibility and access to living kidney donor transplantation had not been comprehensively studied. A number of studies have shown that nephrologists may have inherent biases or assumptions regarding a transplant candidate's expected survival, motivation, adherence and chances of finding a donor.[26,27] [26] These attitudes may result in subconscious differences in the way nephrologists make decisions and discuss transplantation options with patients of ethnic minority backgrounds or socio-economic disadvantage. The hypothesis that ethnic and socio-economic disparities are largely caused by a limited donor pool is prevalent in the literature, but evidence is based on single-centre studies.[13,28-30] These beliefs were also held by some nephrologists in this study (Chapter 6), who expressed a reluctance to unnecessarily raise the expectations of patients when they felt it was unlikely they would find a suitable donor.

Nephrologists also believed that there were centre factors that influence access to living kidney donor transplantation. Epidemiological studies have found that a patient's chance of receiving a living donor kidney transplantation is higher if they are treated at a centre that has a higher annual volume of transplants overall, a higher volume and percentage of living kidney donor transplantation, and longer waiting times for deceased donor transplantation.[31-35] Transplant centres with a higher-volume of living kidney donor transplantation performed a higher proportion of donations from unrelated donors, and they offered programs to overcome biological incompatibility.[32-34] The nephrologists in this study did not refer to these factors, but felt they depended on education, timely referrals, streamlining of evaluations, and effective communication between the independent donor and recipient physicians. Nephrologists believed that their patients often became “lost in the system”, and discussion about living kidney donation and referrals for pre-emptive transplantation were often delayed because of competing responsibilities. In addition, they reiterated that the transplant team had to build a strong culture of living kidney donation by promoting this option positively, encouraging their patients to find potential donors and building trust and confidence in the transplant team.

Donor outcomes

Donors’ perspectives on a range of post-donation outcomes were explicitly and systematically studied, and these outcomes were compared to those that have been measured in recent trials and observational studies (Chapters 6 and 7). Previous qualitative studies of donors motivations’ and their experiences of donation have suggested that donors value highly the psychosocial benefits of donation.[23] Post-donation problems including fatigue, pain, anxiety about their kidney function and difficulties in their relationship with the recipient have been described in qualitative studies.[23] Surveys suggest that only a minority of donors (5-25%) report negative psychosocial and physical outcomes[5,36-38], yet, these were among the highest ranked outcomes for donors. Improvements in family life and emotional wellbeing were rated highly because they were the things that many donors benefited from the most, personally. Others ranked negative psychosocial and functional outcomes highly as they felt they were unrecognised by transplant professionals and inadequately addressed in follow-up care.

Surrogate outcomes are frequently measured because they are easier to collect and detect short-term changes, but offer limited information to inform decision-making as they may not be valid predictors of clinical outcomes.[39] Recent studies have shown that equations for estimating glomerular filtration rate (GFR) underestimate kidney function in living donors.[40-42] Kidney function was most frequently measured by estimated GFR. The nominal group study found that donors were focused on their GFR, and wanted some clarity whether their level of function was normal. A recent qualitative study found that kidney function and blood pressure may be important outcomes to donors, as they allow donors to monitor their health after donation, and provide reassurance about their health.[24] Therefore, some well-known surrogates may be meaningful to patients, despite providing limited information about long-term clinical outcomes. However, it was also found that donor outcomes are reported heterogeneously across studies. This has proved difficult to combine and compare data on donor outcomes across studies, and thus limits the reliability and certainty of evidence available donors to help with decision-making.[5,43-49]

8.4 Implications for clinical practice and policy

Major innovations in transplantation policy and practice have improved access and outcomes in living kidney donor transplantation; however, numbers have decreased in recent years and ethnic and socio-economic disparities are apparent.[50] Overall, the studies in this thesis identified limitations of current guidelines, education, informed consent, pre-transplant psychosocial support and long-term follow up care (Figure 8.1). Addressing these could lead to more equitable access to living kidney donor transplantation, improved satisfaction with the donation process and improved wellbeing for donor-recipient pairs.

Improving access to living kidney donor transplantation and the donation pathway

The fulfilment of living kidney donor transplantation is a complex process, influenced by individual, familial, social, ethical, societal and health care centre and system aspects.[31] In the qualitative systematic review (Chapter 3), potential recipients described the inherent psychosocial and ethical challenges implicated in asking another person to accept risks on their behalf, as well as coping with guilt, responsibility, indebtedness and family resistance. Uncertainties about living kidney donor outcomes, and asking someone to donate, were major obstacles for potential recipients. Therefore, this study identified the need for specific pre-transplant education, psychosocial support and counselling for patients that addresses:

- guilt, ambivalence, decisional-conflict and interpersonal problems
- engaging in discussions with potential donors
- potential risks and outcomes for donors
- acceptance and understanding of their diagnosis
- benefits of pre-emptive transplantation, and
- cultural values and family opposition.

Few psychosocial interventions have been assessed in the pre-transplant setting. A RCT found some promising results with quality of life therapy, which aims to identify specific areas of patient dissatisfaction and problem-solving strategies.[51] The intervention resulted in improved quality of life and psychological functioning for patients awaiting transplantation. The findings in Chapter 3 indicated that recipients choose not to discuss their concerns with their family or potential donor, for example, that they will feel eternally indebted to the donor, or the donor will try to 'control' them. This highlights the need for mediated communication between patients, their family and potential donors to resolve interpersonal issues. This could also help facilitate family support, provide decisional validation and reassurance.

There have been efforts to develop and evaluate interventions to support patients in identifying potential donors. The Talking about Living Kidney Donation Educational and Social Worker intervention encourages patients to identify and resolve self-identified barriers to discussing and pursuing pre-emptive living kidney donor transplantation.[57,60] This intervention increased discussions about living kidney donation with family and clinicians, and the identification of potential donors.[52,53] Indirect discussions about donation in this type of intervention, rather than direct requests to donate, may be effective for donor recruitment[54], and could alleviate patients' concerns about disrespecting or pressuring potential donors. Model conversations[52] and role-playing exercises could be offered to potential recipients to help them make donation requests, directly. It is recommended that patients be provided with access to counselling to cope with the disappointment of refusal to donate and to develop resilience for making subsequent requests.

Pre-transplant education about donor outcomes may be somewhat overlooked for recipients. Evidence-based information about the potential risks and benefits should be communicated to patients. Informing patients about efforts to safeguard donors, such as the use of independent donor advocates, reimbursement schemes, psychological evaluation, and rigorous donor acceptance criteria, may provide reassurance to patients.

Family-oriented education may be particularly effective for culturally and linguistic diverse patients to facilitate social support, improve comprehension of information and address family ambivalence.[52,53] A randomised controlled trial found that a culturally-sensitive home-based family education program improved patients' knowledge and willingness to discuss living kidney donation, decreased patients' concerns, and led to increased donor inquiries, completed evaluations and actual living kidney donation rates.[55,56]

The nephrologist interview study (Chapter 5) primarily identified the need to ensure nephrologists make more explicit and informed decisions concerning recipient eligibility for living kidney donor transplantation. Additionally, improved resources to address patient barriers are required. Therefore, the main recommendations from this study included:

- improving consensus and standardised practice regarding candidates with complex medical or psychosocial issues
- developing an explicit pathway for patient education and referral to transplant services
- using evidence-based guidance for addressing psychosocial risk factors, including non-adherence, depression and low social support[18,39,40]
- ensuring transparency of centre performance and policies
- educating patients with a limited donor pool about options such as ABO incompatible transplantation, paired exchange and unrelated donation[34]
- providing culturally competent educational and psychosocial resources to facilitate shared decision-making and address barriers, and
- clarifying the responsibilities and boundaries of nephrologists in the role of caring for potential recipients.

There is limited research evaluating and implementing interventions to address psychosocial barriers to living kidney donor transplantation.[57,58] Promising interventions to help patients through the pathway to living donor transplantation include a social worker consultation to identify and address individual patient barriers[52], peer support to navigate referral and assessment processes[59], and culturally-sensitive home education.[56]

Training to improve interactions with interpreters might alleviate nephrologists' uncertainties during shared decision-making with non-English speaking patients.[60,61]

Nephrologists distanced themselves from assisting candidates with donor recruitment to avoid a conflict of interest. Some transplant nephrologists also felt they were more "passive" in promoting living donation to patients, because they wanted to protect donors from coercion and unnecessary risk. This may prevent patients from receiving adequate information and counselling regarding living kidney donor transplantation. Therefore, separation of the donor and recipient teams or clinicians is imperative. Moreover, the responsibilities and boundaries of nephrologists representing the recipient, in supporting and facilitating donor education and recruitment, require clarification. With mechanisms protecting the donor from coercion, nephrologists may feel more comfortable in providing advice to their recipients about donor recruitment.

Strategies are also needed to resolve the tensions nephrologists felt between advocating for their patients and protecting the reputation of their transplant program. Trends of risk avoidance for patients with less certain graft outcomes have been observed in the United States.[40,41] This study supports recommendations that both patient outcomes (graft and patient survival) and transplant volume be regarded as equally important in evaluations of centre performance, to ensure that efforts to protect outcomes are not maintained at the expense of expanding access to transplantation.[62] Patients should also be informed about the considerable variability among kidney transplant centres in terms of patient outcomes, unit policy, expertise and resources such as ABO incompatible transplantation. However, many patients are unable to choose a different centre due to financial and geographical constraints.[63-65]

The focus groups with living donors (Chapter 4) demonstrated that more attention is needed to address the psychosocial challenges of live donor evaluation. This includes:

- identifying and addressing fears/concerns and psychosocial issues (e.g. fears of surgery, social support, family conflict, donor-recipient relationship problems and coping with possibility of graft failure)
- mitigating the anxiety of testing (e.g. possibility of being ruled out)
- minimising financial burdens and lifestyle interference, and improving efficiencies in the evaluation process
- preparing potential donors for surgery and recovery (individualised to donor's preferences)
- improving comprehension of risk, and
- clarifying donors' responsibilities in driving the evaluation process.

Since 2007, the Organ Procurement and Transplant Network in the United States has required an independent living donor advocate to assist with informed consent by providing education, support and advocacy to potential donors.[66] An independent live donor advocate, social worker or patient navigator could facilitate more comprehensive support throughout evaluation by addressing donors' needs and concerns as they emerge, limiting lifestyle intrusion, assessing risk comprehension, and providing culturally-sensitive interventions to address family conflict. It is worth noting that a reluctance to burden and intrude on the life of others was a strong deterrent for patients considering living kidney donation. Therefore, limiting the burdens of evaluation may encourage both donors and recipients to be more accepting of living kidney donor transplantation.

Current practice in living kidney donation may prevent many donors from openly discussing their fears, concerns and uncertainties. Guidelines focus on ensuring psychological suitability, motivation and voluntariness, and informing donors of possible outcomes[67,68], rather than providing evidence-based strategies to address these issues. Caution to detect coercion and assess risk comprehension can cause donors to feel scrutinised and become reluctant to express their anxieties. Therefore, it is recommended that a component of the psychosocial evaluation be framed as an opportunity to communicate and resolve concerns without feeling under threat of jeopardising their eligibility. Similarly, deliberately delaying the evaluation process and requiring donors to drive progress of their assessments to ensure donors are motivated can exacerbate delays, burdens and uncertainty. These cautionary measures may be practised more often or intensely in the case of non-directed donation. Overall, greater transparency regarding the purpose and process of donor evaluation could resolve uncertainties, confusion and stress during donor evaluation.

Improving understanding and treatment of living donor outcomes

Living kidney donor candidates accept a range of risks and benefits when they decide to proceed with nephrectomy. Informed consent around this decision assumes they receive reliable data about outcomes they regard as critical to their decision. The nominal group technique study provided a framework to ensure that the outcomes most relevant to donors are consistently included in education, informed consent, assessment and follow-up care. The main recommendations from these studies include:

- improving donor education on long-term outcomes and information about outcomes important to the individual
- assessing and addressing donor-important outcomes during follow-up, and
- keeping donors updated on emerging evidence on donor outcomes and providing advice on protective lifestyle behaviours.

These findings emphasise the importance of identifying donors’ priorities and concerns during the informed consent process, and being cognisant of the donor’s confidence in the transplant process such that they may readily accept or disregard long-term health risks. The recently published Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend informing donors of individualised risks, benefits including medical, surgical psychosocial and economic outcomes during the perioperative period and the remaining lifespan of the donor.[69] The guidelines suggest communicating absolute risks, and disclosing uncertainty in long-term outcomes.[69] However, the donor's strong motivations and confidence in their safety pose additional barriers to comprehending risk information prior to donation.[15,21,22] Donors may also be overwhelmed by information.[15] It remains unclear how to tailor education to donors' varying stages of readiness, learning preferences and health literacy to improve recall and comprehension.[70,71] Therefore, continued education about donor outcomes and emerging evidence is critical after donation.

The assessment of donor-reported outcomes can provide information to help prepare donors for a range of outcomes they may experience and care about, and enable follow-up care to be individualised to the donor's needs.[72] The Organ Procurement Transplant Network (OPTN) mandates the collection of data on a range of post-donation outcomes for two years after donation, including two psychosocial outcomes – employment status and loss of insurance. A broader scope of psychosocial and functional outcomes should be assessed in follow-up. For example, a validated longer-term measure of recovery is needed, that captures donors' full recovery.

Kidney function was the most important outcome to donors, as monitoring their kidney function could provide reassurance that they are not at risk of kidney failure. However, there was some uncertainty whether their GFR was at a normal level, given that they only had one kidney. Equations for estimating GFR underestimate kidney function in living kidney donors, and are less precise than measured GFR.[40-42] The recent KDIGO guidelines recommending routine assessment of both estimated

GFR and serum creatinine during donor follow-up care.[69] This should be explained and emphasised to donors during follow up and may provide greater reassurance about their kidney health and reduce anxieties about their vulnerability to kidney disease.

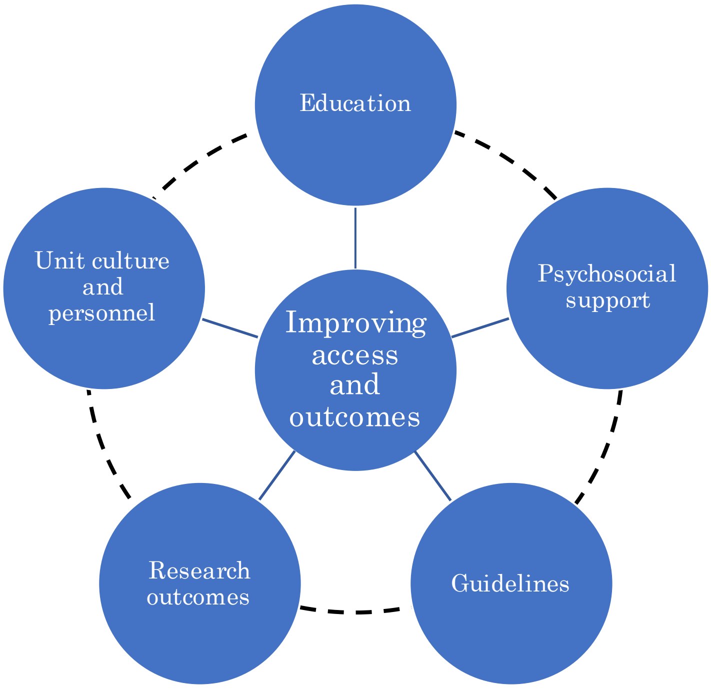

Figure 8.1: Summary of the recommendations derived from this thesis

8.5 Implications for research

The studies in this thesis identified several recommendations for increasing access to living kidney donor transplantation, and improving the donation process. There are some important research gaps that were not addressed in this thesis, and additional research questions were identified from these studies.

Improving the pathway to living kidney donor transplantation

Patients and donors from various ethnic minority groups should be studied to develop a better understanding of cultural barriers, and inform the development of culturally-competent interventions. For example, researchers from the United States have developed and evaluated educational resources about living kidney donation specifically targeted to Hispanic patients and their families.[73,74] There is limited evidence available to inform culturally sensitive interventions in Australia where about 30% of the population was born overseas. Further research is also needed to study:

- the perspectives of patients of low socio-economic backgrounds so as to understand financial barriers
- recipient perspectives on pre-emptive transplantation and non-directed donation
- the experiences of non-directed donors during evaluation and their perspectives of risk
- the perspectives of donors who opt-out of donation during or prior to evaluation, as the barriers they experience may be different to those described included in the focus group study[75]
- the perspectives of surgeons, transplant coordinators, psychiatrists and allied health professionals, as they may have different perspectives on barriers and challenges along the pathway to living kidney donor transplantation, including informed consent, education and psychosocial assessment, and
- the perspectives of nephrologists practising in low-income countries and health care contexts with different regulations and policies for living kidney donor transplantation.

Additional research questions have been developed from the findings of this thesis, including:

- conducting a survey of practices and policies for living kidney donor transplantation across transplant units
- conducting a survey to assess the frequency of opinions among nephrologists to enable comparison across transplant professionals

- conducting a longitudinal study of donors changing priorities for outcomes over time (e.g. prior to donation, in the perioperative period and short-term and long-term follow up)
- developing and evaluating interventions to improve informed consent, psychosocial support and education (including culturally-competent interventions), and
- developing validated screening tools to assess psychosocial and functional outcomes during evaluation and after kidney donation/transplantation.

Outcomes of living kidney donor transplantation

Improved reporting and measurement of donor-relevant and clinical outcomes would ultimately lead to better informed consent practices and evidence-based decision-making in living kidney donation. Heterogeneity in outcome measurement has stifled efforts to pool data across studies.[5,36-38] This makes it difficult to provide donors with reliable data on the outcomes that matter to them. It is increasingly argued that clinical trials should include patient-centred outcomes; standard measures for global, physical, mental and social health are being developed.[76] To facilitate routine collection by transplant centres, researchers, and registries, these measures must also be feasible to measure in large prospective studies and registries, which may be particularly challenging for self-reported outcomes.[77] Generic outcome measures like the SF-36 are frequently used and reported in studies, but provide limited meaningful information to donors and may not capture donation-specific psychosocial experiences e.g. conflict in the donor-recipient relationship. At a minimum, researchers should include meaningful outcomes that are of critical significance to donors, in addition to the outcomes intended to be studied.

Time to recovery was the second most important outcome to donors, yet is infrequently reported in short and long-term studies on the outcomes of donation. Time to discharge was the most frequently reported outcome in therapy studies, which is routinely collected and easily obtained from administrative data. This measure provides limited information to inform donors' expectations of surgical recovery – which, donors defined as the return to "normal" health in terms of their physical and emotional functioning, and resumption of their regular roles and activities. A patient-reported outcome measure is needed that captures their concept of recovery and allowing for long-term assessment. A brief post-operative recovery index (PORI) self-report instrument has been developed, that assesses the quality of recovery across domains, including psychological, physical activity, general symptoms, bowel symptoms and appetite symptoms.[78] However, this would need to be adapted and validated for longer-term assessment (i.e. beyond 30 days) and include participation in the patient's regular roles and activities. This may provide more useful data to better prepare donors for their recovery and understand their needs after donation.

Donor outcomes are central to the decisions of nephrologists and potential recipients and their acceptance of living kidney donor transplantation. As strategies to collect long-term data on donor outcomes are improved, involving donor registries, it is critical that the outcomes reported are useful to all stakeholders, and measured in a more consistent way. Therefore, this study should lead to further work to identify standardised outcome measures which are meaningful and relevant to all stakeholders, including recipients, donors and clinicians.[79,80]

8.6 Conclusion

In conclusion, the studies that form this body of work provide a comprehensive and in-depth understanding of the perspectives and experiences of key stakeholders involved in living kidney donor transplantation. These studies highlight the inherent psychological, cultural and social implications of living kidney donor transplantation, and the importance of identifying and developing interventions to address these issues. The findings also highlight the need for culturally sensitive, family-oriented, educational and psychosocial support to resolve recipient ambivalence and help patients find an acceptable approach to engaging in discussions with potential donors. There is a need for greater consensus and standardised practice regarding complex medical psychosocial transplant candidates, and greater transparency on the part of centre practices. The psychosocial challenges of live donor evaluation must be addressed, including efforts to ensure donors can express their fears and concerns and adequately prepare for donation. Understanding of the risks and benefits of undergoing living kidney donation was shown to be central to the decisions of donors, recipients and nephrologists. Improved reporting and measurement of donor-relevant and long-term clinical outcomes could lead to better informed consent practices and evidence-based decision-making in living kidney donation. Overall, the acknowledgement of stakeholder perspectives in guidelines, education, research and practice could ensure equitable decision-making, alleviate barriers and disparities, and improve satisfaction and outcomes for recipients and their donors.

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APPENDICES

Appendix A: Supporting data for Chapter 3

A.1. Search strategy

OVID Medline 1948 - 19th February 2013
exp Adult/ or exp Young Adult/
exp Patients/
exp Renal Insufficiency/
exp Renal Dialysis/ or exp Dialysis/
exp Peritoneal Dialysis/
exp Peritoneal Dialysis, Continuous Ambulatory/
(haemodialysis or hemodialysis).tw.
peritoneal dialysis.tw.
exp Kidney Transplantation/
kidney transplant recipient$.tw.
exp "Quality of Life"/
exp Psychology, Social/
exp Adaptation, Psychological/
exp Stress, Psychological/
exp Depression/
anxiety/
mental health/
social support/
social adjustment/
communication/
emotions/
interpersonal relations/
satisfaction/
family/
exp Marriage/
Life Change Events/
exp Qualitative Research/
qualitative.tw.
interview$.tw.
focus group$.tw.
exp Living Donors/
(live donor$ or living donor$ or live donation or living donation).tw.
(liv$ adj kidney).tw.

Embase 1996 - 18th February 2013
1996 - 18th February 2013
adult/
exp patient/ or exp chronic patient/
exp chronic kidney failure/
exp dialysis/
exp peritoneal dialysis/
exp continuous ambulatory peritoneal dialysis/
(haemodialysis or hemodialysis).tw.
peritoneal dialysis.tw.
exp graft recipient/ or exp kidney transplantation/
kidney transplant recipient$.tw.
"quality of life"/
social psychology/
adaptation/ or adaptive behavior/

mental stress/
depression/
anxiety/
mental health/
social aspect/ or social support/
self-esteem/
interpersonal communication/
patient satisfaction/
marriage/ or family/
lifestyle/ or lifestyle modification/
life event/
decision making/
qualitative.tw.
interview$.tw.
focus group$.tw.
exp living donor/
(live donor$ or living donor$ or live donation or living donation).tw.
(liv$ adj kidney).tw.

PsycINFO 1809 - 13th February 2013
exp Kidney Diseases/
exp Dialysis/
(haemodialysis or haemodialysis).tw
peritoneal dialysis.tw
kidney transplantation.tw.
kidney transplant recipient$.tw.
exp "Quality of Life"/
qualitative$.tw.
(interview$ or focus group$). tw

CINAHL 1959 to Week 3 2011
TX chronic kidney disease OR TX dialysis OR TX transplantation
Qualitative research (clinical queries – best balance)
TX living donor OR live donor OR living donation
TX live kidney OR living kidney

Appendix B: Supporting data for Chapter 4

B.1. Focus group question guide

Questions	**We would first like you to think about your experiences leading up to the donation:**
1.	What were the factors that made it easier for you to donate and complete the evaluation process? (*Information, education, psychosocial and financial support, family support).*
2.	Were there any barriers or challenges that you had to overcome? How did you overcome them? (*Risk information, fears and concerns, eligibility, family opposition, religious and cultural values)*
3.	Did you have any concerns about outcomes of donation for yourself? (*Medical, lifestyle, psychological, social financial)* What helped you to donate, despite your concerns?
4.	What were your experiences of the informed consent process? What did you think were the goals of informed consent? How effective was this process?

Appendix C: Supporting data for Chapter 5

C.1. Interview guide

Introduction

Briefly, could you describe your role in transplantation?

Beliefs about living kidney donation

What are 2-3 things that you personally consider to be the main benefits of living kidney donor transplantation? Do you have any concerns about any aspect of living kidney donor transplantation?

Compared to your colleagues, would you describe yourself as being more liberal, or conservative, with regards to recipient eligibility for living kidney donor transplantation? Why?

In terms of a patient's eligibility for living kidney donor transplantation, are there any additional or different considerations compared with deceased donor transplantation – why?

Do you think the proportion or number of kidney transplants from living donors should be higher or lower on a national level?

To what extent do you think that living donor transplantation needs 'promotion' in Australia?

Barriers and disparities in living kidney donation (patient, clinician, centre factors)

What do you believe are the main barriers to a patient receiving a living kidney donor transplant?

Do you believe there are any disparities in access to kidney transplantation in Australia – why?

Do you think that any factors relating to the specific nephrologist a patient sees might impact upon their likelihood of considering living kidney donor transplantation?

Can you speculate why some Australian transplant centres have higher rates of living kidney donor transplantation than others?

Suggestions for policy and practice

Do you have any suggestions for changes to policy or practice to:

Address barriers and disparities?

Increase access to living kidney donation?

Improve discussion and patient education around living kidney donor transplantation?

Close

Do you have any other thoughts about living kidney donation that you would like to add?

Appendix D: Supporting data for Chapter 6

D.1. Individual ranking of all outcomes

Rank Position	Outcome	Importance score	N groups listing outcome	N donors ranking outcome	Rank position Australia	Importance score Australia	Rank position Canada	Importance score Canada
1	Kidney function	0.40	14	120	4	0.26	1	0.57
2	Time to recovery	0.27	14	115	2	0.34	5	0.19
3	Surgical complications	0.24	14	120	6	0.20	2	0.29
4	Impact on family	0.22	11	87	1	0.35	19	0.07
5	Donor-recipient relationship	0.21	14	112	3	0.27	8	0.15
6	Life satisfaction	0.18	13	102	7	0.17	4	0.20
7	Lifestyle restrictions	0.18	12	97	5	0.21	6	0.15
8	Kidney failure	0.14	10	81	19	0.07	3	0.22
9	Mortality/survival	0.13	12	97	11	0.12	7	0.15
10	Acute pain/discomfort	0.12	12	99	9	0.15	16	0.10
11	Blood pressure	0.12	14	111	13	0.11	9	0.14
12	Physical function	0.12	9	83	8	0.16	18	0.08
13	Surgical mortality	0.11	13	101	12	0.12	14	0.10
14	Fatigue	0.11	12	94	18	0.08	10	0.14
15	Diabetes	0.10	13	107	15	0.09	11	0.12
16	Financial impact	0.10	14	107	10	0.13	20	0.07
17	Cardiovascular disease	0.20	14	112	14	0.09	13	0.10
18	Depression	0.09	12	94	16	0.09	15	0.10
19	Anxiety	0.09	13	91	17	0.09	17	0.09
20	Chronic pain/discomfort	0.08	11	84	22	0.06	12	0.11
21	Pregnancy	0.06	14	97	23	0.06	21	0.06
22	Weight	0.05	9	64	25	0.05	22	0.05
23	Caregiver responsibilities	0.05	3	27	21	0.09	23	0.03
24	Cholesterol	0.04	5	45	20	0.07	28	0.00
25	Fertility	0.03	7	58	24	0.06	-	-
26	Career impact	0.02	3	27	32	0.02	24	0.03
27	Insurance	0.02	4	35	26	0.04	-	-
28	Gout	0.02	5	43	27	0.03	-	-
29	Self-esteem/body image	0.02	3	24	28	0.03	-	-
30	Anaemia	0.02	1	15	29	0.03	-	-
31	Bone issues	0.02	4	31	30	0.03	-	-
32	Intimacy/sex drive	0.01	2	19	31	0.02	-	-
33	Kidney stones	0.01	1	7	-	-	25	0.02
34	Urinary tract infection	0.01	1	7	-	-	26	0.01
35	Length of stay	0.01	1	8	-	-	27	0.01

D.2. Location and number of participants in each nominal group

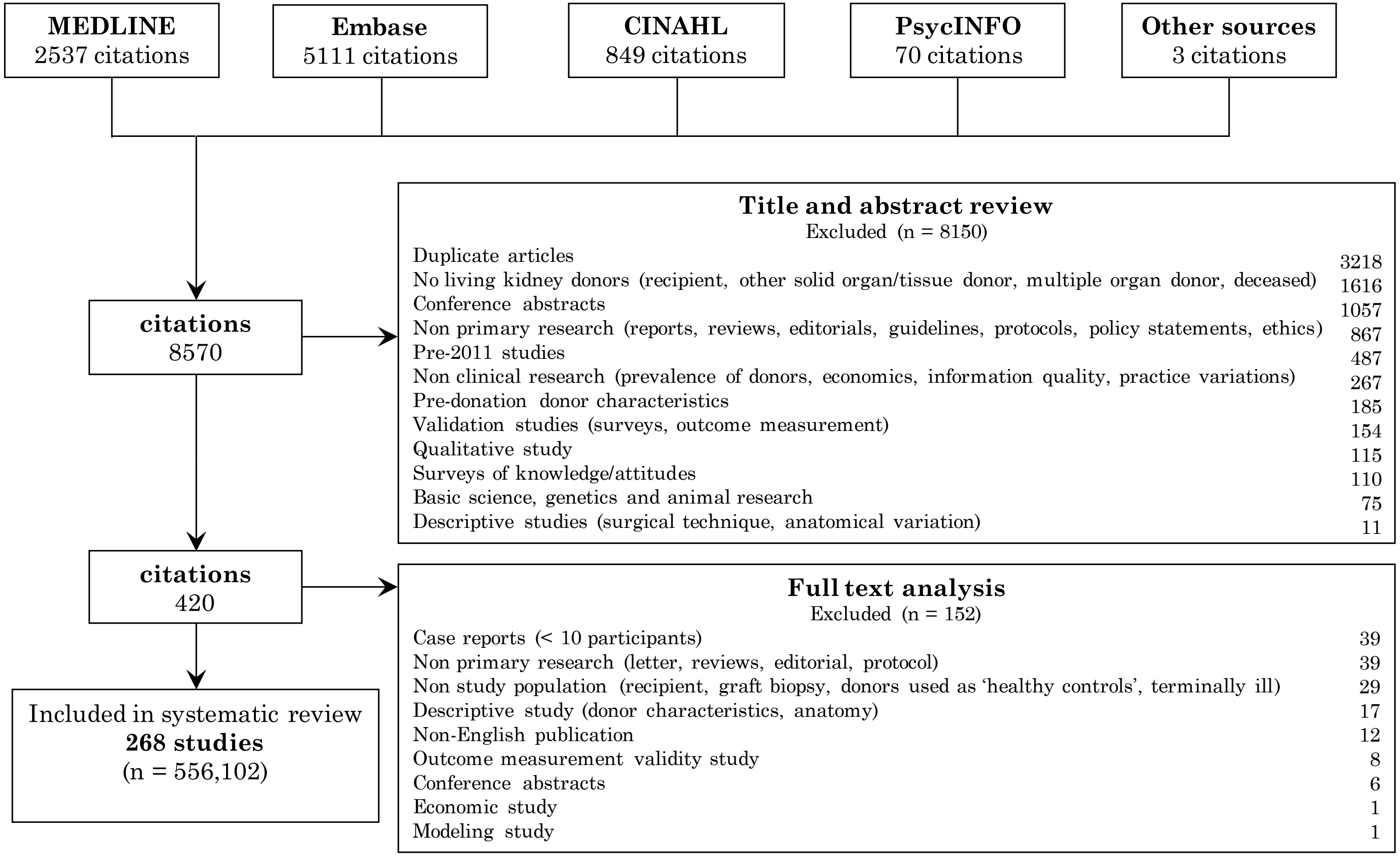
Group ID	**City**	**Participants (n = 123)**
1	Melbourne	7
2	Melbourne	9
3	Melbourne	9
4	Melbourne	10
5	Sydney	5
6	Sydney	10
7	Sydney	8
8	Sydney	9
9	Vancouver	12
10	Vancouver	9
11	Vancouver	11
12	Vancouver	9
13	Vancouver	9
14	Vancouver	6

D.3. Focus group run sheet

Time	**Details**	**Notes**
Phase 1 – Welcome and introductions, ice-breaker and objectives		
10mins	**Welcome** Good [morning/afternoon] everyone. Thank you for attending this focus group to discuss your experiences and perspectives of living kidney donation. My name is ______ from the University of Sydney. **Introduction** We have invited you here because you have experience with living kidney donation. For this session, we would like you to reflect on your experiences **after** living kidney donation. This will help us to understand how donating a kidney has impacted on you, and what aspects of your experience may be more important, and those that may be less important to you. We want you to share insights from your own personal experiences and we encourage you to listen and consider other members' views, and engage in a conversation with each other. The goal of this session is to identify outcomes that are important to you, and to understand the reasons why they are important to you. We want future research to focus on outcomes that are most important to you, as well as information and support that is provided to donors. **Confidentiality and voluntary participation** What you tell us will be recorded but will be kept confidential. Nothing you say will be traced back to you or your name. Also, what you say will not impact the level or type of care you receive. Please note that we are unable to provide clinical advice about your health. You are free to leave at any time without providing a reason. We would also appreciate it if you could please keep this discussion confidential, to respect the other members in the group. **Ice breaker** To get to know you a bit better, could you introduce yourself by telling us: a) Your name b) The first thing that comes to your mind when I say "kidney donor"	
Phase 2 – Focus group discussion		
30 mins	**Experiences/impact of living donation** We would now like to invite you to share your ideas and experiences of donating a kidney: • Has donating a kidney impacted on your life - in what ways? • Did anything happen to you after kidney donation that was unexpected? • What outcomes are most challenging to deal with - why and how do you cope with it?	
Phase 3 – Nominal group Technique (Part 1) (40 minutes)		
40 mins	Now we are going to have a more focused discussion and an activity to find out what outcomes of kidney donation matter to you most and why. Let me give you a bit of context. There are a variety of outcomes that might be experienced by kidney donors. That is, anything that arises or changes, directly as a result of donating a kidney, be it a positive or negative impact. There are research studies being conducted worldwide that are looking to determine the impacts of donating a kidney. For example, they might look at whether kidney	

	donation impacts on the long-term kidney function of donors. We want to know what outcomes matter most to you, so that we can ensure that research focuses on those outcomes. I am going to ask you a question and get you to write down **three** ideas: *What outcomes do you suggest that researchers should include in their study, if they are looking to explore the impact of donating a kidney?* Please write down your 3 ideas now and then we will share them with each other. Now, I would like you to share your ideas. I am going to go around the table and ask each of you to give me one or two ideas from your worksheet. After the entire list is on the board, we will discuss and clarify the ideas. We are now going to include some outcomes [impacts] that other patients told us in the past, or outcomes that have been included in recent research studies. [write on whiteboard, read them out, and clarify] Are any of the outcomes unclear to anyone? If not, we will take a short break while we print out the list of outcomes. We will then rank these items from most important to least important.	
Break **(10 minutes)**		
10 mins	**Break** *Print list of outcomes for ranking.*	
	Phase 3 – Nominal group Technique (Part 2) **(30 minutes)**	
30 mins	Now we are going to look at all the ideas raised by the group and I will ask you to rank them in order of most important to least important to you. If you find it difficult to rank the whole list, please try to rank the top 20. Now we will have a discussion to discuss any similarities and differences in ranking. What did everyone put as: number 1, number 2, number 3, least important? Would anyone like to explain why they ranked (22) or how they made their decisions about ranking? Why do you think most people ranked (22) high/low? Why do you think there are differences in ranking of (22)?	
Wrap up **(1 minute)**		
1 min	**Wrap up** *Wrap up, acknowledgement.* *Thank you and closing remarks.*	

Appendix E: Supporting data for Chapter 7



Title and abstract review

Excluded (n = 8150)

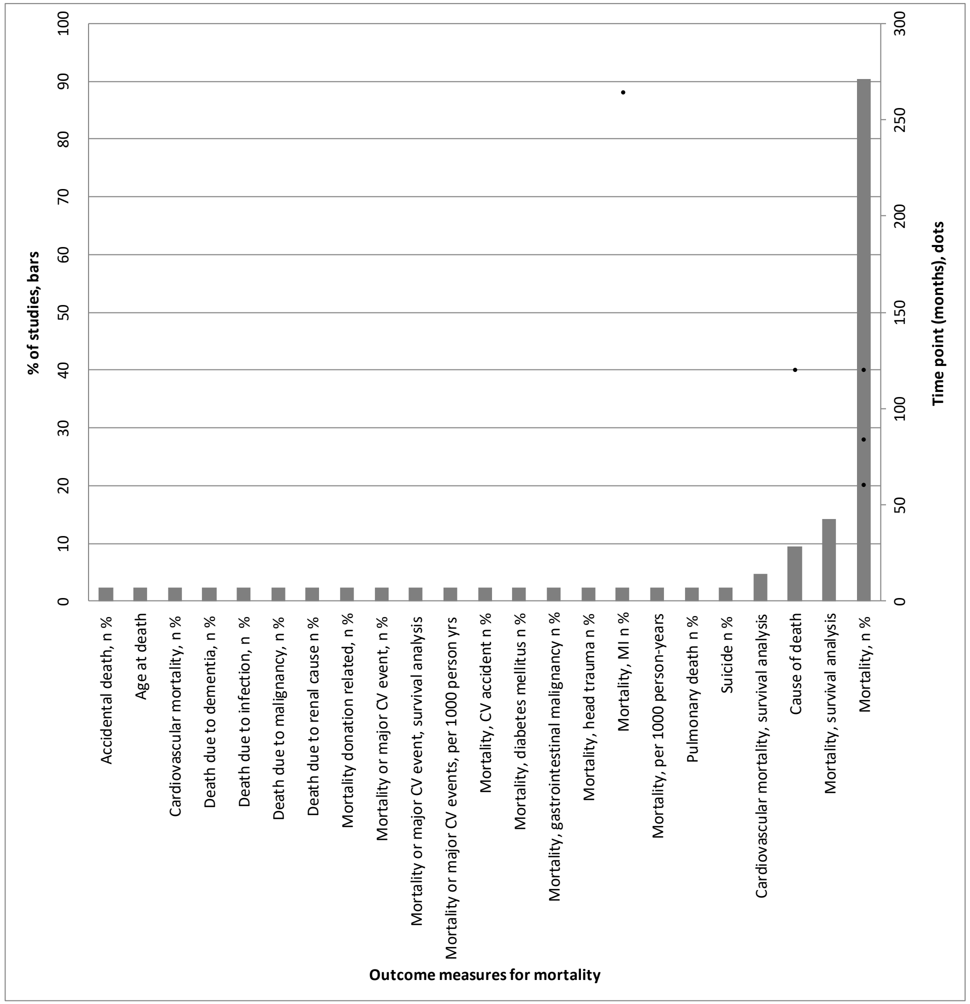
Duplicate articles	3218
No living kidney donors (recipient, other solid organ/tissue donor, multiple organ donor, deceased)	1616
Conference abstracts	1057
Non primary research (reports, reviews, editorials, guidelines, protocols, policy statements, ethics)	867
Pre-2011 studies	487
Non clinical research (prevalence of donors, economics, information quality, practice variations)	267
Pre-donation donor characteristics	185
Validation studies (surveys, outcome measurement)	154
Qualitative study	115
Surveys of knowledge/attitudes	110
Basic science, genetics and animal research	75
Descriptive studies (surgical technique, anatomical variation)	11

Full text analysis

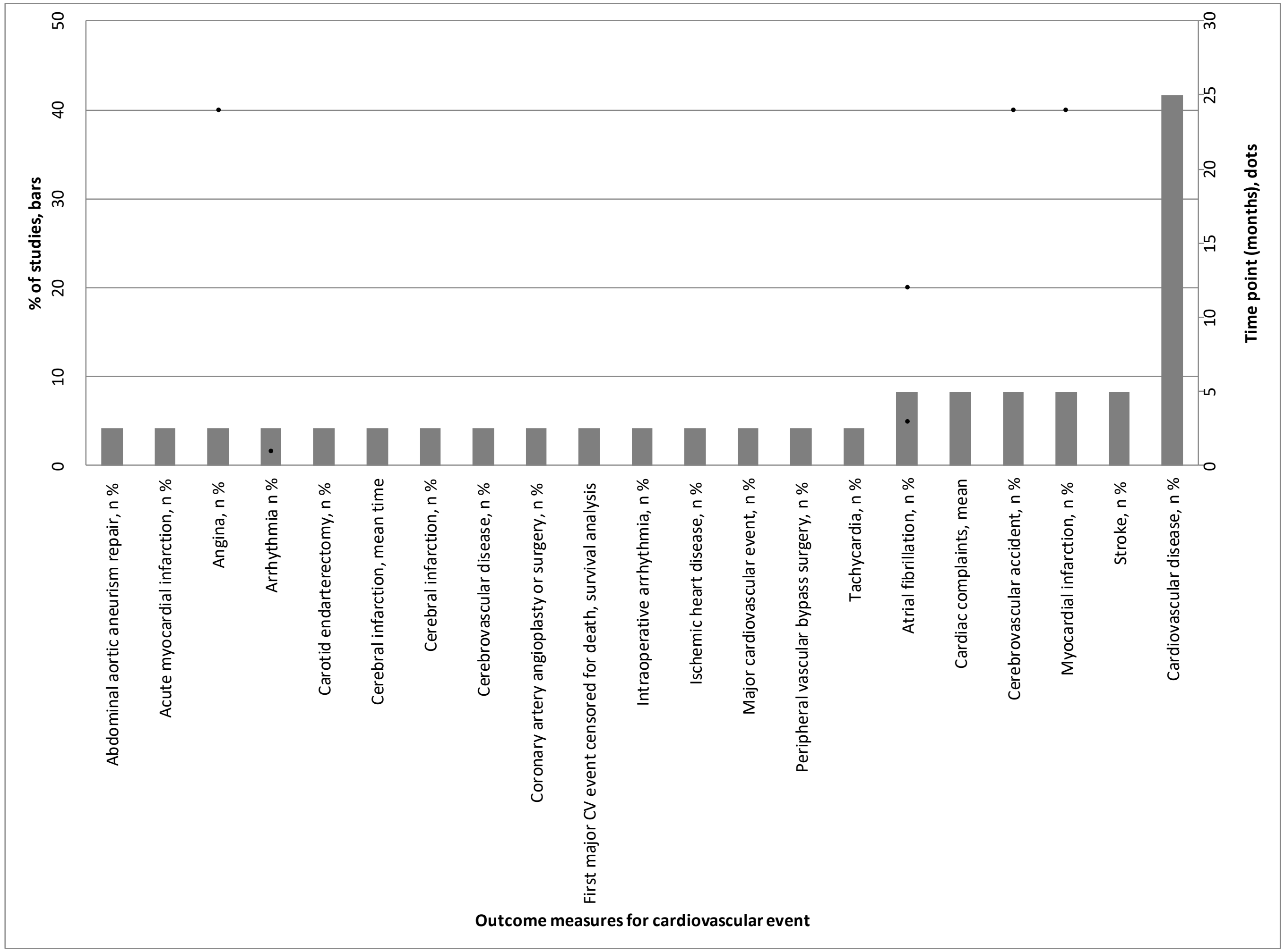
Excluded (n = 152)

Case reports (< 10 participants)	39
Non primary research (letter, reviews, editorial, protocol)	39
Non study population (recipient, graft biopsy, donors used as ‘healthy controls’, terminally ill)	29
Descriptive study (donor characteristics, anatomy)	17
Non-English publication	12
Outcome measurement validity study	8
Conference abstracts	6
Economic study	1
Modeling study	1

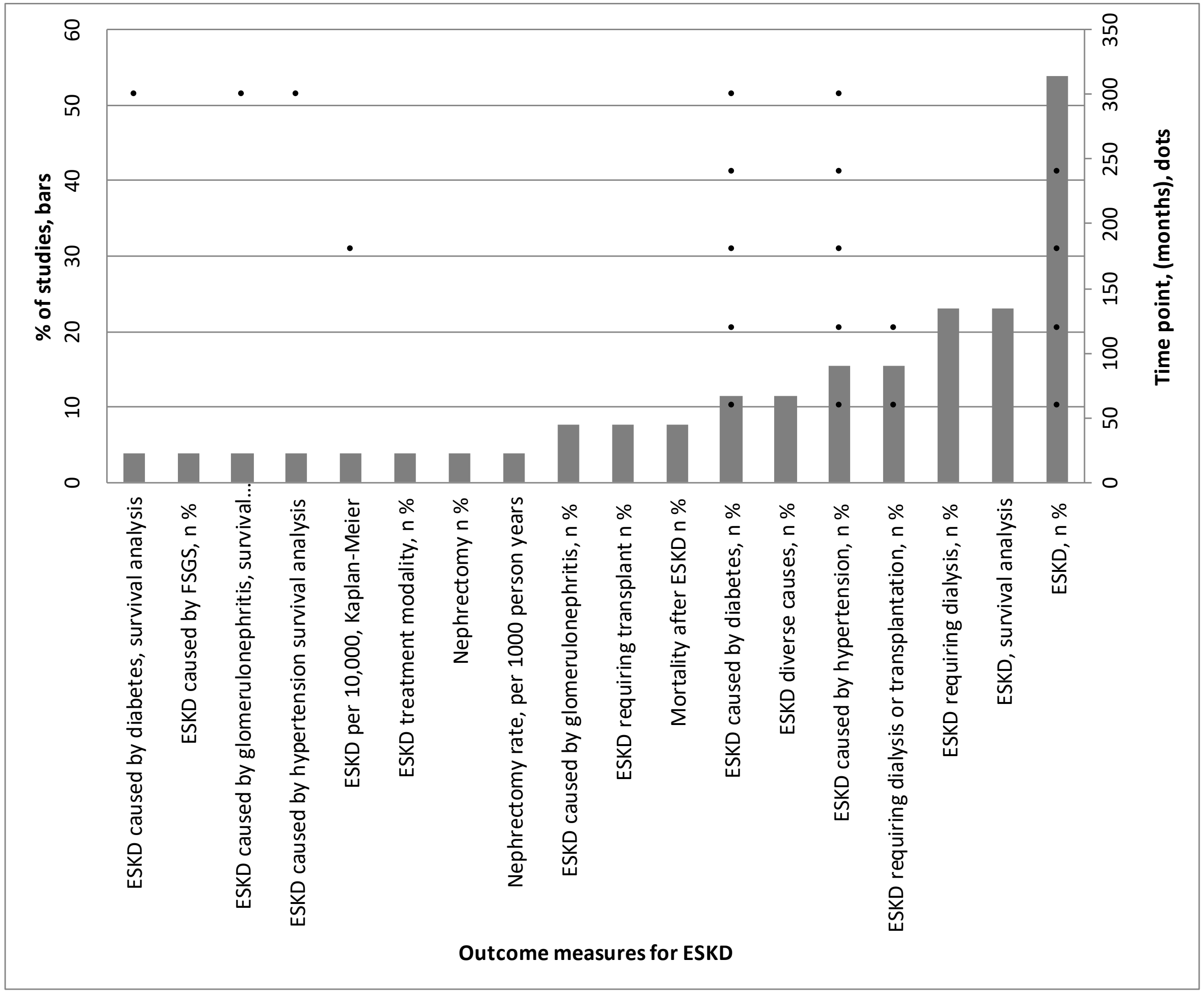
E.1. Search results



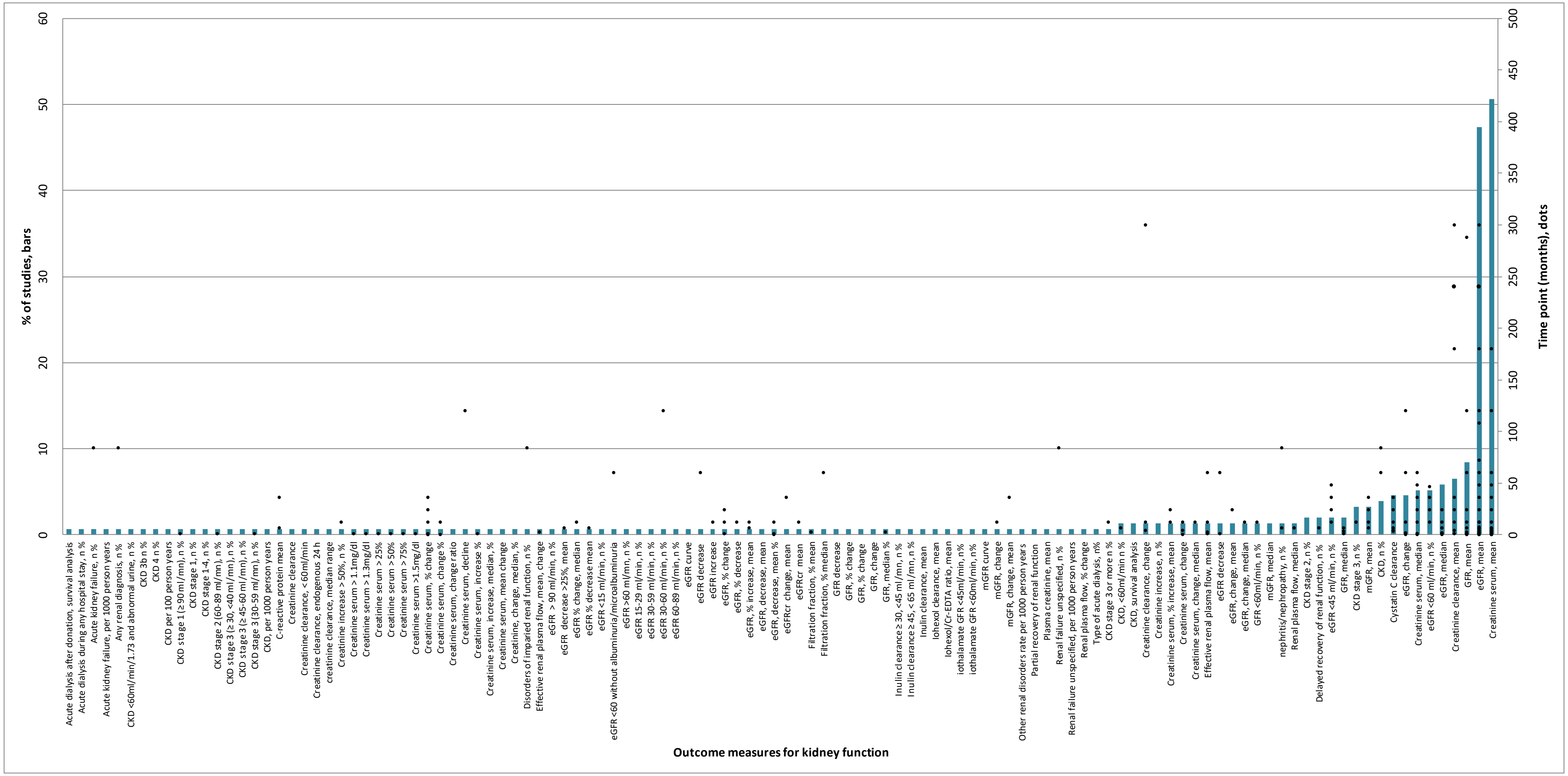
E.2. Frequency of outcome measures (definitions and time points) among trials reporting mortality (42 studies, 23 outcome measures).



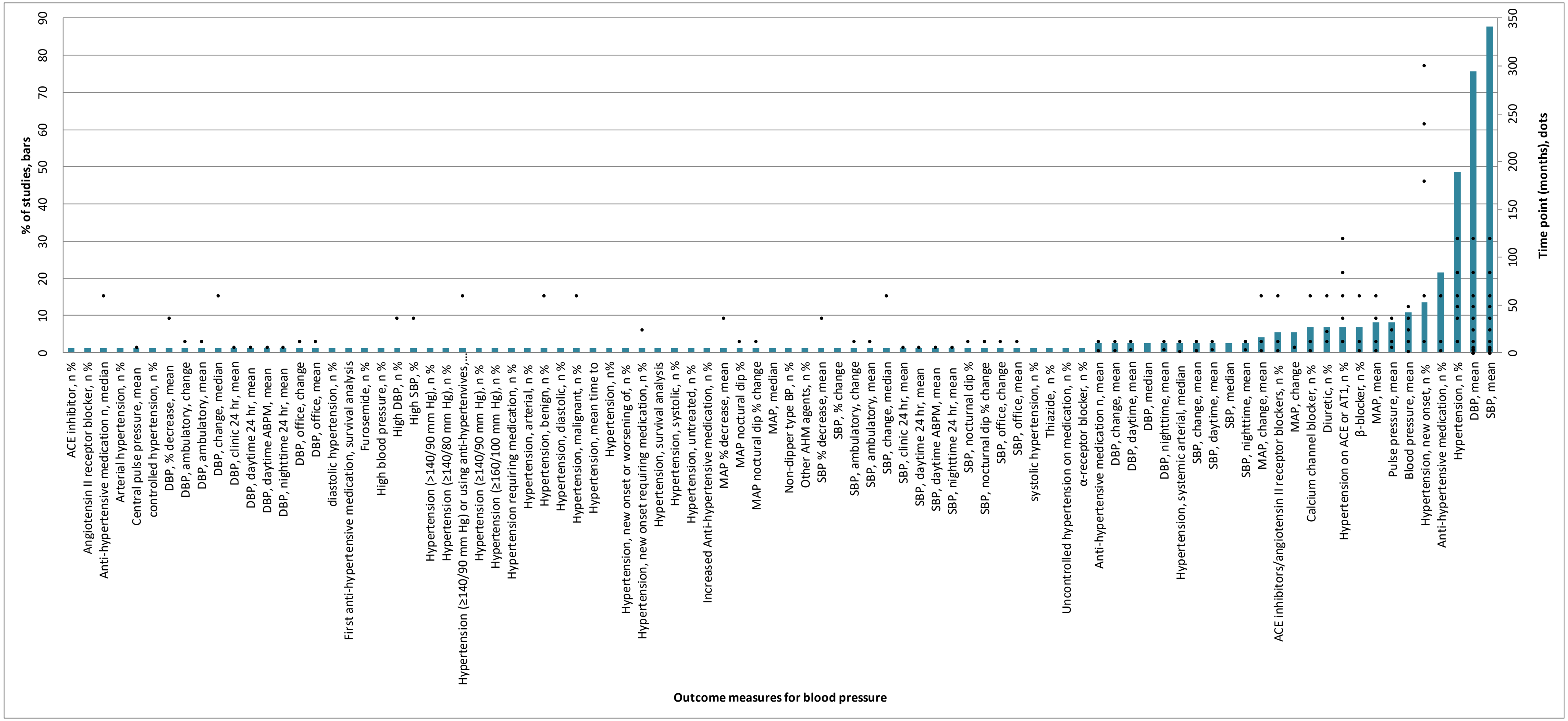
E.3. Frequency of outcome measures (definitions and time points) among trials reporting cardiovascular event (24 studies, 21 outcome measures).



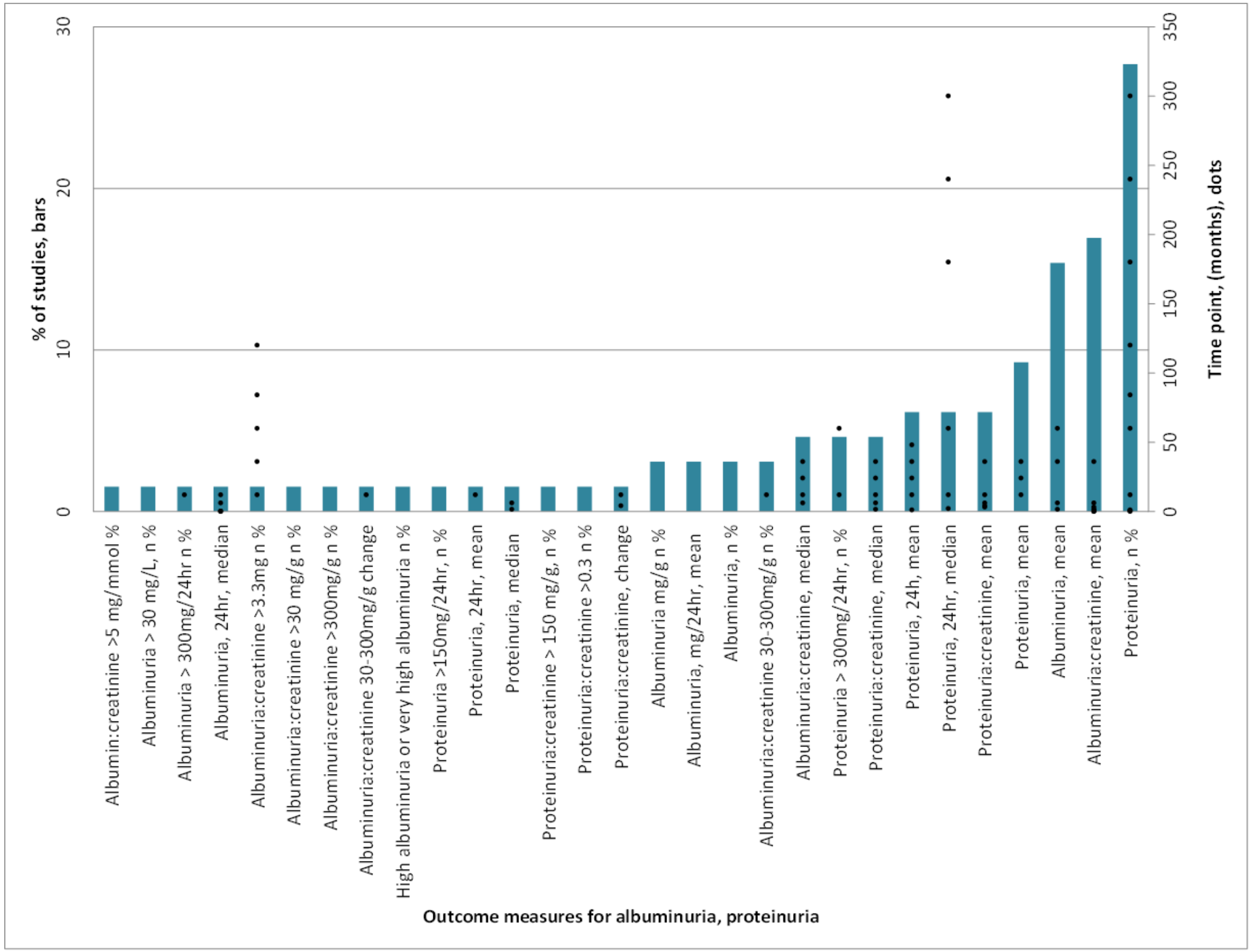
E.4. Frequency of outcome measures (definitions and time points) among trials reporting ESKD (26 studies, 18 outcome measures).



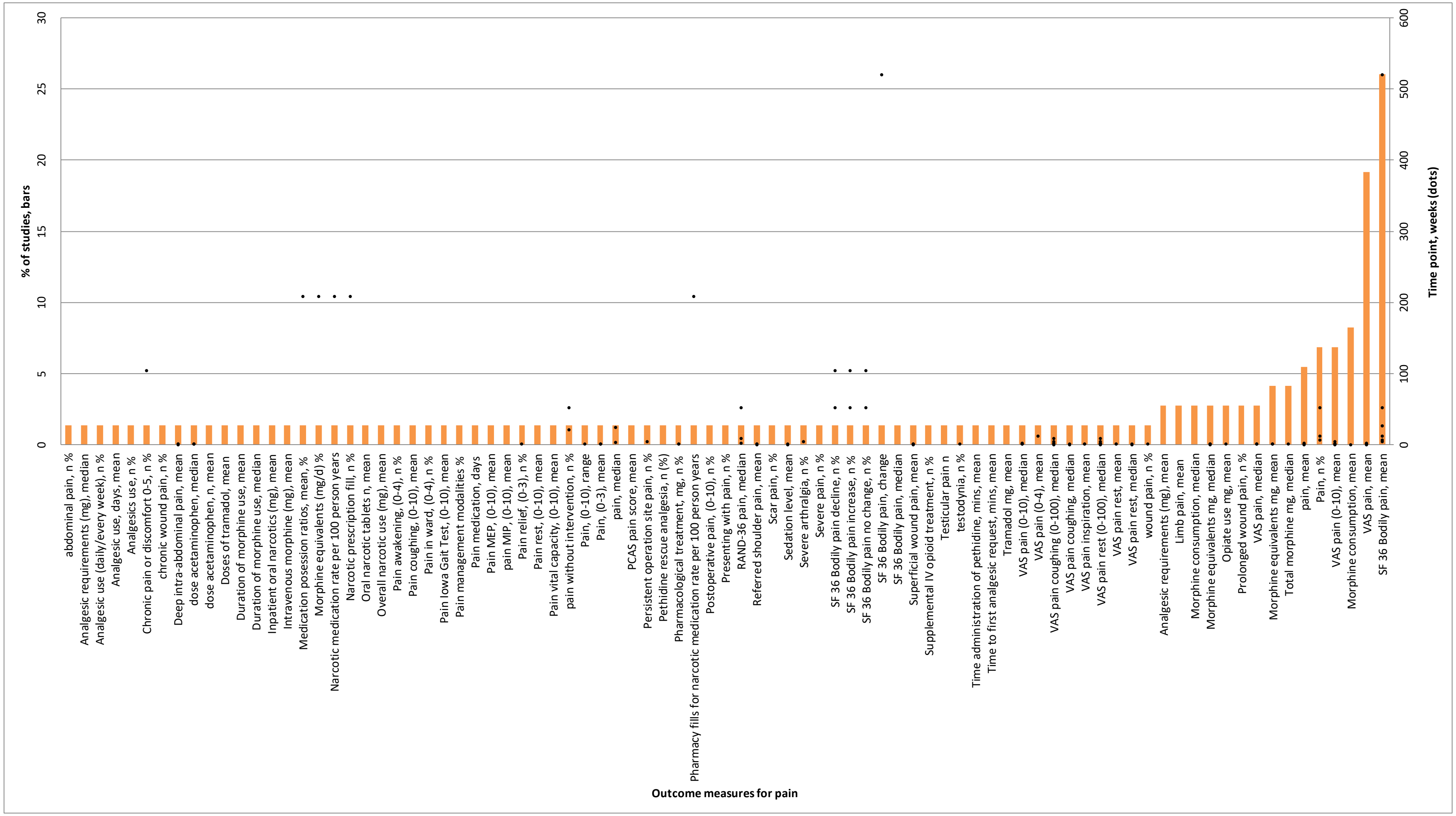
E.5. Frequency of outcome measures (definitions and time points) among trials reporting kidney function (154 studies, 116 outcome measures).



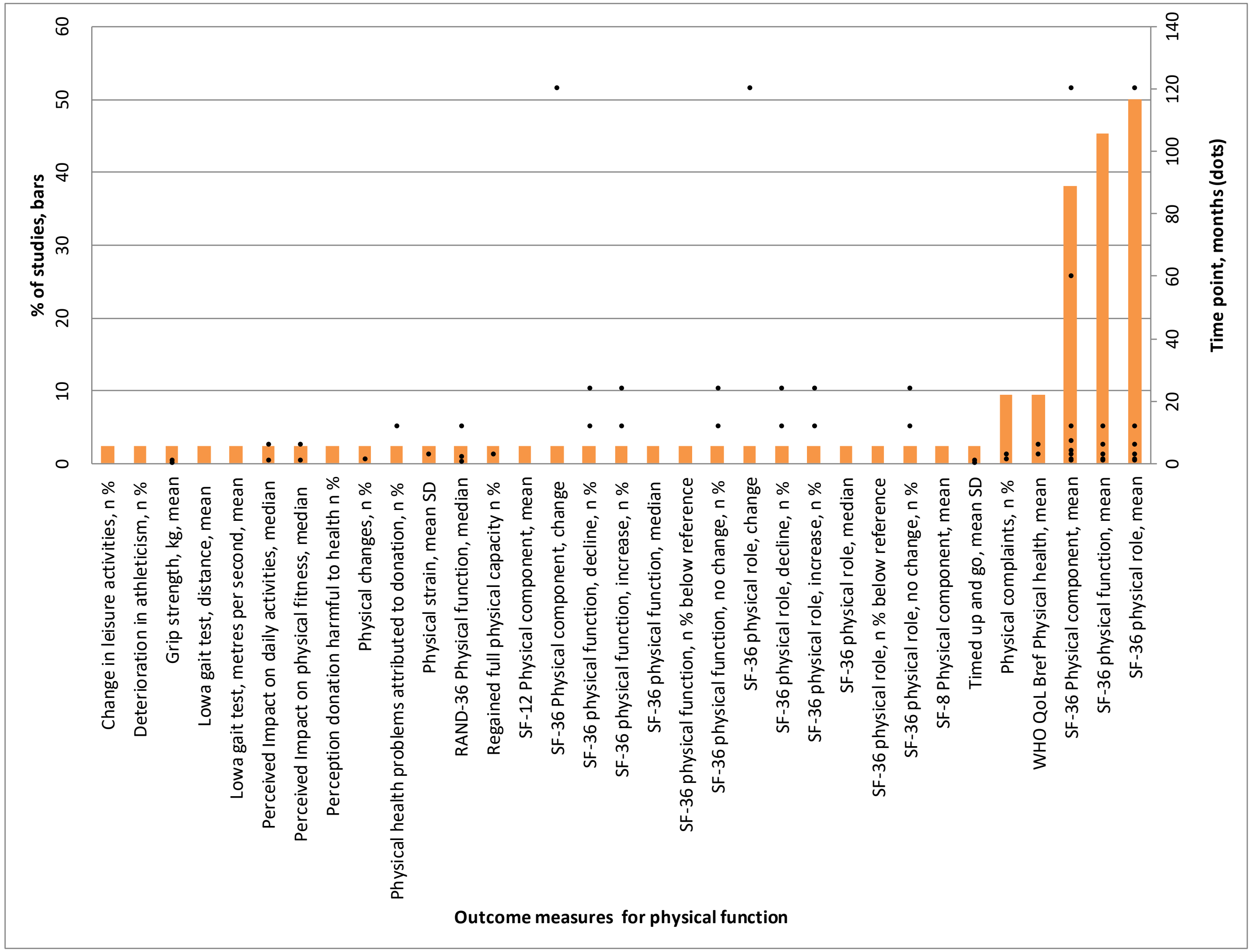
E.6. Frequency of outcome measures (definitions and time points) among trials reporting blood pressure (74 studies, 88 outcome measures).



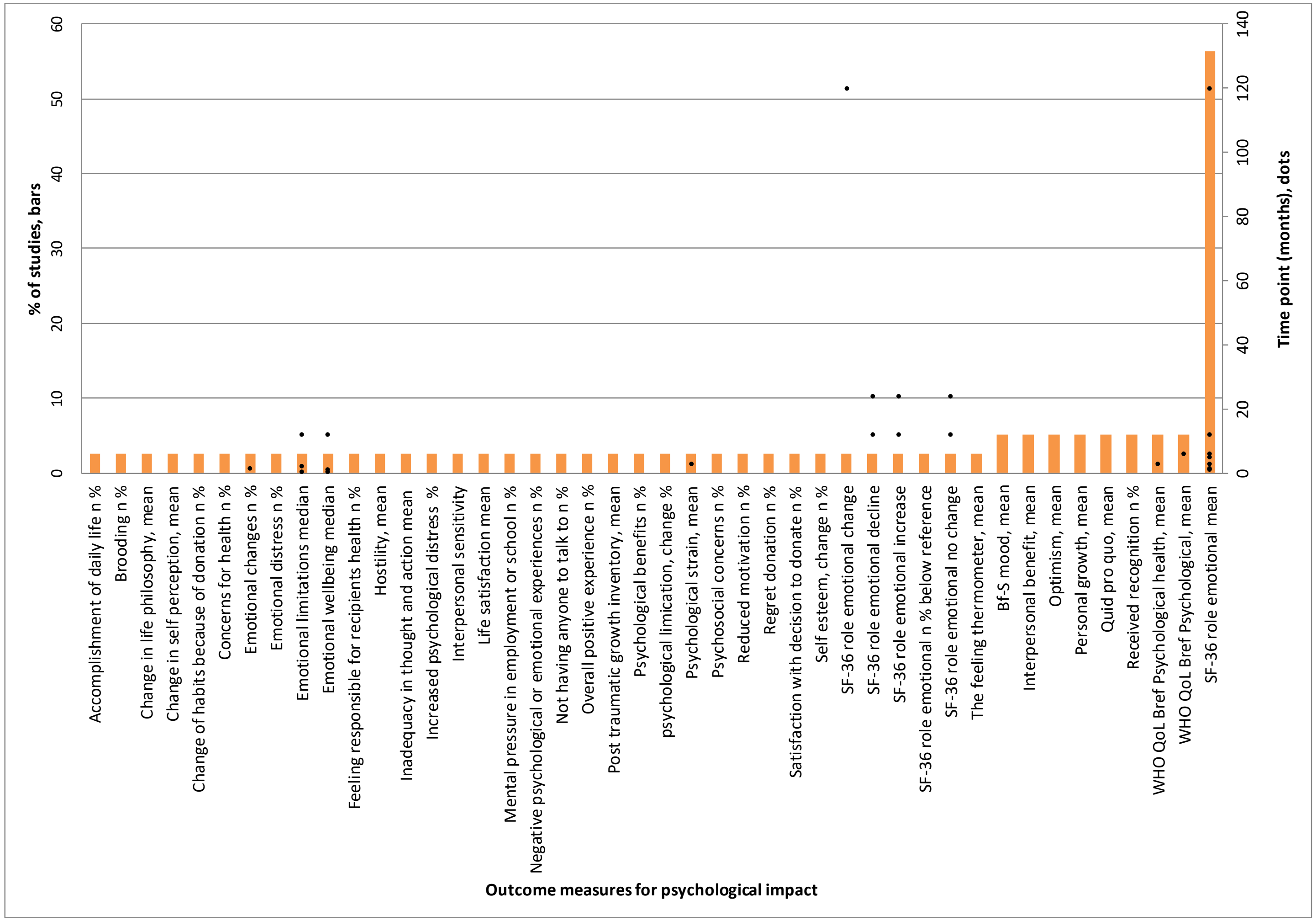
E.7. Frequency of outcome measures (definitions and time points) among trials reporting proteinuria/ albuminuria (65 studies, 29 outcome measures).



E.8. Frequency of outcome measures (definitions and time points) among trials reporting pain (73 studies, 75 outcome measures).



E.9. Frequency of outcome measures (definitions and time points) among trials reporting physical function (42 studies, 33 outcome measures)



E.10. Frequency of outcome measures (definitions and time points) among trials reporting psychological impact (39 studies, 44 outcome measures).

E.11. Search Strategy

MEDLINE **January 2006 - May 2017**	**Embase** **January 2006 - May 2017**	**PsycINFO** **January 2006 - May 2017**
Liv$ donor nephrect$	Liv$ donor nephrect$	Liv$ donor nephrect$
Liv$ kidney donor$	Liv$ kidney don$	Liv$ kidney don$
Living Donors/ and Kidney/	Living donor/ kidney/	

E.12. Proportion of studies reporting each clinical outcome (268 studies, 51 outcome domains)

Domains (clinical outcomes)	**All (n = 268)**
Time to discharge	96 (35.8)
Blood loss	85 (31.7)
Operative time	79 (29.5)
Complication (unspecified)	62 (23.1)
Postoperative complication (unspecified)	43 (16.0)
Mortality	42 (15.7)
Surgical site infection	41 (15.3)
Conversion to open surgery	40 (14.9)
Hospital readmission	31 (11.6)
Perioperative injury	29 (10.8)
ESKD	26 (9.7)
Postoperative bowel function	26 (9.7)
Cardiovascular event	24 (9.0)
Hernia	24 (9.0)
General infection	23 (8.6)
Reoperation	23 (8.6)
Intraoperative complication (unspecified)	21 (7.8)
Diabetes	20 (7.5)
Pulmonary event	18 (6.7)
Genitourinary function	16 (6.0)
Thrombosis/embolization	15 (5.6)
Appearance of incision	13 (4.9)
Wound complication	12 (4.5)
Chylous ascites	11 (4.1)
Nausea/vomiting	11 (4.1)
Gastrointestinal disorder	9 (3.4)
Fat necrosis/seroma	7 (2.6)
Fever	7 (2.6)
Paresthesia/hypoesthesia	7 (2.6)
Oedema	6 (2.2)
Cancer	5 (1.9)
Nephrolithiasis	5 (1.9)
Pruritus	5 (1.9)
Dehydration	3 (1.1)
Fertility	3 (1.1)
Gout	3 (1.1)
Pregnancy complications	3 (1.1)
Skin	3 (1.1)
Lymphatic fistula	2 (0.7)
Thyroid disease	2 (0.7)

Fracture	1 (0.4)
Hydrocele	1 (0.4)
Liver disease	1 (0.4)
Lupus	1 (0.4)
Metabolic syndrome	1 (0.4)
Osteoarthritis	1 (0.4)
Postoperative epigastric function	1 (0.4)
Septicemia	1 (0.4)
Tuberculosis	1 (0.4)

E.13. Proportion of studies reporting each surrogate outcome (268 studies, 35 outcome domains)

Domains (surrogate outcomes)	**All (n = 268)**
Kidney function	154 (57.5)
Blood pressure	74 (27.6)
Proteinuria, albuminuria	65 (24.3)
BMI/weight/composition	37 (13.8)
Lipids	29 (10.8)
Anaemia/haemoglobin/iron	21 (7.8)
Glucose metabolism	16 (6.0)
Uremic toxins and uric acid	14 (5.2)
Cardiovascular function	13 (4.9)
Inflammatory markers/oxidative stress	12 (4.5)
Kidney morphometry	12 (4.5)
Calcium	9 (3.4)
Phosphate	9 (3.4)
PTH	9 (3.4)
Urea	9 (3.4)
Bone metabolism	8 (3.0)
Vitamin D metabolism	5 (1.9)
Blood pressure regulating hormone	4 (1.5)
Kidney biomarker	4 (1.5)
Liver function	4 (1.5)
White blood cells	4 (1.5)
Calcification	3 (1.1)
Endothelial function	3 (1.1)
Kidney pathology	3 (1.1)
Kidney physiology	2 (0.7)
Sodium	2 (0.7)
Adrenal function	1 (0.4)
Calcium x phosphate	1 (0.4)
Cpk	1 (0.4)
Kidney hemodynamics	1 (0.4)
Magnesium	1 (0.4)
Medication (unspecified)	1 (0.4)
Potassium	1 (0.4)
Respiratory function	1 (0.4)
Vitamin A metabolism	1 (0.4)

E.14. Proportion of studies reporting each donor-reported outcome (268 studies, 23 outcome domains)

Domains (patient-reported outcomes)	All (n = 268)
Pain	73 (27.2)
Physical function	42 (15.7)
Psychological impact	39 (14.6)
Mental health	37 (13.8)
Quality of life (global)	35 (13.1)
Social functioning	33 (12.3)
Fatigue/energy	27 (10.1)
Satisfaction with donation	17 (6.3)
Recovery - global return to activity	17 (6.3)
Cosmetic satisfaction	16 (6.0)
Depression	16 (6.0)
Financial impact	15 (5.6)
Employment	13 (4.9)
Anxiety	11 (4.1)
Donor-recipient relationship	9 (3.4)
Sexual function	4 (1.5)
Sleep	4 (1.5)
Muscle weakness	3 (1.1)
Spiritual impact	3 (1.1)
Life satisfaction	2 (0.7)
Caregiver burden	1 (0.4)
Cognition	1 (0.4)
Education attainment	1 (0.4)

E.15. Frequency of all outcome domains reported in therapy studies (91 studies, 70 outcome domains)

Outcome domains	Number of studies	% (/91 studies)	Classification
Time to discharge	72	79.1	Clinical
Blood loss	66	72.5	Clinical
Operative time	62	68.1	Clinical
Donor complication (unspecified)	45	49.5	Clinical
Kidney function	45	49.5	Surrogate
Pain	40	44.0	Donor-reported
Conversion to open surgery	34	37.4	Clinical
Donor postoperative complication (ns)	31	34.1	Clinical
Surgical site infection	27	29.7	Clinical
Perioperative injury	25	27.5	Clinical
Postoperative bowel function	19	20.9	Clinical
Donor intraoperative complication (ns)	18	19.8	Clinical
General infection	16	17.6	Clinical
Hernia	16	17.6	Clinical
Hospital readmission	16	17.6	Clinical
Reoperation	15	16.5	Clinical
Appearance of incision	13	14.3	Clinical
Cosmetic satisfaction	13	14.3	Donor-reported
Physical function	11	12.1	Donor-reported
Thrombosis/embolization	11	12.1	Clinical
Recovery - global return to activity	10	11.0	Donor-reported
Fatigue/energy	9	9.9	Donor-reported
Mortality	9	9.9	Clinical
Pulmonary event	9	9.9	Clinical
Chylous ascites	8	8.8	Clinical
Psychological impact	8	8.8	Donor-reported
Social functioning	8	8.8	Donor-reported
Anaemia/haemoglobin/iron	7	7.7	Surrogate
Genitourinary function	7	7.7	Clinical
Nausea/vomiting	7	7.7	Clinical
Quality of life (global)	7	7.7	Donor-reported
Wound complication	7	7.7	Clinical
Cardiovascular event	6	6.6	Clinical
Fat necrosis/seroma	6	6.6	Clinical
Mental health	6	6.6	Donor-reported
Blood pressure	5	5.5	Surrogate
Fever	5	5.5	Clinical
Oedema	4	4.4	Clinical
Paraesthesia/hypoesthesia	4	4.4	Clinical

Proteinuria, albuminuria	4	4.4	Surrogate
Satisfaction with donation	4	4.4	Donor-reported
Employment	3	3.3	Donor-reported
Financial impact	3	3.3	Donor-reported
Gastrointestinal disorder	3	3.3	Clinical
Sexual function	3	3.3	Donor-reported
Anxiety	2	2.2	Donor-reported
ESKD	2	2.2	Clinical
Fertility	2	2.2	Clinical
Kidney biomarker	2	2.2	Surrogate
liver function	2	2.2	Surrogate
lymphatic fistula	2	2.2	Clinical
Pruritus	2	2.2	Clinical
Skin	2	2.2	Clinical
Adrenal function	1	1.1	Surrogate
Blood pressure regulating hormone	1	1.1	Surrogate
BMI/weight/composition	1	1.1	Surrogate
Creatinine phosphokinase (Cpk)	1	1.1	Surrogate
Dehydration	1	1.1	Clinical
Depression	1	1.1	Donor-reported
Glucose metabolism	1	1.1	Surrogate
Hydrocele	1	1.1	Clinical
Inflammatory markers/oxidative stress	1	1.1	Surrogate
Lipids	1	1.1	Surrogate
Postoperative epigastric function	1	1.1	Clinical
Pregnancy complications	1	1.1	Clinical
Respiratory function	1	1.1	Surrogate
Septicaemia	1	1.1	Clinical
Sodium	1	1.1	Surrogate
Uremic toxins and uric acid	1	1.1	Surrogate
White blood cells	1	1.1	Surrogate

E.16: Frequency of all outcome domains reported in prognosis studies (177 studies, 100 outcome domains)

Outcome domains	Number of studies	% (/177studies)	Classification
Kidney function	109	61.6	surrogate
Blood pressure	69	39.0	surrogate
Proteinuria, albuminuria	61	34.5	surrogate
BMI/weight/composition	36	20.3	surrogate
Mortality	33	18.6	clinical
Pain	33	18.6	donor-reported
Mental health	31	17.5	donor-reported
Physical function	31	17.5	donor-reported
Psychological impact	31	17.5	donor-reported
Lipids	28	15.8	surrogate
Quality of life (global)	28	15.8	donor-reported
Social functioning	25	14.1	donor-reported
ESKD	24	13.6	clinical
Time to discharge	24	13.6	clinical
Diabetes	20	11.3	clinical
Blood loss	19	10.7	clinical
Cardiovascular event	18	10.2	clinical
Fatigue/energy	18	10.2	donor-reported
Complication (unspecified)	17	9.6	clinical
Operative time	17	9.6	clinical
Depression	15	8.5	donor-reported
Glucose metabolism	15	8.5	surrogate
Hospital readmission	15	8.5	clinical
Anaemia/haemoglobin/iron	14	7.9	surrogate
Surgical site infection	14	7.9	clinical
Cardiovascular function	13	7.3	surrogate
Satisfaction with donation	13	7.3	donor-reported
Uremic toxins and uric acid	13	7.3	surrogate
Postoperative complication (unspecified)	12	6.8	clinical
Financial impact	12	6.8	donor-reported
Kidney morphometry	12	6.8	surrogate
Inflammatory markers/oxidative stress	11	6.2	surrogate
Employment	10	5.6	donor-reported
Anxiety	9	5.1	donor-reported
Calcium	9	5.1	surrogate
Donor-recipient relationship	9	5.1	donor-reported
Genitourinary function	9	5.1	clinical
Phosphate	9	5.1	surrogate
PTH	9	5.1	surrogate

Pulmonary event	9	5.1	clinical
Urea	9	5.1	surrogate
Bone metabolism	8	4.5	surrogate
Hernia	8	4.5	clinical
Reoperation	8	4.5	clinical
General infection	7	4.0	clinical
Postoperative bowel function	7	4.0	clinical
Recovery - global return to activity	7	4.0	donor-reported
Conversion to open surgery	6	3.4	clinical
Gastrointestinal disorder	6	3.4	clinical
Cancer	5	2.8	clinical
Nephrolithiasis	5	2.8	clinical
Vitamin D metabolism	5	2.8	surrogate
Wound complication	5	2.8	clinical
Nausea/vomiting	4	2.3	clinical
Perioperative injury	4	2.3	clinical
Sleep	4	2.3	clinical
Thrombosis/embolization	4	2.3	clinical
Blood pressure regulating hormone	3	1.7	surrogate
Calcification	3	1.7	surrogate
Chylous ascites	3	1.7	clinical
Cosmetic satisfaction	3	1.7	donor-reported
Intraoperative complication (unspecified)	3	1.7	clinical
Endothelial function	3	1.7	surrogate
Gout	3	1.7	clinical
Kidney pathology	3	1.7	surrogate
Muscle weakness	3	1.7	donor-reported
Paresthesia/hypoesthesia	3	1.7	clinical
Pruritus	3	1.7	clinical
Spiritual impact	3	1.7	donor-reported
White blood cells	3	1.7	surrogate
dehydration	2	1.1	clinical
Fever	2	1.1	clinical
Kidney biomarker	2	1.1	surrogate
Kidney physiology	2	1.1	surrogate
Life satisfaction	2	1.1	donor-reported
Liver function	2	1.1	surrogate
Oedema	2	1.1	clinical
Pregnancy complications	2	1.1	clinical
Thyroid disease	2	1.1	clinical
Calcium x phosphate	1	0.6	surrogate
Caregiver burden	1	0.6	donor-reported

Cognition	1	0.6	donor-reported
Education attainment	1	0.6	donor-reported
Fat necrosis/seroma	1	0.6	clinical
Fertility	1	0.6	clinical
Fracture	1	0.6	clinical
Kidney hemodynamics	1	0.6	surrogate
Liver disease	1	0.6	clinical
Lupus	1	0.6	clinical
Magnesium	1	0.6	surrogate
Medication (unspecified)	1	0.6	surrogate
Metabolic syndrome	1	0.6	clinical
Osteoarthritis	1	0.6	clinical
Potassium	1	0.6	surrogate
Sexual function	1	0.6	donor-reported
Skin	1	0.6	clinical
Sodium	1	0.6	surrogate
Tuberculosis	1	0.6	clinical
Viral hepatitis	1	0.6	clinical
Vitamin A metabolism	1	0.6	surrogate