Living kidney donation: outcomes, ethics, and uncertainty

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Since the first living-donor kidney transplantation in 1954, more than half a million living kidney donations have occurred and research has advanced knowledge about long-term donor outcomes. Donors in developed countries have a similar life expectancy and quality of life as healthy non-donors. Living kidney donation is associated with an increased risk of end-stage renal disease, although this outcome is uncommon (<0·5% increase in incidence at 15 years). Kidney donation seems to elevate the risks of gestational hypertension and pre-eclampsia. Many donors incur financial expenses due to factors such as lost wages, need for sick days, and travel expenses. Yet, most donors have no regrets about donation. Living kidney donation is practised ethically when informed consent incorporates information about risks, uncertainty about outcomes is acknowledged when it exists, and a donor's risks are proportional to benefits for the donor and recipient. Future research should determine whether outcomes are similar for donors from developing countries and donors with pre-existing conditions such as obesity.

Introduction

The first successful kidney transplantation from a living donor was 60 years ago between identical twins. More than 27 000 living-donor kidney transplants are now done each year across developed and developing countries.[1] In practice, a perioperative death or major complication from kidney transplantation is a rare event.[2,3] At the time of nephrectomy, kidney donors typically only spend a short time in hospital.[4] Yet, living with one kidney has lifelong implications. Research has advanced knowledge about donor life expectancy, quality of life, costs (donor-related and health-care system), and the risks of end-stage renal disease, hypertension, and adverse pregnancy outcomes. This new information creates the need for important revisions to the processes of informed consent and decision making about living kidney donation, particularly for donors in North America, Europe, Australia, and New Zealand, where most of the research originated. For transplant professionals, improved strategies are needed to communicate risks to donors, especially when adverse health outcomes such as end-stage renal disease are uncommon or unlikely to occur in the first few years after donation. Additionally, helping donors balance considerations of risk in the presence of strong emotions around the decision to donate is a difficult task.

In this Review, we provide a perspective on living kidney donation with data about long-term donor outcomes. We describe ethical implications and challenges related to decision making for donors. The Review does not address the practice of illegal and unregulated living kidney donation (eg, transplant tourism).

Epidemiology of living kidney donation

Worldwide trends in living kidney donation

Since 1954, we estimate that more than half a million living-donor kidney transplantations have been done worldwide. The highest number of living kidney donations happened in the USA (5600–6600 annually) and India (an estimated >6000 annually, although India does not have a formal registry). Brazil, Iran, Mexico, and Japan each do almost 1500 living-donor kidney transplantations annually.[1] About 60% of donors are women,[5–7] and the average age at the time of donation is between 40 and 45 years.[8–11]

Living-donor kidney transplantation has recently stagnated in the USA, Canada, Australia and New Zealand, and Brazil, but has continued to grow substantially in other countries such as Japan and South Korea (figure 1).[1] In the USA, the annual number of living kidney donors reduced by 10%, from 6647 to 5989, between the years 2004 and 2013. Declines in donation disproportionately took place in male, black, genetically related donors, and donors younger than 50 years.[3,12,13] In Canada, the number of living kidney donations rose steadily until 2006, remaining stable since then at 454–491 annually.[14] The number of living kidney donations in Australia and New Zealand peaked at 423 in the year 2008 and declined by 31% to 292 in the year 2012.[15] The rate of growth in living kidney donor transplantation has slowed considerably in Europe.[16] These declines in donation are not easily explained, but seem temporally associated with the economic recession, drawing attention to the financial risks of kidney donation for individuals with little savings or income.

Unequal access to living-donor kidney transplantation

Unlike deceased-donor organs, living-donor organs are not usually treated as a public resource. Living kidney donation generally takes place as a directed gift between individuals after careful assessment by the transplant
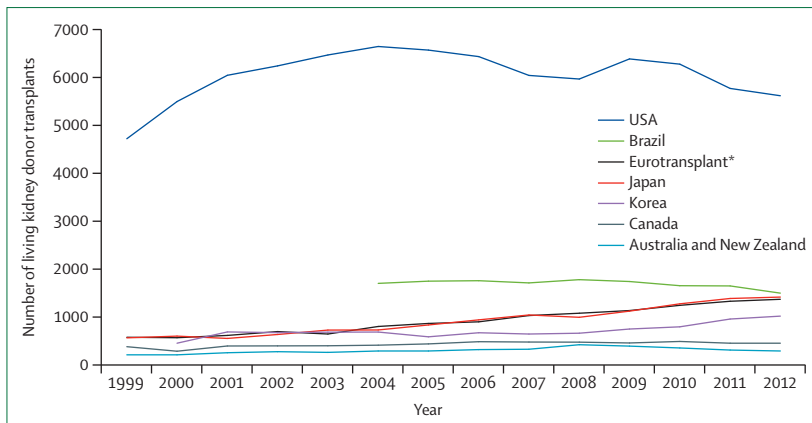
Figure 1: Temporal trends in the annual number of living kidney donation transplants
*Eurotransplant membership has changed over time; to show temporal trends, we restricted the counts to living-donor transplants in original member countries of Germany, Austria, Luxembourg, Belgium, and the Netherlands.

team. In the USA and Australia, patients with kidney failure are much more likely to receive a living-donor kidney transplant, if they are white, young, wealthy, privately insured, and well educated.[12,17–19] These disparities in access to transplants might be partly explained by high rates of contraindications to donation such as obesity in some minority populations and great difficulties in the management of donation costs.[20]

In many countries, living kidney donation is the only affordable treatment for kidney failure. This is evident across large regions of India and Pakistan, for example, where chronic dialysis is rationed in units supported by government or community donations, or is only available with payments that are prohibitive for most patients. In this respect, chronic dialysis is viewed as a bridge to a life-saving kidney transplant from a living donor. In many developing countries, the infrastructure to procure deceased-donor organs does not exist.[21–23]

Unrelated and incompatible donors
Living kidney donation in unrelated donors (eg, friends, spouses, or distant relatives of the recipient) are becoming more common.[3,12] In the USA, the proportion of living kidney donations from unrelated donors increased from 30% to 57% between 1999 and 2013. Similar trends are evident in Europe, Australia, and New Zealand.[16]

This rise in unrelated living kidney donation is largely associated with a declining emphasis on close HLA matches between donor–recipient pairs.[24] With advances in immunosuppressive therapy, the longevity and function of the transplanted organ is now less dependent on the genetic donor–recipient relationship than in the past. The rise in unrelated donors has also been helped by so-called kidney paired donation, a strategy used to overcome donor–recipient incompatibility if the transplant candidate has antibodies to the donor's blood or HLA type. Such antibodies greatly increase the risk of donated-organ rejection and, in the case of

anti-HLA antibodies, might develop because of previous pregnancies, blood transfusions, or transplants.[25] As shown in figure 2, registries of incompatible donor–recipient pairs have enabled transplantation to proceed through paired exchanges, or donation chains in which each donor provides a kidney to an unrelated compatible recipient. Paired exchange has been helped by the transportation of living-donor kidneys between centres and by non-synchronous transplants, in which one or more donors wait to donate until new pairs enter the chain.[26,27] In some cases, a transplantation chain begins when an individual with no relationship to any recipient donates a kidney (termed non-directed donation). In 2012, this type of altruistic donation enabled a 30-transplant chain to proceed.[28]

Disadvantages of kidney paired exchange include the logistical demands of coordinating transplants across multiple centres. Additionally, pairs without a blood type O donor might face prolonged delays to transplantation because it is more difficult to find matches in the available pool of donors. Despite these difficulties, paired exchange is an important pathway to transplantation for an increasing number of patients. In 2013, 10% of living kidney donations in the USA were paired exchanges.[5]

Desensitisation protocols offer an alternative approach to enable living kidney donation between incompatible pairs. The recipient undergoes intensive pretransplant immunosuppression, which typically includes plasma-pheresis and intravenous immunoglobulin to reduce antidonor antibody titres.[29] Although desensitised recipients might have an increased risk of infections and antibody mediated rejection, life expectancy is still improved compared with dialysis.[30]

Chronic kidney disease
To meet the demand for kidneys, transplant teams are increasingly allowing older individuals than previously allowed and individuals with health conditions such as obesity, prediabetes, kidney stones, or hypertension, to become living kidney donors.[31] Prominent guidelines do not stipulate an upper age limit for living donors, and donation in older adults is increasing.[20,32–36] Between 2002 and 2009, the number of living kidney donors aged 55 years or older in the USA nearly doubled, increasing from 407 to 726. During that period, the percentage of donors aged 55 years or older in Australia and New Zealand increased from 27% to 38%. This trend is not surprising since, in many countries, the median age of patients on the kidney transplant waiting list is rising and these patients might attract donors in the same age group.

About 25% of living donors in the USA, Canada, Australia, and New Zealand have a body-mass index (BMI) of 30 kg/m² or higher. On trend with the general population, the proportion of living kidney donors with obesity in the USA has increased steadily over time.[37]

By contrast, donors who meet contemporary definitions of prediabetes and hypertension—but whose blood pressure and glucose tolerance were deemed to be normal at the time of donation—have been accepted for several decades.[38] Unfortunately, long-term outcomes for donors with these pre-existing conditions have not been well defined.

Assessment and selection of living kidney donors

Psychosocial assessment

As shown in table 1, the assessment includes an in-depth health and psychosocial assessment. The process is guided by ethical principles to protect the donor. To provide informed consent, donors should be free from coercion, have the capacity to make the donation decision, have all relevant information disclosed, and have sufficient comprehension of potential outcomes.[34] The transplant team should understand the donor's motives, commitment, and views on the trade-off between the risks and non-medical benefits of donation.

Contraindications to living kidney donation

Many major guidelines identify evidence of kidney disease and diabetes as absolute contraindications to living kidney donation.[33,34,39,40] Some guidelines list active malignancy, hypertension with end-organ damage, and uncontrolled psychiatric conditions as contraindications.[33]

Relative contraindications to living kidney donation include obesity (BMI≥35 kg/m²), hypertension, prediabetes, recent nephrolithiasis, vascular disease such as fibromuscular dysplasia, substantial proteinuria, and haematuria caused by conditions such as thin basement membrane disease.[33,35,36,40] The risk posed by these conditions might plausibly depend on the donor's age at donation, race, lifestyle, and the availability of postoperative health care. However, reliable data on the lifetime chance of complications for individuals who differ in age, baseline kidney function, or race, are not available, nor is clear information on risks attributable to donation versus other baseline factors such as genetics (in cases in which the donor is related to the recipient). Perhaps as a result, substantial practice variation exists with respect to these risk factors.[41] For example, in a survey of US transplant centre policies, 10% of centres excluded donors based on a cutoff of BMI of more than 30 kg/m², 52% excluded donors with a BMI more than 35 kg/m², and 20% excluded donors with a BMI more than 40 kg/m², while 12% had no policy and 6% would exclude donors on the basis of BMI only if other cardiovascular risk factors were present.[42]

Health outcomes after living kidney donation

Outcomes for organ recipients

Although this Review focuses on donors, the excellent outcomes for recipients provide the main motivation for
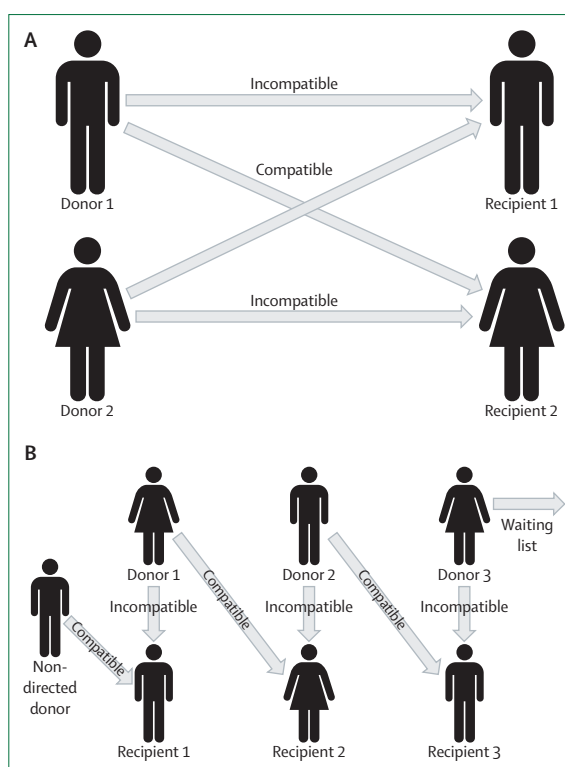

Figure 2: **Kidney paired donation**
(A) Donation across two pairs and (B) open chain paired donation.

living kidney donation and merit brief consideration. Recipients of living kidney donation have a better quality of life and a much longer survival versus chronic dialysis treatment. Compared with recipients of deceased-donor kidneys, recipients of living-donor kidneys wait less time for transplantation, have a lower risk of rejection, and have better allograft survival and longer life (although outcomes might depend on donor age and predonation kidney function).[3,12,43] Unlike deceased-donor transplantation, living kidney donation can be scheduled when the recipient's health is optimum, and the kidney avoids injury from donor brain death, prolonged transport, or associated events.

Assessment of outcomes for donors

Randomised trials could generate very reliable estimates of the risks for donors; however, randomised trials of organ donation are not ethical. Living kidney donors undergo extensive medical and psychosocial assessment and are therefore healthier than the general population. However, in many observational studies, donor outcomes were compared with general population controls, which could mask any increased risk attributable to donation. Historically, the validity of many studies of donor outcomes was also limited by high rates of loss to follow-up, recall bias, and inadequate sample sizes to detect clinically important risks.

	Testing	Main purpose	Related absolute contraindications
Kidney structure and function	Assessment of filtration function; screening for present or previous proteinuria or haematuria, or both; imaging, typically with contrast enhancement	To estimate whether postdonation renal function will be sufficient; to screen for kidney disease, including kidney stones, and to characterise the kidney's structure and vascular anatomy	Evidence of chronic kidney disease
Haematological or oncological assessments	Blood typing; coagulation; review of age-appropriate cancer screening, and any family history of cancer	To ensure blood type compatibility with recipient; to assess bleeding risk; to confirm overall donor health, and in some rare cases, prevent cancer transmission to the recipient	Blood type incompatibility needs recipient desensitisation or donor exchange; untreated malignancy
Cardiovascular function	Blood pressure; lipid screening; preoperative stress testing, per clinician judgment	To determine whether blood pressure postdonation is likely to be sufficiently controlled to protect the remaining kidney; cardiovascular health assessment; operative risk assessment	Transplant team might decline donor if findings show risk of future poor health
Infectious disease risk	Screening for HIV, hepatitis B and C, syphilis, tuberculosis; where appropriate, infections endemic to specific regions	To identify diseases that might impair the donor's future health or harm the immunosuppressed recipient if infection transmitted through donated organ	Transplant team might decline donor if findings show risk of future poor health
Endocrine function	Assessment of glycaemic abnormalities, often with oral glucose tolerance testing in high-risk patients; body-mass index	To confirm absence of diabetes and low risk of future diabetes	Diabetes
Other health aspects (gastrointestinal, pulmonary, dermatological, and rheumatological)	Interview; physical assessment; routine laboratory assessment; chest radiograph	General health assessment	Transplant team might decline donor if findings show risk of future poor health
Family history	Renal disease; diabetes; cancer	Assessment for genetic predisposition to kidney disease (eg, polycystic kidney disease); to confirm low risk of future diabetes; general health assessment	Transplant team might decline donor if findings show risk of future poor health
Histocompatibility	HLA typing; donor and recipient tissue cross-matching	Ensure HLA compatibility of donor organ with recipient's immune system	High levels of recipient antibodies against donor antigens needs desensitisation or paired kidney exchange
Psychosocial assessments	Interview to determine capacity for decision making; mental health history; substance misuse history; social support, financial resources; detailed assessment of donor's motives, values, and understanding	To assess donor's capacity for decision making; to assess donor's risks for future health problems; where relevant (eg, injection drug use), to assess risks of acquiring blood-borne infections; to assess support and resources for donor during surgical recovery period; to assess whether coercion or financial inducements are present; understanding of risks and benefits; and whether decision is consistent with the donor's values	Inability to understand or little insight into risks and benefits because of mental illness or other reasons; evidence of coercion
Counselling by an independent donor advocate	Additional assessment of the elements of informed consent	Assessment by a professional whose judgment should be independent from the needs of the recipient or the centre	Processes of informed consent not satisfied

Table represents synthesis of guidelines from multiple countries.

Table 1: Elements of the extensive health and psychosocial assessment for potential living kidney donors

More recent studies[9,11,44] have succeeded in assembling comparator groups that have undergone some health assessment, and matched these comparators to donors with key baseline characteristics such as demographics, comorbidities, and health habits (table 2).

Mortality and cardiovascular disease outcomes

Many studies, including cohorts from Sweden, Japan, and the USA, have showed that living kidney donors have similar or better life expectancy than the general population.[2,45–47,66] Four large studies have also compared mortality in living kidney donors with healthy matched controls who did not have evidence of chronic diseases that would preclude kidney donation at many transplant centres.[2,10,11,44] Segev and colleagues[2] matched 80 347 living kidney donors to a smaller group of healthy non-donors selected from the third US National Health and Nutrition Examination Survey and found similar survival during median follow-up of 6·3 years. By contrast, Mjøen and colleagues[10] reported an increased risk of death in 1901 Norwegian kidney donors with median follow-up of 15·1 years compared with healthy matched comparators from a regional population survey. The cumulative incidence of mortality at 25 years was about 18% in donors versus 13% in healthy non-donors (adjusted hazard ratio 1·30, 95% CI 1·11–1·52). The Segev and Mjøen studies were limited by the use of comparator cohorts from different time periods than when the donations took place. This approach creates the potential for bias because of changes in medical care or mortality trends across eras.

Cohorts of Canadian living kidney donors, US living kidney donors aged 55 years or older, and healthy controls, were assessed for death or major cardiovascular events by use of claims data and death registries.[44] Neither study found an increased risk of the outcome associated with kidney donation.[11,44] Together, the results from these two studies are generally

	Comparison group	Outcome for previous kidney donors*	Additional study information
Survival	Healthy matched non-donors	Most data show that donors have similar survival	Four studies: from the USA, Norway, Canada;[2,10,11,44] Norwegian cohort showed higher mortality associated with donation
Survival	General population	Longer-term survival than non-donors	Three studies from Sweden, and from single centres in the USA and Japan[45-47]
End-stage renal disease	Healthy matched non-donors; general population	Increased relative risk, but low cumulative incidence of end-stage renal disease; lower risk of end-stage renal disease (vs general population)	Two studies from the USA and Norway;[9,10] estimated cumulative incidence is less than 0·5% at 15 years; one study from Sweden[48]
Cardiovascular disease	Healthy matched non-donors	No increased risk of cardiovascular disease	Two studies from the USA and Canada[11,44]
Pre-eclampsia or gestational hypertension	Predonation and postdonation	Increased risk	Provincial cohort from Ontario, Canada;[49] single US centre;[50] national cohort from Norway[51]
Hypertension and elevated blood pressure	Healthy matched non-donors; predonation and postdonation	Increased blood pressure; increased systolic blood pressure of 4 mm Hg; increased diastolic blood pressure of 6 mm Hg at least 5 years postdonation	Two studies from the USA (black donors) and Canada;[52,53] various studies[54]
Quality of life	General population	Quality of life as good or better for living donors	Various studies from many countries[55-65]

Only the quality-of-life studies include donors from the developing world in the studies cited in the table. *Versus comparison group.

Table 2: **Summary of medium-term and long-term health outcomes after living kidney donation**

reassuring. However, concerns persist about whether the findings can be generalised to donors in the developing world. Some transplant leaders have also argued that, on the basis of present data, the lifetime risk of these complications or others cannot be accurately estimated in young donors (defined for this article as <30 years), who will spend many decades in a single-kidney state.[67]

End-stage renal disease

Evidence suggests that living kidney donation greatly elevates the relative risk of end-stage renal disease, although this outcome remains uncommon: less than 0·5% over 15 years.[10,68] Unfortunately, few data for long-term renal outcomes have been published outside North America and Europe.[69]

Immediately after nephrectomy, living kidney donors have a glomerular filtration rate of about 50% of predonation rate. Because of adaptive hyperfiltration in the remnant kidney, the glomerular filtration rate usually increases to 60–75% of predonation levels by a year after donation.[70] Kidney donors might also have small increases in concentration of serum uric acid, FGF-23, parathyroid hormone,[71,72] and non-albuminuric proteinuria.[73] Kidney donation might also cause blood pressure to increase.[52,54] These factors could contribute to an accelerated loss of renal function.

End-stage renal disease outcomes were investigated in the US donor cohort previously assembled by the group led by Segev.[2] 99 (0·1%) of 96 217 donors developed this disease with median follow-up of 7·6 years. The incidence of end-stage renal disease in donors was lower than in unscreened general population controls,

but higher than in matched healthy non-donors.[9,45] Muzaale and colleagues[9] extrapolated data to a longer time horizon and estimated that the 15-year cumulative incidence of end-stage renal disease was 0·31% in living kidney donors versus 0·03% (p<0·001) in healthy non-donors. Although the 15-year cumulative incidence of end-stage renal disease was twice as common in biologically related (0·34%) versus unrelated donors (0·15%), the difference was not significant.[9]

A concordant finding was identified in the cohort of Norwegian kidney donors, in which nine (0·47%) of 1901 donors developed end-stage renal disease (median follow-up time 15·1 years). Kidney donation was associated with a hazard ratio of 11·38 (95% CI 4·37–29·63) for this disease versus healthy non-donors.[10]

These studies have greatly expanded our understanding of postdonation renal outcomes; however, important gaps in knowledge remain. First, because comparison groups were not matched on family history, the extent to which the higher rate of end-stage renal disease in donors is attributable to genetic predisposition is unclear. However, all donors did not have substantial evidence of early kidney disease at the time of donation, which makes it less likely that genetics can fully explain the reported risk of this disease. Second, data do not enable precise estimates of the lifetime risk of developing end-stage renal disease.

Renal outcomes in black and Aboriginal donors

The very high rates of kidney disease in black individuals and Aboriginal communities have generated concern about outcomes for living kidney donors from these communities.[74,75] In the general population, black race is

associated with a four-times increased risk of end-stage renal disease.[76] An association of similar magnitude has been described in black versus white living kidney donors.[77] For example, Cherikh and colleagues[78] identified 126 US living kidney donors with end-stage renal disease and reported a relative risk of end-stage renal disease of 4·9 in black versus white donors.[78]

Fewer data are available about outcomes for Aboriginal donors. A case series reported outcomes of 22 indigenous kidney donors from the Northern Territory of Australia. From 16 with follow-up data, three (19%) had end-stage renal disease and two (12%) had died. A cohort of 38 Aboriginal living kidney donors from a Canadian centre noted that Aboriginal donors were much more likely to have hypertension (43% vs 19%, p=0·02) and diabetes (19% vs 2%) than randomly selected white donors.[79]

These findings and others have focused attention on the genetic versus social determinants of renal disease associated with race.[75] The G1 and G2 coding variants of the *APOL1* gene on chromosome 22 have a strong association with renal disease and are almost always inherited only by individuals with African ancestry.[80] The mechanism of disease associated with *APOL1* risk variants is not known. Screening for *APOL1* is not routinely done for black race donors at most centres. However, some transplant leaders have argued for taking race into account, for example by adopting more stringent criteria for blood pressure, when clinicians decide whether to accept black donors.[74]

Pregnancy after kidney donation

Some female living kidney donors are in their reproductive years. Because pregnancy leads to renal hyperfiltration and volume expansion, living kidney donors—whose remaining kidney is also subject to hyperfiltration—might be at increased risk of pregnancy complications.

Three retrospective cohort studies[49–51] from Canada, Norway, and the USA have examined pregnancy outcomes after kidney donation. The Canadian study ascertained postdonation pregnancies and proportion of pregnancy complications in 85 donors who were matched on relevant characteristics to non-donors. Gestational hypertension or pre-eclampsia were more common in kidney donors than matched non-donors (11% vs 5%). The incidence of pre-eclampsia (6% in donors) was similar across all three studies.[49] Reassuringly, in the Canadian study, most previous donors had uncomplicated pregnancies, and other important maternal and faetal outcomes did not differ significantly between the two groups.

Quality of life and decisional regret

Studies from many countries have generally shown good health-related quality of life after donation.[55] However, much of the data consist of generic quality of life instruments that might not capture donor-specific experiences. For example, some donors report difficulties including pain control during surgical recovery and a feeling of vulnerability to future health problems.[56,57]

The RELIVE cohort of 2455 US donors (mean follow-up of 17 years) showed that more than 80% had average or better self-rated health on the Medical Outcomes Study Short-Form 36.[58] Quality of life in the physical and mental component scores was similar to or more than norms for both black and white donors.[59] Generally, good health-related quality of life has been reported in donors in Canada, Australia, Scotland, Brazil, Taiwan, and several European countries.[56,60–63] Investigators have also asked donors whether they would make the donation decision the same way, in view of their experiences. Only a small minority of donors expressed regret about donation.[62–65] The RELIVE study revealed that predonation psychiatric diagnoses, younger age, a longer time to full recovery from surgery, and the feeling of having received inadequate attention from the transplant team were associated with worse mental health-related quality of life after donation.[58] Some donors also expressed regret or disappointment in the rare event that the donated kidney fails soon after surgery.[65,81] Notably, a randomised trial in potential kidney donors with use of motivational interviews to discuss the donation decision has suggested that this intervention might improve perceptions of postdonation recovery.[82]

Financial consequences of living kidney donation

Living kidney donation can be financially costly to donors, even in countries where the donor's medical expenses are paid by the recipient's insurance or the health-care system. Major costs can include transportation, child care, lost income (or holiday time) from missed work, and fees associated with medical care.[83] In a prospective follow-up of 100 Canadians, the mean cost associated with donation was CAN$3268. However, for 15% of donors, costs exceeded CAN$8000.[84]

In the USA, some donors have experienced difficulty in obtaining health or life insurance, although most data are self-reported.[85] A study of premiums for donors in Canada, on the basis of estimates provided directly by insurance representatives during the first stage of applications for life insurance, did not find increased rates.[86]

Ethical implications of new knowledge about donor outcomes

Informed consent process

Information about kidney-donor outcomes needs incorporation into the processes of informed consent. Transplant centres should ensure that potential donors understand that nephrectomy increases their risk of end-stage renal disease, but for most donors, the rate of this disease over 15 years is less than 1%. Estimates of the lifetime chance of end-stage renal disease are imprecise

particularly for young donors (younger than 30 years), and this uncertainty should be acknowledged. Female donors with childbearing potential should be counselled about future reproductive plans, with about 8–14% (*vs* 3–7% of women in the general population) of these women expected to have gestational hypertension or pre-eclampsia in a future pregnancy.[87] The informed consent process should include plans for financial consequences of donation. Consent should also incorporate information about good quality of life for donors, and any anticipated benefits to the recipient. Although most data suggest that live donors have excellent longevity, the informed consent process might also include discussion of a Norwegian study[10] that reported higher death rates in kidney donors versus healthy controls.

Some of these elements, particularly the contrast between relative and absolute rates of end-stage renal disease, might be difficult for donors to understand. To put rare outcomes into a familiar context, centres might need to develop more effective educational approaches, such as visual aids. The consent process should include serial meetings and diverse opportunities for potential donors to ask questions.[88]

Risk assessment and benefits from the donor's perspective

Transplant professionals should be guided by principles of beneficence and non-maleficence toward the donor, while taking the donor's autonomy into account.[89] Kidney donors often have a strong desire or duty to improve the life of the recipient.[57,90] Some individuals describe the donation experience as a morally meaningful act.[57] Many donors report making a rapid decision that does not change when shown the data about risks.[91] Many potential donors are already fully committed to the donation of a kidney by the time they contact the transplant programme. For a donor whose welfare is closely linked to the potential recipient (such as a spouse), the donor might hope that their mutual welfare will improve with transplantation. In summary, many donors describe non-medical benefits from donating.

For transplant professionals, helping a donor to achieve these benefits from donation is consistent with the principle of beneficence.[89] However, donors have a diversity of motives, expectations, and relationships to the recipient.[90] Some potential donors have reservations about the donation decision or expect few benefits. The assessment of potential non-medical outcomes (such as quality of life and psychological health) from donation needs members of the transplant team to understand the donor's perspective on how donation will affect many aspects of his or her life. Therefore, the transplant team needs the expertise to do a thorough psychosocial assessment.[33,92] In the USA, UK, Canada, and Australia, guidelines recommend or regulations mandate the use

of an independent donor advocate who verifies the donor's informed consent. The donor advocate should be an individual whose position in the health system offers some protection from any undue pressure to accept a donor.[20,33,34,36] For example, the advocate might not be directly employed by the transplant centre or might have a reporting structure to a leader outside transplantation.

The decision to accept a donor is generally made by an interdisciplinary committee. Although donor autonomy is an essential component, the committee members must also consider their own consciences and professional standards.[35] Transplant professionals might later encounter a donor who developed end-stage renal disease or another poor outcome. These professionals should feel comfortable that the decision making and informed consent processes were ethically sound.

For donors from the developing world, the processes of informed consent should include discussion of how outcomes data might not be generalisable to their situation. Transplant professionals should seek to confirm that donors will have the resources to obtain good preventive care and needed treatments if complications such as hypertension arise. Donation should not proceed until the team is satisfied with the follow-up plan.

Thresholds of acceptable absolute risk for adverse outcomes

The new data for donor outcomes draw attention to the unresolved problem of thresholds of acceptable risk for living kidney donors. By use of the end-stage renal disease example, the relative risk associated with kidney donation would lead to important differences in the expected absolute lifetime incidence of end-stage renal disease between donors without baseline risk factors for kidney disease (eg, a 45-year-old white donor with no health problems) versus donors with strong risk factors (eg, a 45-year-old black donor with family history of kidney disease).[93]

This scarcity of guidance about acceptable risk is, in part, because of the fact that each donor's risks must be weighed against the expected benefit to that donor and the intended recipient. Additionally, setting thresholds on the lifetime probability of complications such as end-stage renal disease might perpetuate or worsen disparities in access to kidney transplantation in minority groups that have a high baseline prevalence of end-stage renal disease, such as Aboriginal Australians.

Financial incentives for living kidney donation

New insights about donor outcomes could have implications for policy aimed to create financial incentives for live organ donation. First, evidence about financial costs has led to recommendations that donors receive financial counselling, and has fostered pro-grammes to reimburse donors for their legitimate

	Policy	Outcomes
Kidney donors might experience substantial financial costs of donation from mechanisms including lost wages, incurred travel and accommodation expenses, and, in some cases, barriers to obtaining affordable insurance	Health system provides appropriate reimbursement for donation-related expenses; laws protect donor's employment for a reasonable period after donation; elevated insurance premiums due to kidney donation prohibited	Remove financial risks to the donor; possible outcome of increased living kidney donation in interested potential donors who are financially vulnerable; treat donors fairly
Long-term health complications of kidney donation, such as end-stage renal disease	Transplant centre or health system provides medical care for complications, routine follow-up care, and payment for treatment; in countries with deceased donor transplantation, priority for former live organ kidney donors in allocation might be considered	Adverse health outcomes from kidney donation identified early and treated
Scarcity of thresholds of acceptable risk of complications for the acceptance of kidney donors	As research findings develop, clinical practice guidelines should incorporate input from stakeholders and identify a lifetime incidence of complications that precludes donation; because long-term risks are more difficult to predict in younger versus older donors, centres might preferentially recommend older donors when more than one donor is available	Standardisation and transparency related to the acceptance of kidney donors across centres

Table 3: Proposed policies and practice guidelines to protect living kidney donors from medical and financial risks

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Panel: **Key research needed to improve the informed consent process for living kidney donors**

1. Long-term outcomes for donors with pre-existing chronic health conditions, including obesity, hypertension, metabolic syndrome, and kidney stones
2. Outcomes for donors in developing countries
3. Genetic and social risk factors for end-stage renal disease in living kidney donors
4. Estimation of lifetime risks in young (eg, <30 years of age) kidney donors
5. Novel educational approaches to educate potential donors—particularly those with low numeracy—about the risks associated with kidney donation

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expenses.[94] Second, new data about donation-related complications might support the contention that donors deserve a financial reward to offset the acceptance of risk. Although societies of transplant professionals support reimbursement of expenses, regulated direct incentives for living kidney donation is a polarising issue, with many leaders in the transplant community providing compelling arguments for and against incentive programmes.[95]

Needed policy and research related to living kidney donor transplantation

New policies to address the medical and financial risks of living kidney donors are needed. Potential policies are described in table 3. Additionally, funding agencies should support research to determine long-term outcomes for living kidney donors, particularly for donors with predonation health conditions (panel). In particular, developing countries should consider investment in transplant registries that advance research into living-donor outcomes. New research is also needed to reduce disparities in access to living-donor transplantation, and improve efficient evaluation procedures for motivated donors. For many transplant candidates, the option of living-donor kidney transplantation and the process of engagement with potential donors are not thoroughly explored by the transplant team. Yet, some research supports the idea that targeted education, counselling, or coaching transplant candidates might lead to increased access to living kidney donation—particularly in ethnic minorities and older patients who have historically had lower rates of living-donor kidney transplantation.[96–98,12]

Conclusion

Since 1954, more than half a million living-donor kidney transplants have been done worldwide. Recent studies have greatly clarified our understanding of the risks and benefits of kidney donation over the short and long term. Continuing efforts to resolve uncertainties related to living kidney donation, particularly in the developing world, are necessary to safeguard the ethical practice of living kidney donation for the future.

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