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PRACTICE



CLINICAL UPDATE

Living kidney donation

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Globally each year more than 30 000 people become living kidney donors.¹ In the UK there have been more than 1000 living kidney donations every year since 2009.² There are two types of kidney donation, living and deceased. Living donor kidney transplantation offers the best treatment in terms of life expectancy and quality of life ²⁻⁹ for most people with kidney failure (see box 1), the prevalence of which is steadily rising. Living kidney donation is constantly evolving, with new ways of maximising recipient opportunities and increasing information regarding long term outcomes associated with donation. This review presents an overview of current practice covering who can donate, to whom, and the possible impact of donation on the donor's health.

Why do non-specialists need to know about this?

Non-specialists might be approached for information about living kidney donation and need to know where to access up-to-date relevant information. Refer interested potential donors to a living donor kidney transplant centre for advice. General practitioners or family physicians may be asked by a specialist team for information about a potential donor undergoing assessment, or to assist with organisation of investigations in the pre-donation stage. Given that the prevalence of living donors in increasing (currently about 1000 per annum in the UK) doctors are increasingly likely to encounter people who have donated and should be aware of what impact donation may have on their health. Some patients prefer to see their regular general practitioner for long term follow-up after donation.¹⁸

Who can donate a kidney, and to whom?

Most living kidney donors donate to relatives or friends, which is termed directed (or specified) donation. Alternatively, individuals can donate a kidney to a recipient with whom they do not have a pre-existing relationship—termed non-directed altruistic donation (or "Good Samaritan" or unspecified donation).^{19 20} This was formally legalised in the UK in 2007. Altruistic donors now account for about 10% of all living kidney donations.²

In the UK in 2012 the British Transplantation Society and Human Tissue Authority provided guidance on "directed altruistic donation." This term is used to describe organ donation that happens either between individuals who have a genetic relationship but no established emotional relationship, or between a donor-recipient pair who had no pre-existing emotional or genetic relationship. This definition was an attempt to overcome some of the confusion brought about by the use of social media to recruit potential living kidney donors, which caused blurring of the lines between directed and non-directed donations. Terminology varies, however, and a working group from the European Society for Organ Transplantation alternatively describes publically solicited donors as "solicited specified donors."²¹ The stimulus for a potential donor to come forward is the publication of an individual's need for a transplant on social networks or through the media.^{20 22}

Historically, all transplants had to occur between ABO blood group and HLA antigen compatible donor and recipient pairs, to prevent hyperacute rejection of the transplanted kidney. However, donors no longer need to be have such compatibility. Most transplants are still between compatible pairs, but desensitisation techniques have been developed to reduce anti-donor antibody titres in the recipient to allow immunologically incompatible kidney transplants.²³⁻²⁵ It is not always possible to lower antibody titres sufficiently to proceed, and such transplants do carry increased risks to the recipient, particularly of infection and rejection in the early post-transplant period. Long term graft survival, though improving,²⁵ is compromised compared with compatible living donor graft survival. Immunologically matched transplants remain preferable, and in many countries this is achieved via a regional or national living donor kidney exchange scheme (fig $1 \downarrow$).²⁶⁻³⁰

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What you need to know

- · Living donor kidney transplantation is the best treatment for most people with renal failure
- There is no upper age limit and few absolute contraindications to living kidney donation
- · A living kidney donor does not always need to be the same blood group as the intended recipient
- · Most donors have no long term ill effects from living with a single kidney
- Ensure living kidney donors have annual follow-up including blood pressure assessment, urine analysis for protein, and estimation of renal function

Box 1: Advantages of living donor over deceased donor kidney transplants

- Living donor kidney transplants reduce the number of individuals on waiting lists for deceased donor transplants and offer the possibility of a transplant to more patients, who would otherwise be dialysis dependent¹⁰
- · Living donor kidney transplants typically last longer, and recipient survival is greater²⁻¹¹
- · Living donor transplants are associated with shorter hospital stays, minimising disruption to recipients' lives
- · Planned desensitisation of recipients can occur more easily to allow immunologically incompatible transplants
- The elective nature of the surgery permits transplantation in patients who would be unsuitable for emergency surgery
- The recipient costs of living donor kidney transplants are less, because of shorter hospital stays and the decreased incidence of delayed transplant function and early transplant failure.^{12 13}
- Living donor kidney transplants are more likely to take place before the recipient has started dialysis (pre-emptive). Shorter periods spent on dialysis are associated with less comorbidity and better post-transplant outcomes.^{14 15} Pre-emptive transplants are also associated with cost savings from the avoidance of dialysis^{16 17}

What motivates people to become living kidney donors?

A thematic synthesis of qualitative studies has described directed and non-directed living kidney donors as being compelled by altruism, inherent responsibility, family expectation, personal benefit, and spiritual beliefs.³¹ Non-directed altruistic donors, much like directed donors, report being motivated by a desire to benefit other people or society as a whole, a compelling desire to donate and recognise personal psychosocial gains.^{32,34} Where commercial organ trading exists, or where donation is financially incentivised, most unrelated donors report financial motivation.^{35,38} Payment for donation is illegal in almost all countries.³⁹

What are the risks of living kidney donation?

Short term risks

Mortality in living kidney donation is estimated to be between 0.01 and 0.03%.⁴⁰⁻⁴² A recent systematic review reported that perioperative complications, such as wound infection and bleeding, occur in about 7.3% of cases.⁴¹ Immediately after nephrectomy, the glomerular filtration rate of the donor roughly halves. However, a year after donation, this is expected to increase to 60-70% of pre-donation levels,⁴³ due to adaptive hyperfiltration in the remaining kidney.

Longer term risks

Our knowledge of the long term risks of living kidney donation is incomplete, especially for specific donor subgroups (such as those defined by age, ethnicity, socioeconomic position, and with comorbidities). Observational data are limited by duration of follow-up and identifying an appropriate comparative group. In addition, when living donation was first introduced only relatively young and healthy individuals were accepted for kidney donation. As the criteria for donation have expanded to include older donors and those with comorbidities,⁴⁴ however, the current donor population is now demographically different from the cohort for whom long term follow-up data are available. This limits the generalisability of findings from studies of early donor populations to currently accepted donors.

Advising donors about risks

In order for a living donor to provide informed consent, potential donors and recipients require information on the known risks, and the limits to our understanding of these risks. When counselling a potential donor, risk must be considered on an individual basis. Establish whether younger, non-white,⁴⁵ overweight individuals or those with pre-existing hypertension or impaired glucose tolerance are prepared to make lifestyle changes to minimise long term risks. A small case-control study of long term risks in US army personnel 45 years after unilateral nephrectomy due to trauma reported that mortality was not increased in servicemen with one kidney compared with age matched controls with two kidneys.⁴⁶ Other small single centre studies have also reported that the survival of living kidney donors is better than that of the general population.^{47 48}

Two recent large cohort studies have reported a higher risk of kidney failure among donors compared with healthy non-donors, but the absolute 15 year reported incidence of kidney failure in both studies was <1%.^{49 50} These observational studies had limitations, and criticisms have included concerns regarding the comparability of non-donor controls⁵¹⁻⁵³ and relatively short follow-up.⁵⁴

A recent US analysis attempted to estimate an individual's risk of renal failure if they did not donate a kidney, and compared 15-year projections with the observed risk among a large cohort of living kidney donors.⁵⁵ This concluded that the relative risk for donors was 3.5-5.3 times higher than the predicted risks in the absence of donation.⁵⁵ Overall, the absolute risk for donors was <1% over this period, comparable with other observational studies, but the risk was greater in black donors as well as current or former smokers.

Two meta-analyses have suggested that kidney donors may have a small increase in blood pressure ⁵⁶ (<6 mm Hg) and in urinary protein,⁵⁷ although the quality of research included in both analyses was reported as poor.⁵⁸ The data on an increased cardiovascular event rate in donors is equivocal.⁴⁰⁻⁶⁰ Although the risks of gestational hypertension and pre-eclampsia seem to be higher in pregnancies among donors than among healthy non-donors,⁶¹⁻⁶³ adverse outcomes for mother or offspring have not been documented.

Work exploring the mental health of living kidney donors is limited, but a recent case-control study from the Netherlands suggested that donation is not associated with short term changes in mental health.⁶⁴ Multiple studies suggest that the quality of life of most living kidney donors seems to be at least equal to that of the general population ⁶⁵⁻⁷² and usually returns to pre-donation levels after donation. A thematic synthesis of qualitative work from Europe, the United States, Canada and Australia, however, identified some negative donation-specific experiences among the overall positive experiences, including a sense of loss, fear, vulnerability, and neglect.³¹

Several studies have reported that potential donors are more willing to accept greater donor risks than potential recipients and transplant professionals.⁷³ Greater risks seem to be accepted when the intended recipient is closely related and when his or her prognosis is poor.^{74 75} In addition, potential donors have been found to be more likely than potential recipients or clinicians to agree that living donation is acceptable when long term donor risks are uncertain.⁷³

In addition to evaluating the risks, consideration of living kidney donation must also involve an evaluation of the benefits to potential donors, which can be substantial, and the harms of non-donation.⁷⁶

How are living donors assessed and how long does it take?

National guidelines exist for living kidney donor evaluation.¹⁸⁻⁸⁰ Details of the guidance differ between countries,⁸⁰ and the international Kidney Disease: Improving Global Outcomes (KDIGO) committee is developing a global, evidence based guideline which is currently available for public consultation.⁸¹

The primary goals of donor evaluation are to determine the suitability of an individual for donation, to ensure a donor is making an informed choice free from coercion or monetary incentive, and to confirm that the kidney is suitable to be transplanted into the intended recipient.

In the UK the living donor evaluation process typically encompasses the steps outlined in figure $2\parallel$.

The duration of living donor evaluation varies between and within countries.⁸² Potential donors need to be given a suitable period to consider donation, often described as a "cooling off" period.⁸³ The clinical assessments and investigations can be carried out in one day, and some centres in the UK run one-day assessments.⁸⁴ To be a donor, an individual needs to be suitable to undergo surgery under general anaesthesia and to be able to cope with one kidney for the longer term.

Who cannot donate?

Very few absolute contraindications to living kidney donation exist (box 2).⁴⁴

The United Kingdom Guidelines for Living Donor Kidney Transplantation¹⁸ specify the minimum measured glomerular filtration rate (mGFR) required for donation in order to ensure that the mGFR of the remaining kidney is predicted to be more than 37.5 mL/min/1.73 m² at 80 years of age. The data on which this was based were limited, and there is variation between UK centres in the measurement of GFR.⁸⁶

In most transplant programmes living kidney donors are required to be over 18 years of age,¹⁸ but cases where adolescents have donated do exist.⁸⁷ Caution is recommended when accepting donors under 25 years of age as younger people have more time to develop comorbidities and an increased lifetime risk of renal failure.⁵⁵ Women who wish to have children need to be counselled regarding the small increased incidence of gestational hypertension and pre-eclampsia among kidney donors,⁶¹⁻⁶³ and alternative donors are preferred if available. Other relative contraindications to donation include obesity and diabetes, and factors that might affect a potential donor's decision-making capacity (such as cognitive impairment, undertreated psychiatric conditions, or active substance misuse).

In most countries potential donors are prevented from donating if there is evidence of donor coercion, as identified by any member of the donor evaluation team or by an independent assessor or donor advocate.^{20 80}

What is the surgical procedure?

Laparoscopic kidney removal is preferred¹⁸ as it is associated with less pain, shorter hospital stay, and earlier return to normal activities.⁸⁸ Minimally invasive surgical techniques for donor nephrectomy include robot assisted laparoscopy⁸⁹ and a laparoendoscopic single site approach.^{41 90} After surgery, living donors tend to stay in hospital for two to three days, and full recovery is expected within 6-12 weeks.¹⁸

What is the global picture?

Almost 100 of the World Health Organization member states now report transplantation services, but the rates of living kidney donation and the proportion of kidney transplants from living donors vary widely (fig 3 and $4\downarrow$).⁹¹⁻⁹³

Reasons for variation include differences in the underlying prevalence of renal failure, the acceptability and rates of deceased donor transplantation, the healthcare funding for preoperative and postoperative donor care, and differing donor reimbursement or incentives. Iran is currently the only country in the world to have a compensated and government regulated programme for unrelated living donor renal transplantation.³⁹ Payment for donation in most other countries is illegal. However, there remains an international trade in both organs and living donors.^{94 95} The Declaration of Istanbul on organ trafficking and transplant tourism outlines the circumstances in which removing organs from a living or deceased donor are unacceptable and aims to halt unethical transplant activities, including organ trafficking, transplant tourism, and transplant commercialism.⁹⁶

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Provenance and peer review: Not commissioned; externally peer reviewed.

Patient consent obtained.

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Box 2: Absolute contraindications to living kidney donation¹⁸⁻⁸⁵

- Active malignancy* or chronic infection
- · Nephrolithiasis secondary to a metabolic abnormality
- · Uncontrolled hypertension
- · Overt proteinuria, glomerular pathology, or an inadequate glomerular filtration rate (GFR)
- Bilateral renal artery atherosclerosis or fibromuscular dysplasia involving the orifices of both renal arteries
- · Sickle cell disease

*In some countries donors with certain types of cancer or successfully treated low grade tumour may be considered for kidney donation (such as small (<4 cm) subcapsular renal cell carcinoma with excision at time of donation and no distant spread, or low grade non-melanoma skin cancer)

Methods box

A PubMed Medline search was undertaken in May 2016 based on the following key words and variants: living, donor(s), donation, transplant(s), kidney, renal. The Cochrane Collaboration database was also screened for relevant articles. The Kidney Disease Improving Global Outcomes (KDIGO) reports *Summary of Published Living Kidney Donor Guidelines, Guideline Evidence Report*, and *Outcomes of Living Kidney Donation*, and the draft of *Clinical Practice Guideline on the Evaluation and Follow-up Care of Living Kidney Donors* were reviewed, along with the *United Kingdom Guidelines for Living Donor Kidney Transplantation* and references.

The authors' own knowledge, clinical experience, research, and personal archives of references were used. Research published since article submission was highlighted by reviewers. AE Courtney is chair of the UK NHS Blood and Transplant's Living Donor Kidney Transplantation 2020 Strategy Implementation Group.

Living kidney donation-a donor and family's experience

Our daughter thrived without illness for the first 18 months of her life, but then we noticed a swelling on one side of her stomach and took her to the doctor. A number of scans and x rays later, we were finally given the news that she had completely no function in one kidney and her other kidney was under severe pressure due to hydronephrosis. Our whole family was shocked and traumatised.

With appropriate drains and stents, our daughter had reasonable kidney function for a number of years, but at the age of 11 years her creatinine levels were creeping up and her consultant discussed dialysis. We raised the option of live donation. We had no idea really at this point what it entailed so had a list of questions to ask: how long the process will take, the likelihood of a match, whether it will take straight away, and numerous others. We wanted to do it to get our daughter healthy again without the dialysis if at all possible. Decision made, we wanted to proceed.

My husband was a slightly better match than me, and was put in contact with the living kidney donor coordinator. At the first appointment, we were told that the process takes approximately nine or 10 months, and all I could think of was whether we had this amount of time, as our daughter's kidney was failing and she was determined not to have dialysis if she could avoid it.

A few weeks later my husband had the first of the tests. A number of weeks later the next and so on. We asked whether a lot of these tests could be run on the same day to avoid disruption and minimise impact on his employment. We were informed that unfortunately the process was slow. Our daughter at this stage was losing a lot of weight and her condition was deteriorating quickly.

After the first date was cancelled four days before the surgery, which was devastating, on 8 August 2007 all went ahead. I was surprised at how well my husband looked that afternoon, and at around 4.30 pm our daughter was back onto the intensive care ward and sitting up looking amazing. The kidney worked straight away and all was good. My husband was discharged the following afternoon and returned to work six weeks later. Our daughter experienced instant improvement in her health, and joked about how tanned she looked, to which I replied "That's normal skin tone."

All went well for four years, until a virus known as BK attacked the kidney, and then rejection developed. With appropriate treatment, our daughter's kidney function stabilised but deteriorated again in 2014. She was in need of another kidney. Timing was not good. She was about to enter the final year of her master's degree and was determined to finish it alongside her peers. However, around Christmas we recognised the familiar signs that she had shown many years before—weight loss, vomiting, and extreme tiredness.

In January I rang the living donor coordinator to ask if I could be tested—and was informed that all the tests were now carried out in one day! A few weeks later, I arrived on the ward at 8.30 am for my tests to commence. The coordinator had a list of appointments and went to each department alongside me. By 4.30 pm that afternoon I was on my way home, exhausted but delighted to know that in a week or two we would know for sure if my kidneys were healthy enough for donating. They were, and surgery was booked for 23 March 2015 (when our daughter had no lectures due to the Easter break).

All went well, I returned to work after seven weeks, and our daughter graduated from university three months later. She started a PhD in physics that same year.

As a family having been through the living donation process twice, we would most certainly recommend the one day testing. The process for my husband was long and drawn out and impacted greatly on family and work life. During the time waiting, we were further traumatised watching our daughter become increasingly unwell, and there was little we could do. On the second occasion, it was a full day in hospital, but by the time I was leaving most of the tests had been conducted, we knew things were progressing quickly, and I only had to take one day off work.

Nine years on, and my husband remains well. One year on, I had my review at the hospital and all is good. Most importantly our daughter's results are excellent and she is living life to the full.

We are truly grateful for the staff that cared for us during both these transplants. As a family we thank them all.

Jacqueline Johnston, donated at Belfast City Hospital, Belfast Health and Social Care Trust

Previous accounts of living kidney donation have been published in the BMJ:

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Resources for healthcare professionals

- Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline on the Evaluation and Follow-up Care of Living Kidney Donors, released for public consultation in November 2015 and expected to be formally published in 2016
- Joint Working Party of The British Transplantation Society and The Renal Association. United Kingdom Guidelines for Living Donor Kidney Transplantation. 3rd ed. 2011. https://www.bts.org.uk/Documents/Guidelines/Active/UK%20Guidelines%20for%20Living% 20Donor%20Kidney%20July%202011.pdf
- Details the UK guidelines for the evaluation of both living kidney donors and transplant recipients. Includes the legal framework and guidance on financial reimbursement
- Plus "Addendum to Living Kidney Donor Guidelines." 2015. http://www.bts.org.uk/BTS/Guidelines_Standards/Current/BTS/Guidelines_ Standards/Current_Guidelines.aspx—Provides an update on the risks of living kidney donation based on recent research findings
- NHSBT Organ Donation and Transplantation. Living donor kidney transplantation http://www.odt.nhs.uk/donation/living-donation/living-donor-kidney-transplantation
- UK's national transplant website with information on all aspects of donation and transplantation, including guidelines and activity reports
- Kidney Disease Improving Global Outcomes (KDIGO). Outcomes of Living Kidney Donation. www.kdigo.org/clinical_practice_guidelines/ LivingDonor/KDIGO%20Guideline%20Evidence%20Report.pdf
 - Reports findings from a systematic review of research into the outcomes of living kidney donation
- Thiruchelvam PT, Willicombe M, Hakim N, Taube D, Papalois V. Renal transplantation. *BMJ* 2011;343:d7300 (http://dx.doi.org/10. 1136/bmj.d7300)
- Provides further details on renal transplantation, including details of transplant candidate eligibility and details of deceased donor transplantation. However, the content regarding living donor transplantation has been updated for this review
- Reese PP, Boudville N, Garg AX. Living kidney donation: outcomes, ethics, and uncertainty. Lancet 2015;385:2003-13
 Summarises data on long term donor outcomes and the ethical implications and challenges related to decision making for donors

Information for patients

- NHSBT Organ Donation. Living organ donation. https://www.organdonation.nhs.uk/faq/living-organ-donation
- Give a Kidney—One's Enough. How to give a kidney. http://www.giveakidney.org/2015/uncategorized/how-to-give-a-kidney
- British Kidney Patient's Association. Donating a kidney: what to expect. http://www.britishkidney-pa.co.uk/images/stories/downloads/
 patientinfopage/BKPA_leaflet_leaflet-donating.pdf
- healthtalk.org. People's experiences: organ donation. http://www.healthtalk.org/peoples-experiences/organ-donation-transplant/organdonation/topics—Video accounts of the experiences of living donors
- National Kidney Foundation. The big ask: the big give. https://www.kidney.org/transplantation/livingdonors—US website about living kidney donation

Ongoing research

Ongoing research aims to determine the long term outcomes for living kidney donors, especially for younger donors, those with comorbidities such as hypertension and obesity, and donors of all ethnic groups and socioeconomic positions. Determining the long term outcomes for donors is one of the "Top 10 kidney transplant research priorities" set by the UK James Lind Alliance and Centre for Evidence in Transplantation Priority Setting Partnership in February 2016 (http://www.jla.nihr.ac.uk/priority-setting-partnerships/kidney-transplant/top-10-priorities/)

Examples of active trials:

- Kidney Donor Outcomes Cohort (KDOC) Study USA. ClinicalTrials.gov identifier: NCT01427452 (https://clinicaltrials.gov/ct2/show/ NCT01427452)
- The Long Term Medical and Psychological Implications of Becoming a Living Kidney Donor: A Prospective Pilot Study USA, Canada and Australia. ClinicalTrials.gov identifier: NCT00319579 (https://clinicaltrials.gov/ct2/show/NCT00319579)
- Long-term Effects of Becoming a Living Kidney Donor Study Canada, Australia. ClinicalTrials.gov identifier: NCT00936078 (https://clinicaltrials.gov/ct2/show/NCT00936078)

Further research is also required to better understand barriers to living kidney donation, in order for socioeconomic and racial disparities in living donor kidney transplantation to be addressed and to facilitate living kidney donation when individuals are motivated to donate:

• LaPointe Rudow D, Hays R, Baliga P, et al. Consensus conference on best practices in live kidney donation: recommendations to optimize education, access, and care. Am J Transplant 2015;15: 914-22.

How patients were involved in the creation of this review

A living kidney donor was invited to provide an account of her experiences. Jacqueline Johnston had donated a kidney to her daughter, and her husband had also donated previously. Her account contrasts the experience her husband had of donor evaluation over several months with that of her own assessment, which took place in one day.

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Figures



Fig 1 Paired and pooled living kidney donation. Donor-recipient pairs who are immunologically incompatible and between whom a direct transplant is not viable are registered in the national scheme to achieve a compatible transplant match with other donor-recipient pairs. When two pairs are involved it is termed paired donation; pooled donation comprises more than two pairs. Donor-recipient pairs who have poor compatibility or substantial age-disparity and would like to achieve a better match can also register in this scheme.



MRI = magnetic resonance imaging; MDT = multidisciplinary team.

Fig 2 Steps in the evaluation of potential living kidney donors. Adapted with permission from Graham JM, Courtney AE. Oral presentation: 5 years of 1-days: Outcomes of potential living kidney donors undergoing a 1-day assessment pathway. British Transplantation Society Congress; Scottish Exhibition and Conference Centre, Glasgow 2016⁸⁴



Fig 3 Kidney transplants from living donors 2014 (per million population). Adapted with permission from International Registry in Organ Donation and Transplantation IRODaT Newsletter - Final numbers 2014. December 2015⁹¹

Fig 4 Kidney transplants in 2014 (or last year with data available) for WHO member states (per million population). DCD=donation after circulatory death. DBD=donation after brain death. *Data from 2013. **Data from 2012. ***Data from 2011. ****Data from 2010. Data source: WHO-ONT Global Observatory on Organ Donation and Transplantation Adapted with permission from Elsevier and Muller E, et al. Kidney transplantation across the globe: the good and bad. The Lancet Kidney Campaign. *Lancet*^{®2}