

**A report for
Universitätsklinikum Schleswig-Holstein/Campus Kiel
on shared decision making
for living kidney donation**



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LIST OF ABBREVIATIONS

AER	Albumin excretion rate
AST	American Society of Transplant
β-hCG	Human chorionic gonadotropin
BMI	Body mass index
CDSR	Cochrane Database of Systematic Reviews
CI	Confidence interval
CKD	Chronic kidney disease
CVD	Cardiovascular disease
DARE	Database of Abstracts of Reviews of Effects
ESRD	End-stage renal disease
FAQ	Frequently asked question
GFR	Glomerular filtration rate
G-I-N	Guidelines International Network
HALS	Hand-assisted laparoscopic nephrectomy
HARP	Hand-assisted retroperitoneoscopic nephrectomy
HRQoL	Health-related quality of life
HTA	Health technology assessment
IR	Incidence rate
KDIGO	Kidney Disease: Improving Global Outcomes
KSR	Kleijnen Systematic Reviews Ltd
LESS	Laparoendoscopic single-site nephrectomy
MA	Meta-analysis
MFI	Multidimensional Fatigue Inventory
NA	Not applicable
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NOS	Newcastle-Ottawa Scale
NOTES	Natural orifice transluminal endoscopic surgery
NR	Not reported
PICOS	Participants, intervention, comparators, outcomes and study design
RCT	Randomised controlled trial
RR	Relative risk
SDM	Shared decision making
SMD	Standardised mean difference
SR	Systematic review
UK	United Kingdom
USA	United States of America
VAS	Visual analogue scale

1. PROJECT OBJECTIVE

A key aim of the research project “Making SDM a reality” is to create interactive websites to inform patients as part of shared decision making (SDM).

To support this, Kleijnen Systematic Reviews Ltd (KSR) has prepared an evidence report with a synthesis of the literature underpinning the supporting evidence table of the relevant treatment options.

The topic of this evidence report is living kidney donation.

2. METHODS

2.1 INCLUSION CRITERIA

The research question underpinning the literature searches for this topic was developed in conjunction with clinical departments at Universitätsklinikum Schleswig-Holstein/Campus Kiel. The question was framed in terms of participants, intervention, comparators, outcomes and study design (PICOS), see Table 1.

As detailed below, literature searches were carried out using a stepwise approach to identify relevant studies according to study design. In the first step, searches aimed to identify relevant systematic reviews and guidelines.

Table 1: Inclusion criteria for searches

PICOS	
Patient population	Healthy potential kidney donors
Intervention/Comparators	Donor nephrectomy (laparoscopic, open or robot-assisted) compared to no donor nephrectomy
Outcomes	• Donor survival • Donor postoperative recovery • Risks to the donor (short and long-term) • Long-term implications • Ethical issues
Study design	Systematic reviews (SR)/meta-analyses (MA) (or randomised controlled trials (RCTs), or studies of lower evidence levels (non-randomised/observational studies), if needed.
MA = meta-analysis; RCT = randomised controlled trial; SR = systematic review	

In consultation with the commissioner, questions frequently asked by patients in conjunction with outcomes identified in the literature were developed into an evidence table outline.

2.2 FREQUENTLY ASKED QUESTIONS

The following research questions were identified as frequently asked questions (FAQs):

- 1. What does kidney donation involve?**
 - a. Rationale
 - b. Eligibility for donation
 - c. Practicalities for donation
 - d. Surgical techniques
- 2. What is the impact of kidney donation on long-term donor survival?**
 - a. Cause-specific mortality
 - b. Survival time
- 3. How long does a donor take to recover?**
 - a. Length of stay in hospital
 - b. Time to return to usual activity
 - c. Return to work
 - d. Return to driving

4. What are the short and long-term risks of kidney donation?

- a. Perioperative mortality
- b. Perioperative morbidity (e.g. need for reoperation, infectious complications, pain, wound-related complications, internal haemorrhage, reduction in glomerular filtration rate (GFR))
- c. Long-term morbidity (e.g. risks of hypertension and / or proteinuria, kidney disease including need for dialysis, cardiovascular disease, risk of cancer, psychological impairment, gout, fatigue syndrome, loss of physical fitness, metabolic bone disease, needing medication or special diet, diabetes)

5. What are the long-term implications of kidney donation?

- a. Consequences of living with one kidney
- b. Impact on quality of life and lifestyle
- c. Impact of life-long medical follow-up
- d. Impact on pregnancy
- e. Impact on future employment

6. What are ethical issues involved in kidney donation?

For example, guarantee that kidney donation is genuine and voluntary, motivation of the donor, emotional relationship with the recipient, irreversibility of kidney donation, expected outcome of transplantation for the recipient (difference between living and cadaveric kidney donation), alternative treatments available to the recipient, i.e. dialysis or waiting for cadaveric kidney grafts), safety of the procedure for the donor, opportunities to spend rehabilitation time together (donor/recipient).

2.3 LITERATURE SEARCHES

Literature searches were carried out to identify relevant systematic reviews and evidence-based guidelines on living kidney donations. To inform FAQs, a second targeted database search on living kidney donation and shared decision making was also undertaken.

The search strategies were developed specifically for each database and the keywords adapted according to the configuration of each database. Searches were limited by date range for systematic reviews and guidelines to 2012-2019. Targeted searches on SDM and living kidney donation were limited to the last three years as current and up-to-date evidence in this area was considered to be most relevant. Searches were not limited by language or publication status.

2.4 SEARCH SOURCES

Literature searches

Literature searches were conducted on 29 and 30 May 2019 to identify evidence to inform questions (FAQs) and to answer these FAQs based on systematic reviews, meta-analyses and evidence-based guidelines.

For this evidence report, searches for systematic reviews and guidelines were supplemented by targeted web searches to find information for the more narrative aspects of FAQs. The bibliographies of included studies and review articles were also checked for additional relevant articles.

Systematic reviews and guidelines

The following systematic review specific databases were searched from 2012 to present:

- Cochrane Database of Systematic Reviews (CDSR) (Wiley): 2012-2019/05/Iss5
- Database of Abstracts of Reviews of Effects (DARE) (www.crd.york.ac.uk): 2012-2015/03/31
- Health Technology Assessment (HTA) database (www.crd.york.ac.uk): 2012-2018/03/31
- KSR Evidence (KSR): up to 2019/05/30
- Epistemonikos (www.epistemonikos.org): 2012-2019/05/30

The following guidelines resources were searched from 2012 to present:

- Guidelines International Network (G-I-N) (www.g-i-n.net): up to 2019/05/30
- NHS Evidence (www.evidence.nhs.uk): 2012/01/01-2019/05/30
- ECRI Guidelines Trust (<https://guidelines.ecri.org/>): up to 2019/05/30
- NICE (www.nice.org.uk): up to 2019/05/30

Full details of all search strategies are presented in Appendix 1.

Targeted searches

To identify questions relevant to shared decision making, targeted searches were undertaken in the following databases from 2015 - 2019:

- EMBASE (Ovid): 1974 to 2019 May 29
- MEDLINE and In-Process & Other Non-Indexed citations (Ovid): 1946 to 2019 May 29
- MEDLINE Epub Ahead of Print and Daily Update: up to 2019 May 29

Full details of all search strategies are presented in Appendix 1.

Handling of citations

Identified references from the bibliographic database searches were downloaded into EndNote bibliographic management software for further assessment and handling.

Supplementary searches

Internet searches were performed to add more qualitative patient-related information to inform the more narrative FAQs.

2.5 METHODS OF STUDY SELECTION, QUALITY ASSESSMENT AND DATA EXTRACTION

Study selection

Two reviewers independently screened the title and abstract of each record identified by the search and determined the potential relevance of each record. For potentially relevant records, the full paper was obtained, independently checked, and inclusion criteria applied. Any disagreements were resolved through discussion.

An evidence hierarchy was used to select the most appropriate study(ies) to populate the evidence tables. Where more than one study could provide evidence, the most relevant studies were selected using the following criteria: recency (most recent preferred), quality (highest quality preferred), representativeness (populations representative of the general target population preferred). Where there were gaps in the evidence (no systematic review or guideline available), as described before, relevant randomised controlled trials (RCTs) would have been searched for and extracted, and where no RCTs would have been identified, observational studies would have been employed.

Data extraction

For each study, data were extracted by one reviewer and checked by another. Any disagreements were resolved by consensus.

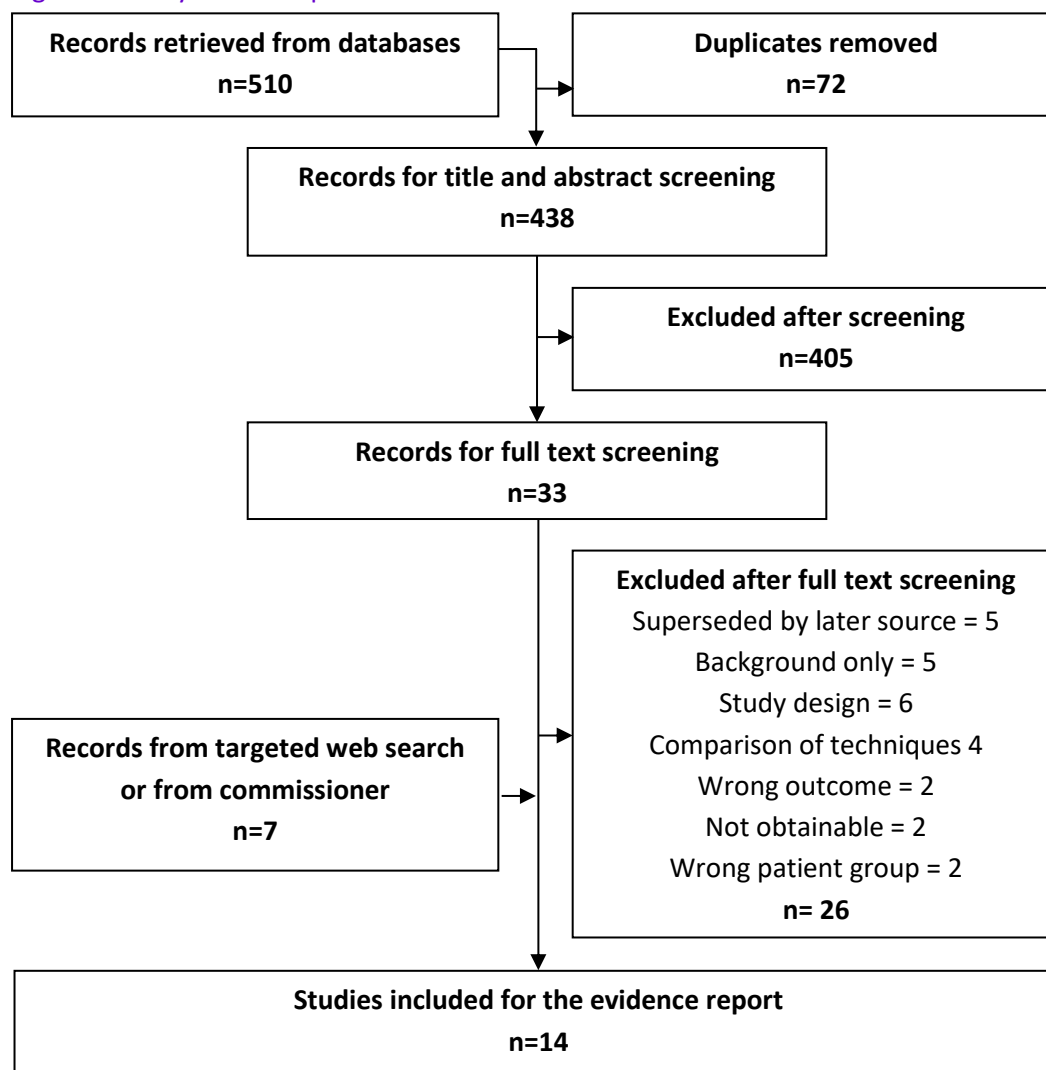
3. RESULTS

3.1 LITERATURE SEARCH RESULTS AND INCLUSION ASSESSMENT

A total of 510 records were retrieved from literature searches. After de-duplication, 438 titles and abstracts were screened by two reviewers. Thirty-three full papers were identified as potentially relevant. After further review, 26 records were excluded. In addition, internet searches were performed and retrieved 7 records which were used to inform FAQs 1, 2, 4 and 5. Thus, 14 records were selected for this report, please see Table 2.

A summary of the study selection process according to a modified PRISMA flow chart is reported in Figure 1.

Figure 1: Study selection process



3.2 OVERVIEW OF THE EVIDENCE

Table 2 summarises the studies used to answer the FAQs.

Table 2: Evidence sources

Study	Evidence type	What does kidney donation involve?	What is the impact of kidney donation on long-term donor survival?	How long does a donor take to recover?	What are the short and long-term risks of kidney donation?	What are the long-term implications of kidney donation?	What are ethical issues involved in kidney donation?
Arai 2018 ¹	SR qualitative studies	-	-	-	-	-	✓
Bundesgesetzblatt Verlag 2019 ²	Web site	-	-	-	-	✓	
Chen 2019 ³	Registry data	-	-	-	✓	-	-
Hanson 2015 ⁴	SR qualitative studies	-	-	-	-	-	✓
IQTIC 2018 ⁵	Registry data	-	✓	-	✓	-	-
Janki 2015 ^{6*}	Literature review	✓	-	-	-	-	-
Kortram 2016 ⁷	SR	-	-	✓	✓	-	
Lentine 2017 ⁸	Guidelines	✓	-	-	-	-	✓
Meyer 2016 ⁹	Qualitative review	-	-	-	✓	-	-
O'Keeffe 2018 ¹⁰	SR	-	✓	-	✓	✓	-
Organspende-info.de ^{11*}	Web site	✓	-	-	-	-	-
Ruck 2018 ¹²	Primary study (qualitative)	-	-	-	-	✓	-
Thiel 2005 ¹³	Registry data	-	-	-	-	✓	

Study	Evidence type	What does kidney donation involve?	What is the impact of kidney donation on long-term donor survival?	How long does a donor take to recover?	What are the short and long-term risks of kidney donation?	What are the long-term implications of kidney donation?	What are ethical issues involved in kidney donation?
Wirken 2015 ¹⁴	SR qualitative studies	-	-	-	✓	-	-
* Obtained from targeted web search SR = Systematic Review							

FAQ 1: WHAT DOES KIDNEY DONATION INVOLVE?

This section covers the rationale for living kidney donation, eligibility issues and surgical procedures. This is set out as Table 3.

Table 3: Description of living kidney donation

Rationale
A living kidney donor is a person who gives one of their healthy kidneys to someone with kidney failure who needs a transplant (the recipient). This could be a friend or family member. In Germany, an organ can be donated only to relatives, spouses, life partners or close friends, who are especially connected to the recipient. A kidney transplant can be transformational for someone with kidney disease, whether or not they are already having dialysis treatment. A successful transplant from a living donor is considered to be the best treatment option available for most people with kidney disease.¹⁵ Generally, people who receive a kidney from a living donor live for longer than those who receive one from a deceased donor.¹⁶ Quality of life is also better than they would be expected if they did not receive a kidney transplant.¹⁵ Living kidney donation allows the operation to be planned at a time that is convenient for the recipient, donor and clinical team. The average waiting time for a kidney transplant from someone who has died is approx. 6 years. For some ethnic groups and people with rare tissue types the wait can often be much longer.¹¹
Eligibility for donation
Donors will be provided with individualised estimates of short-term and long-term risks. Furthermore, risk will be assessed with respect to predetermined acceptance thresholds.⁸ Several online risk calculators are available^{17,603} Prior to any donation, informed consent is sought for donors to be evaluated and subsequently, if appropriate, informed consent for donation.⁸ Eligibility is assessed following a number of medical and surgical tests to check overall fitness and health. Medical history of nephrolithiasis (kidney stones), gout, blood pressure and risks of cardiovascular disease will all be checked as part of the eligibility process.⁸ Additionally screening will also be provided for evidence of transmittable infections and cancer to assist with eligibility decisions. Family history of kidney disease will be checked as well as a face-to-face psychological evaluation with one or more trained health professionals.⁸ A kidney will never be removed from someone unless the doctors are satisfied that the risks to the individual, in the short and long-term, are acceptably low, and all living kidney donations will be assessed by the hospital's living donation commission, which will make its recommendation accordingly. Some people who wish to donate find that they are not able to do so because of the results of the assessment process.^{11,18}
Surgical techniques
The following alternative techniques are offered at UKSH, but there may be other surgical techniques at other clinics: Open donor nephrectomy – minimal pararectal incision A minimally invasive incision is made near the rectus muscle in the abdominal region. The incision can be expected to measure between 7 cm and 15 cm depending on weight of the donor. Full robot-assisted laparoscopic nephrectomy The operating surgeon sits behind the console operating with 3-4 robot-arms while the operating assistant stands beside the patient. The position of the trocars and extraction site of the kidney is similar to conventional laparoscopic nephrectomy. Whilst, no randomised controlled trials comparing robot-assisted donor nephrectomy with laparoscopy have been

published so far, the procedure is thought to be safe and effective alternative to laparoscopy.⁶

Sources: Janki 2015⁶; Lentine 2017^{8,18}; Organspende-info.de¹¹

FAQ 1: EVIDENCE SUMMARY

What does kidney donation involve?

Rationale

A kidney can be donated to a close friend or family member. A successful transplant from a living donor is the best treatment option available for most people with kidney disease, by increasing life expectancy, quality of life and the need for ongoing intrusive treatment.

Eligibility

Donors will be provided with individualised estimates of short-term and long-term risks. Furthermore, risk will be assessed with respect to predetermined acceptance thresholds. Informed consent is required prior to eligibility testing and prior to decision to proceed.

Surgical techniques

Different surgical techniques are available:

- Open donor nephrectomy – minimal pararectal incision
- Full robot-assisted laparoscopic nephrectomy

FAQ 2: WHAT IS THE IMPACT OF KIDNEY DONATION ON LONG-TERM DONOR SURVIVAL?

The main evidence for mid- and long-term risks (including mortality) for living kidney donors comes from a recent, well-conducted systematic review by O’Keeffe and colleagues.¹⁰ This review evaluated studies of living kidney donation in adults between April 1964 and July 2017, including 118,426 donors and 117,656 control participants. Observational studies with at least one year of follow-up that compared health outcomes in adult living kidney donors versus non donor populations were included. The review was based on evidence from 52 studies from 17 countries and the average follow-up ranged from one to 24 years. The review evaluated the quality of included studies in terms of their population representativeness, comparability of groups and ascertainment of outcomes. The authors noted that only five studies selected the control population on the basis of successful completion of living donor screening or eligibility for nephrectomy based on medical status and renal function tests. The authors based the main analyses on 28 studies from 2000 onwards rated as medium or high quality according to these criteria.

FAQ 2a: Cause-specific mortality

The specific systematic reviews identified in this report did not provide data on cause-specific mortality. However the well conducted systematic review by O’Keeffe and colleagues provided data on all-cause mortality only, see Table 4.¹⁰

O’Keeffe found no statistically significant difference in overall survival between donors and non-donors, indeed there was a clear overall tendency for donors to have better survival (RR, 0.60 (CI, 0.31 to 1.10)). However, this might well be explained by the pre-selection for good health before a person is allowed to donate.

The included studies were similar with regards to quality. Most of the included studies had a follow up time of under 10 years, whereas the median follow up time of just one of the included primary studies was 15 years (Mjoen as reported in O’Keeffe¹⁰), and this study showed a higher mortality for donors compared to non-donors (224/1901 (11.8%) donor deaths compared to 2425/32621 (7.4%) non-donor controls). In a letter to the editor of the Annals of Internal Medicine, Mjoen argues that effects on mortality would likely not be visible until after 10 years, due to the pre-selection of donors based on health.¹⁹ However, it is worth noting that the recruitment period for kidney donors in this study was 1963 to 2007, so applicability to current circumstances is questionable.

Table 4: All-cause mortality

Outcome	No of studies / name	Follow up time (years) ^a	No events / N Donors (%)	No events / N Non-donors (%)	Pooled adjusted RR (95% CI) ^b	Pooled IR in donors (95% CI) ^c	Pooled IR non-donors (95% CI) ^c
All-cause mortality	4	6 to 15 (medians)	1467/84495 (1.7%)	3121/62484 (5.0%)	0.60 (0.31 to 1.10)	4.3 (1.3 to 14.1)	5.9 (1.6 to 22.1)
	Segev et al, 2010 ²⁰	6.3 median (IQR 3.2-9.8)	1206/80347 (1.5%)	272/9364 (2.9%)			
	Garg et al, 2012 ²¹	6.5 median	16/2028 (0.7%)	365/20280 (1.7%)			
	Mjøen et al, 2014 ²²	15.1 median (donors)	224/1901 (11.8%)	2425/32621 (7.4%)			
	Berger et al, 2011 ^{23*}	Unclear (all patients over 70)	22/219 (10.0%)	59/219 (26.9%)			
Source: O’Keeffe 2018 ¹⁰ a) Mean or median follow-up time in donors; b) Risk estimates from the four studies with baseline recruitment ending after 2000 and a Newcastle Ottawa Scale (NOS) ²⁴ score ≥4 were pooled using the random-effects profile likelihood meta-analysis method; c) Incidence rates per 1000 person-years for disease outcomes. *These numbers cannot be found in the source paper CI = confidence interval; IR = incidence rate; RR = relative risk							

The 2018 IQTIC report⁵ presents in hospital mortality and death of donor within 3 years following live kidney donations in Germany. Table 5

Table 5: Mortality, hospital and within 3 years

Outcome	Events/total number of donations	
	2016	2017
Hospital mortality	0/597	0/548
Death of donor within one year after living kidney donation	0/643	$\leq 3^*/582$
Death of donor within two years after living kidney donation	0/613	0/632
Death of donor within three years after living kidney donation	$\leq 3^*/715$	0/603
Source: IQTIC 2018 ⁵ *Please note that ≤ 3 seems is a standard term to present data when anonymization would be an issue with absolute numbers. The accompanying text reads no deaths		

FAQ 2b: Survival time

No reviews were found which reported the impact of kidney donation on long-term survival. However as discussed in FAQ2a, Mjoen as referenced in O’Keeffe¹⁰ suggests that there is a difference in survival comparing follow up times of under and over 10 years.

FAQ 2: EVIDENCE SUMMARY

What is the impact of kidney donation on long-term donor survival?

Based on a recent systematic review analysis of four studies including 84,495 living kidney donors and 62,484 non-donors, there was no evidence of increased risk of death from any cause at between six and 15 years after kidney donation. However, if the follow up time is segregated into under and over 10 years follow up, there seems to be an impact on mortality, where donors have a lower mortality in the first 10 years (probably due to pre-selection for good health), but that after more than 10 years mortality is adversely affected for donors compared to non-donors.

FAQ 3: HOW LONG DOES A DONOR TAKE TO RECOVER?

The main evidence for recovery time comes from a recent high-quality systematic review by Kortram and colleagues of minimally invasive live donor nephrectomy covering a range of operative techniques.⁷ The review included 190 studies (32,038 donors) up to March 2016.

FAQ 3a: Length of stay in hospital

Currently, average length of stay for removal of kidney in Universitätsklinikum Schleswig-Holstein is 4.9 days (s.d. 2.0 to 8.0)

FAQ 3b: Time to return to usual activity

The systematic review by Kortram and colleagues provided data on duration of convalescence for patients undergoing minimally invasive live donor nephrectomy, see Table 7.⁷

Table 6: Duration of convalescence

No of studies	No of donors	Mean (range) duration of convalescence (days)
Unclear	2,363	24.1 (4 to 60)
Source: Kortram 2016 ⁷		

FAQ 3c: Return to work

No studies were found which reported the impact of returning to work. However, impact on future employment is discussed in FAQ 5e.

FAQ 3d: Return to driving

No studies were found which reported times for return to driving. Indeed, the study by Hanson 2019²⁵ suggested that this issue was not evaluated as an outcome in any of the 268 studies (5% were randomised and 95% observational) which were reviewed as part of an investigation into the spectrum and consistency of outcomes after living kidney donation.

FAQ 3: EVIDENCE SUMMARY

How long does a donor take to recover?

A systematic review of studies of patients undergoing kidney donation with minimal procedures found an average length of stay in hospital of about 4 days. The same systematic review found an average duration of convalescence of about 24 days.

No evidence was found for return to work or return to driving times.

FAQ 4: WHAT ARE THE SHORT AND LONG-TERM RISKS OF KIDNEY DONATION?

The main evidence for short-term risks (including postoperative risks) comes from a recent systematic review by Kortram and colleagues of minimally invasive live donor nephrectomy covering a range of operative techniques.⁷ The main evidence for long-term morbidity for living kidney donors comes from the systematic review by O’Keeffe and colleagues.¹⁰

FAQ 4a: Perioperative mortality

A systematic review by Kortram and colleagues provided data on perioperative mortality in minimally invasive live donor nephrectomy, see Table 8.⁷ Please also see table 5 in FAQ2 for recent German data.

Table 7: Perioperative mortality

Outcome	No of studies	No of donors	No of events	Percentage
Mortality within 30 days	142	25,116 ^a	3	0.01 ^a
Source: Kortram 2016 ⁷ ^a There are discrepancies in the total number of patients reported in the text and in the table. The number reported for the two relevant subgroups in the text corresponds to the number reported in the table though so this was used. Depending on the population used, the percentage would be either 0.010% or 0.012%				

FAQ 4b: Perioperative morbidity

A systematic review by Kortram and colleagues provided data on perioperative events and complications in minimally invasive live donor nephrectomy, see Tables 9 and 10.⁷

Table 8: Perioperative morbidity: complications and re-interventions

Outcome	No of studies	No of donors	No of events	Percentage
Intraoperative complications	173	27,776	612	2.2
Postoperative complications	187	30,970	2,174	7
Infectious complications	163	26,729	697	2.6
Surgical re-intervention	163	28,516	165	0.6
Readmissions	NR	3084	95	3.1
Source: Kortram 2016 ⁷ NR = Not reported				

Table 9: Perioperative morbidity: Intraoperative and postoperative parameters

Outcome	No of donors	Value (range)
Pain day 1 (VAS score): mean (range)	1004	4.1 (0.37 to 8)
Pain at discharge (VAS score): mean (range)	757	2.2 (2 to 5)
Pain at 14 to 30 days post-op	488	1.3 (0.8 to 1.25)
Source: Kortram 2016 ⁷ VAS = visual analogue scale		

FAQ 4c: Long-term morbidity

The well conducted systematic review by O’Keeffe and colleagues provided data on risks of several chronic diseases (cancer, cardiovascular diseases, diabetes, hypertension, and end-stage renal disease),¹⁰ while the systematic review and meta-analysis by Wirken 2015 reported on fatigue,¹⁴ see Table 11. Wirken mentions that clinically significant changes between pre- and post-donation

assessments of fatigue were found in the early postoperative recovery period in all studies and in 50% of studies long term after donation. However Wirken also mentions that long-term fatigue levels were comparable to general population norms.¹⁴

No comparative data (donor vs non-donor) were found for fatigue levels. However a study by Meyer 2016⁹ examined fatigue levels experienced by over 200 donors in Norway, 8-12 years after donation, using the Multidimensional Fatigue Inventory (MFI). They described overall fatigues scores as being low. No differences were observed between donors < 70 years and ≥ 70 years, but Meyer and colleagues did find that females had significantly higher scores than males for general fatigues, physical fatigue, reduced motivation and mental fatigue. Activity levels (the remaining dimension of the MFI) were similar for males and females. It is important to bare in mind, however, that fatigue levels in non-donor populations were not analysed, so these patterns might be reflective of what happens for non-donors.⁹

Table 10: Long term morbidity

Outcome	No of studies	Average follow up time (years) ^a	No events / N Donors	No events / N Non-donors	Pooled adjusted RR (95% CI) ^b	Pooled IR in donors (95% CI) ^c	Pooled IR non-donors (95% CI) ^c
Cancer	3	8 to 15	160 / 7174	451 / 11712	0.72 (0.58 to 0.87)	2.9 (1.2 to 6.9)	4.3 (1.3 to 14.4)
Cardiovascular disease	4	6 to 15	107 / 4274	991 / 53246	1.11 (0.64 to 1.70)	2.4 (1.6 to 3.5)	1.9 (0.8 to 5.1)
Diabetes	5	6 to 12	47 / 3038	181 / 8261	1.03 (0.77 to 1.25)	3.8 (2.6 to 5.4)	4.1 (3.4 to 5.2)
Hypertension	4	6 to 12	297 / 1726	862 / 6949	1.08 (0.46 to 2.34)	26.3 (12.8 to 53.7)	25.9 (14.4 to 48.0)
ESRD	3	7 to 15	109 / 100145	53 / 62255	8.83 (1.02 to 20.93)	0.5 (0.1 to 4.9)	0.1 (0.02 to 0.6)
Fatigue*	1-2 months post-donation		3-6 months post-donation		≥12 months post-donation		
	No of studies	SMD (95%CI)	No of studies	SMD (95%CI)	No of studies	SMD (95%CI)	
	9	-0.93 (-1.03 to -0.83)	7	-0.22 (-0.49 to 0.05)	10	-0.26 (-0.35 to -0.18)	

Source: O’Keeffe 2018¹⁰, and *Wirken 2015¹⁴
^a Mean or median follow-up time in donors; ^b Risk estimates from studies with baseline recruitment ending after 2000 and an NOS score≥4 were pooled using the random-effects profile likelihood meta-analysis method; ^c Incidence rates per 1000 person-years for disease outcomes. CI = confidence Interval; ESRD = end-stage renal disease; IR = incidence rate; RR = relative risk; SMD = standardized mean difference before versus after donation

The 2018 IQTIC report⁵ presents morbidity outcomes following live kidney donations in Germany. See Table 12. Please note that these numbers are non-comparative, i.e. they do not compare the incidence/prevalence of a particular outcome to the incidence/prevalence in a matched non-donor population.

Table 11: Donor dialysis and reduced kidney function within 3 years of donation

Outcome	Events/total number of donations	
	2016	2017
Donor requiring dialysis	0/597	0/548
Reduced kidney function of donor within one year after living kidney donation	≤3*/546	0/512
Reduced kidney function of donor within two years after living kidney donation	0/514	≤3*/545
Reduced kidney function of donor within three years after living kidney donation	≤3*/589	≤3*/517
Source: IQTIC 2018 ⁵ *Please note that ≤3 is a standard term to present data when anonymization would be an issue with absolute numbers. The accompanying text reads no events		

Other post-donation outcomes have been reported using registry data from American live kidney donation post-donation outcomes see Table 13. A total of 9558 living kidney donors with post-donation data for up to 40 years were analysed. Overall, 1406 LDs (14.7%) had post-donation events. As with the German numbers above the below American data is non-comparative. Likely some of the conditions listed would have occurred to the individuals regardless of their kidney donation.

Table 12: Long term morbidity

Post-donation condition	No of live kidney donors with condition	Occurrence Rate (% out of all 9558 live kidney donations)
New Hypertension Diagnosis (posttransplant)	806	8.43
Diabetes	190	1.99
Proteinuria	171	1.79
Post-operative Ileus/SBO	147	1.54
Myocardial Infarction	114	1.19
Pneumothorax	106	1.11
Stroke	74	0.77
Dysrhythmia	61	0.64
Chronic Incisional Pain	53	0.55
Sudden Death	40	0.42
Chronic/Maintenance Dialysis	28	0.29
Testicular Pain	27	0.28
Post-operative Hemorrhage	21	0.22
Cardiac Arrest	20	0.21
Wound Dehiscence	16	0.17
Wound Seroma	15	0.16
Hematuria	14	0.15
Nephrolithiasis	13	0.14
Incisional Hernia	9	0.09
Kidney transplant waiting list	9	0.09
Kidney transplant	8	0.08
Pulmonary Embolism	8	0.08
Pancreatitis	7	0.07
Reoperation for Incisional Hernia	7	0.07
Complication of Intubation	6	0.06
Epididymitis	6	0.06
Microalbuminuria	6	0.06
Post-operative Reintubation	6	0.06
Post-operative Renal Failure	6	0.06
Bladder Injury	5	0.05
Bowel Injury	3	0.03
Post-operative Dialysis	3	0.03
Post-operative deep vein thrombolism	3	0.03
Splenic Injury	3	0.03
Rhabdomyolysis	2	0.02
Vascular Injury	2	0.02
Source: Chen 2019³ 36 post-donation conditions that are found in the living kidney donors in RELIVE ImmPort. Total number of donors with one or more condition is 1401. Total number of donors is 9558 including the majority of those that do not have a recorded condition.		

FAQ 4: EVIDENCE SUMMARY

What are the short and long-term risks of kidney donation?

A systematic review of over 25,000 donors undergoing minimally invasive kidney removal reported three deaths in the postoperative period (usually defined as up to 30 days after operation). The same systematic review found that just over 2% of people had complications during surgery and about 7% had complications after surgery. Almost 3% had complications due to infection. Fewer than 1% needed a further surgical procedure and approximately 3% had to be readmitted to hospital. In a group of just over 1,000 donors the average level of pain on day one was about 4 on a scale of 0 to 10 where 0 is no pain and 10 is unbearable pain. This went down on average to just over 2 at the time of discharge and just over 1 at 14 to 30 days after the procedure.

No comparative data (donor vs non donor) were found in regard to long term fatigue after donation. Non comparative evidence suggests that fatigue levels are generally low, although females appear to exhibit higher levels of fatigue than males.

Based on the higher quality evidence from a recent well-conducted systematic review including 84,495 living kidney donors and 62,484 non-donors, there was no evidence of an increased risk of cancer, cardiovascular disease, type 2 diabetes or hypertension when assessed between five and 15 years after kidney donation. There was an increased risk of end-stage renal disease. However in real terms the increase in risk is small. If 1,000 kidney donors were followed up for ten years, five might have end-stage renal disease. If 1,000 non-donors were followed up for ten years, one might have end-stage renal disease.

FAQ 5: WHAT ARE THE LONG-TERM IMPLICATIONS OF KIDNEY DONATION?

Two sources of evidence were assessed to inform the long-term implications of kidney donation that have not already been addressed by FAQs, namely the high-quality systematic review O’Keeffe 2018¹⁰ and a primary qualitative study by Ruck 2018¹² which was based on semi-structured interviews of 50 living kidney donors.

FAQ 5a: Consequences of living with one kidney

The study reported by Ruck 2018¹² attempted to elicit concerns about kidney donation (before and after) as well as reporting the views of family members and friends (as reported from donors). Results from this study suggested over one fifth of donors considered living with one kidney to be a genuine concern prior to transplant. This proportion almost halved after donation which suggests that some concerns had been alleviated, see Table 14.

A statement from the Swiss live donor registry²⁶ related to donor life after kidney donation. When donors were asked if with the benefit of hindsight they would redo the donation, 4.3% of the donors said no, 94.4% said yes. Reasons for saying no was in most instances that the result for the kidney receiver was not satisfactory.¹³

Cosmetic satisfaction is not a well-researched area. According to Hanson 2019,²⁵ cosmetic satisfaction was reported as an outcome in only 6% of the 268 studies included within their investigation into the spectrum and consistency of outcomes studied after living kidney donation. No results of significance were reported from any of these studies. Results from Ruck 2018¹² suggested that a low percentage of patients (2%) were concerned about the incision/scar pre-donation. This increased to 4% post-donation. Family and friends (as reported from donors) did not consider this to be a concern (0%), see Table 14.

Financial issues were identified as patient-reported outcomes in only 5.6% of the 268 studies included within the review undertaken by Hanson 2019²⁵ although, once again, no specific evidence was reported.

According to German insurance requirements, when transplanting live organ donation, it is generally the case that the costs of inpatient treatment of the donor, transplantation of the organ and all other benefits associated with organ donation are covered by the health insurance of the recipient. Thus, the organ donor has a comprehensive benefit claim against the health insurance of the organ recipient for his entire outpatient, inpatient and pre- and post-treatment and further aftercare.²

Insurance issues were identified as an issue of concern for patients prior to donation in the study by Ruck 2018¹². However, this was not considered to be an issue post-donation, suggesting any concerns were alleviated, see Table 14.

Table 13: Concern with consequences of living with one kidney

Concern	Pre-donation	Post-donation	Family/Friends
Donors remaining kidney failing	22%	12%	2%
Incision or scar	2%	4%	0%
Insurance Issues	4%	0%	2%
Employment	4%	2%	0%
Source: Ruck 2018 ¹²			

FAQ5b: Impact on quality of life and lifestyle

The systematic review undertaken by O’Keeffe identified thirteen studies reporting Health Related Quality of Life in living kidney versus control populations.¹⁰ All used the standardized Short Form-36 or Short Form-12 Health Survey to measure psychosocial and physical health. In overall terms, no important differences were detected for any of the domains between donors and non-donors. The exception was for vitality, where donors appeared to respond more favourably than non-donors. It is notable, that there was no single quality of life component where non donors reported more favourably than donors (statistically significant or not). This being said, donors will have been heavily pre-assessed for health effects, whereas this will not necessarily be the case for non-donors. None of the studies included by O’Keeffe to inform quality of life had controls that had successfully completed living donor screening, or were eligible for nephrectomy based on medical status and renal function tests. To this extent, results might not be as surprising as they first appear, see Table 15.

Table 14: Pooled mean difference in HRQoL Scores Between Living Kidney Donors and Non donors

Number of studies	Outcome	Donors (n)	Non donors (n)	Standardised mean difference (95% CI)
7	Physical Component summary	6,903	29,460	0.24 (0.00 to 0.48)
8	Mental Component summary	7,207	29,643	0.00 (-0.20 to 0.19)
7	Physical function	6,973	22,594	0.04 (-0.07 to 0.11)
7	Role physical	6,956	22,594	0.08 (-0.08 to 0.16)
7	Bodily pain	6,958	22,594	0.12 (-0.12 to 0.34)
7	General health	6,960	22,594	0.17 (-0.08 to 0.42)
7	Vitality	6,962	22,594	0.2 (0.10 to 0.31)
7	Social function	6,964	22,594	0.07 (-0.05 to 0.19)
7	Role emotional	6,957	22,594	0.04 (-0.15 to 0.24)
7	Mental health	6,962	22,594	0.11 (-0.09 to 0.32)

Source: Table in O’Keeffe 2018¹⁰
CI = confidence interval; HRQoL = health-related quality of life; SMD = standardised mean difference

FAQ5c: Impact of long medical follow up

No studies were found which reported the impact of long term medical follow up. Indeed, the study by Hanson 2019 suggested that this issue was not evaluated as an outcome in any of the 268 studies which were reviewed as part of an investigation into the spectrum and consistency of outcomes after living kidney donation.²⁵ The 2017 KDIGO guideline suggests that all donors be offered psychosocial services during the first year of donation.¹⁸ Additionally, measurement of blood

pressure, BMI, serum creatinine measurement with GFR estimation and albuminuria measurement should be performed at least annually post-donation. Reviews and promotion of a healthy lifestyle including regular exercise, healthy diet and abstinence from tobacco are also recommended.

FAQ5d: Impact on pregnancy

Two studies were identified by O’Keeffe 2018¹⁰ which looked at the long term impact of kidney donation on pregnancy-related outcomes. One of the studies was of good quality (Garg 2015, as reported in O’Keeffe) whereas the other was rated as poor (Reisasaeter 2019, as reported in O’Keeffe) as judged by the NOS. Meta-analysis undertaken by O’Keeffe suggested that there was a higher risk of pre-eclampsia for living donors when compared to non-donors which was significant at the 95% level (RR, 2.12 (CI, 1.06 to 4.27). Risks were also found to be higher for gestational hypertension (RR, 2.27 (CI, 0.94 to 5.36) , pre term birth (RR, 1.47 (CI, 0.78 to 2.64) and low birthweight (RR, 1.70 (CI, 0.91 to 3.16), although there was a much higher degree of uncertainty around these findings, as they were not statistically significant, see Table 16.

Table 15: Pregnancy-related outcomes

Outcome	Number of studies	Average follow up time (years)*	Events (donors, n=237)	Events (non-donors, n=22,299)	Pooled adjusted Risk Ratio (95%CI) †	Pooled Incidence Rate per 100 pregnancies (95% CI) (donors)	Pooled Incidence Rate per 100 pregnancies (95% CI) (non-donors)
Gestational hypertension	2	5-11	10	331	2.27 (0.94, 5.36)	3.8 (1.4, 6.3)	1.6 (1.0, 2.2)
Pre-eclampsia	2	5-11	14	687	2.12 (1.06, 4.27)	5.9 (2.9, 8.9)	3.1 (2.9, 3.3)
Preterm birth	2	5-11	21	1449	1.47 (0.78, 2.64)	8.7 (5.1, 12.3)	6.5 (6.2, 6.8)
Low birthweight	2	5-11	17	1141	1.70 (0.91, 3.16)	7.0 (3.8, 10.2)	4.7 (3.6, 5.9)

Source: O’Keeffe 2018¹⁰

* Mean or median follow-up time in donors; † Risk estimates from the two studies with baseline recruitment ending after 2000 and a NOS score≥4 were pooled using the random-effects profile likelihood meta-analysis method

CI = confidence interval; NOS = Newcastle-Ottawa Scale

FAQ5e: Impact on future employment

According to Hanson 2019,²⁵ employment was reported in 4.9% of the 268 studies included within their review of the literature. No results were reported from these studies. Results from Ruck 2018¹² suggested that a very small percentage of patients (4%) were concerned about employment pre-donation. This reduced to 2% post-donation, family and friends did not consider this to be a concern, see Table 14.

FAQ 5: EVIDENCE SUMMARY

What are the long-term implications of kidney donation?

Consequences of living with one kidney

Cosmetic satisfaction may be an issue for a small proportion of patients, with evidence that it is a higher concern post transplant compared to pre-transplant.

Financial consequences

Financial consequences have not been studied in detail but checklists are available to consider where impact might occur. There is some evidence to suggest that pre-donation insurance concerns were alleviated post-donation, although specific policies will no doubt need to be scrutinised.

Impact on quality of life and lifestyle

There is no evidence to suggest any quality of life aspect is negatively impacted by a choice to donate a kidney. Indeed, as a whole, quality of life is better for those donating a kidney compared to those not donating (possibly because their eligibility for transplant suggests their overall health status may be better than that of the non donor population).

Impact of long medical follow up

No studies were found which reported the impact of long term medical follow up. However, the guidelines mention medical follow up, which should take place annually.

Impact on pregnancy

Meta analysis based on two studies suggested that there was a higher risk of pre-eclampsia for living donors when compared to non donors. Risks were also found to be higher for gestational hypertension, pre term birth and low birthweight (though non-significant in all cases). It appears that those contemplating pregnancy will have additional factors to consider prior to donation of a kidney.

Impact on future employment

No results of significance were reported from studies identified in systematic reviews considered in this report. Results from a structured questionnaire suggested, that for a small proportion of patients, employment impact was a particular concern prior to transplant. However this appears to have been less of a concern post-transplant.

FAQ 6: WHAT ARE ETHICAL ISSUES INVOLVED IN KIDNEY DONATION?

The 2017 KDIGO guideline (Kidney Disease: Improving Global Outcomes) addresses ethical aspects of the donation process.^{8,18,27}

The guideline contains a checklist of items to discuss, inform and examine in conjunction with kidney donation from a living donor. Most of the checklist items relate to physical tests to ensure health status, prognoses and compatibility (or exchange programs), but some items are specifically relevant for the ethics of the donation process, see Table 17. The process of kidney donation must follow the laws and regulations of the country and its governing regulatory bodies.⁸ Particular legal issues usually need to be considered in order to protect vulnerable people, e.g. cognitively impaired, young and/or dependent people.¹⁸ Other aspects with ethical implications cover respect of autonomy (e.g. the required informed consent) and the prohibition of incentives to donate that may create undue influence (e.g. payment for organs in money or kind).¹⁸ Physicians need to inform potential donors regarding the regulatory aspects (e.g. regarding ongoing payment of salaries and remuneration, insurance in the case of complications etc.).²⁷

Transplant professionals have an ethical duty to act in the best interest of the donor. *‘Donor candidate autonomy does not overrule medical judgement and transplant professionals are ethically justified to decline a donor candidate when they believe that the risk of poor post-donation outcomes is too high. A poor outcome can have a very negative impact on the donor, on their recipient, and on public opinions about living donation’.*¹⁸

Table 16: Extract of items from the KDIGO checklist with ethical implications

Guideline chapter ^a	Checklist of test, information, and discussion items
1	• Provide the donor candidate with individualized estimates of short- and long-term risks • Evaluate risks with respect to predetermined transplant program acceptance thresholds
2	• Obtain consent from the donor candidate for evaluation and donation
16	• Perform face-to-face psychosocial evaluation, education and planning session with one or more trained, experienced health professionals
18	• Respect donor autonomy during all phases of evaluation and donation
19	Perform annual post donation follow-up care including: • Review and promotion of healthy lifestyle practices including exercise, diet, and abstinence from tobacco • Review and support of psychosocial health and well-being

Based on Table 1 of Lentine 2017⁸

^a Chapter numbers refer to the full English guideline ⁸

AER = albumin excretion rate; β -hCG = human chorionic gonadotropin; BMI = body mass index; CKD = chronic kidney disease; CVD = cardiovascular disease; GFR = glomerular filtration rate

FAQ6a: Donor perspective

Arai 2018¹ did a qualitative systematic review on factors influencing kidney donors' decisions. The systematic review distinguished between four different areas influencing the decision making in kidney donors, see Table 18.

Table 17: Themes of factors influencing kidney donors' decision-making

Four themes of kidney donors' decision-making	
Donor's role, personality, and personal values	• Individual donors' thoughts • Intrinsic nature of a donor's position • <i>Feelings supporting the will to donate</i> • <i>Negative donor feelings about donation</i>
Donor's understanding level	• Lacking judgment • Insufficient understanding despite decision ability
Personal influences on donor	• Personal relationships or situations that may cause pressure • Acts and values on the side of healthcare professionals that may cause pressure
Donor's environment and situation	• <i>Environment in which donor hesitates to express their feelings</i> • Uncertainty in medicine which makes it difficult to evaluate risks and benefits • Positive economic benefit • <i>Surroundings showing no understanding of the donor's intent to donate</i>
Based on Table 2 and page 3038 of Arai 2018 ¹ <i>Italicised</i> = issues into which individual discussion is needed, according to Arai 2018 ¹ UK = United Kingdom; USA = United States of America	

A good understanding level of the procedure, risk and benefits is a prerequisite for a donor's decision making ability. Further, the donor should make the decision in an environment free from influence on her or his decision making.

However, Arai et al. further described sub sets of issues for which individual discussion would be needed regarding the appropriateness of the intervention from the donor point of view.¹ These issues were found in areas of "Donor's role, personality, and personal values" and "Donor's environment and situation" specifically: "Feelings supporting the will to donate"; "Negative donor feelings about donation"; "The environment in which the donor hesitates to express their feelings"; "Surroundings showing no understanding of the donor's intent to donate" (*italicised in the table*).

FAQ6b: Recipient perspective

Hanson 2015⁴ undertook a qualitative systematic review on attitudes of patients with chronic kidney disease toward live donor kidney transplantation. The systematic review identified six themes and concluded that '*enhanced education and psychosocial support may help clarify, validate, and address patients' concerns regarding donor outcomes, guilt, relationship tensions, and donor recruitment*', see Table 19.

Table 18: Themes of recipient expectations and attitudes toward live kidney donation

Six themes of recipient expectations and attitudes	
Prioritizing own health	• Better graft survival • Accepting risk • Desperate aversion to dialysis
Guilt and responsibility	• Jeopardizing donor health • Anticipating donor regret • Causing donor inconvenience
Ambivalence and uncertainty	• Doubting transplant urgency • Insufficient information • Confronted by unfamiliarity • Prognostic uncertainty
Seeking decisional validation	• A familial obligation • Alleviating family burden • Reciprocal benefits for donors • Respecting donor autonomy • External reassurance • Religious approval
Needing social support	• Avoiding family conflict • Unrelenting indebtedness • Emotional isolation
Cautious donor recruitment	• Self-advocacy • Lacking self-confidence • Avoiding donor coercion • Emotional vulnerability • Respecting cultural and religious taboos
Based on Table 3 and page 541ff of Hanson 2015 ⁴	

FAQ 6: EVIDENCE SUMMARY

Ethical Issues

Donor perspective

The donor candidate should be provided with individualized estimates of short- and long-term risks. Evaluate risks with respect to predetermined transplant program acceptance thresholds.

Face-to-face psychosocial evaluation, education, and planning should be given. Donor autonomy should be respected during all phases of evaluation and donation. This would include protecting the donor candidate from making decisions in an environment in which donor hesitates to express their feelings.

Annual post- donation follow-up care should be performed.

Recipient perspective

The recipient will face a number of decisions and issues of a physical and psychosocial nature related to the living organ donation. Education and psychosocial support may help process the recipient's concerns.

Legal issues

The process of kidney donation must follow the laws and regulations of the country and its governing regulatory bodies. Particular legal issues usually need to be considered in order to protect vulnerable people (e.g. cognitively impaired, young and/or dependent people). Transplant professionals have an ethical duty to act in the best interest of the donor and donor autonomy should not overrule medical judgement.

3.3 ASSESSMENT OF THE CLINICAL REVIEW EVIDENCE

A summary of studies providing clinical evidence is set out in Table 20 below. Studies which merely provided descriptive evidence are not listed here (see footnote)

Table 19: Overview of the clinical evidence (studies only)

Study ID	Participants	Interventions	Outcomes	Study Design	Follow-up
Arai 2018¹	75 studies Participants were considering making a live kidney donation Number of participants NR	Potential living kidney donation	Questionnaires on donor decision making autonomy	Systematic review of qualitative evidence	NR
Hanson 2015⁴	≥ 1,791 adults with chronic kidney disease At least 58% had received or were undergoing evaluation for a living donor transplantation	Potential living kidney donation	In-depth or semi structured interviews, focus groups, and open-ended surveys on expectations and attitudes toward living kidney donation	Review of qualitative evidence	NR
Kortram 2016⁷	32,038 donors	Minimally invasive live donor nephrectomy	Recovery time, perioperative risks and complications	Systematic review	Peri-operative (approx. 30 days)
Lentine 2017⁸	Participants contemplating living organ donation Age and number NR	Potential living organ donation	NA	Guideline	NA
Meyer 2016⁹	217 donors representing 63% of donors in Norway who donated 8-12 years ago	Living kidney donation	Fatigue. HRQoL was also reported but not used in this review because O'Keefe ¹⁰ was considered a more valid source.	Cross sectional survey	8-12 years after donation
O'Keefe 2018¹⁰	118,426 donors and 117,656 control participants	Living kidney donation	All-cause mortality, mid and long-term risks of diseases, complications of pregnancy and HRQoL	Systematic review	At least one year

Study ID	Participants	Interventions	Outcomes	Study Design	Follow-up
Ruck 2018¹²	50 donors and their families/friends (proxies)	Living kidney donation	Concerns about donation before or after donation or heard from family members or friends	Primary study (qualitative)	Pre and post - donation
Wirken 2015¹⁴	3,201 living kidney donors from 34 studies	Living kidney donation	Fatigue (long term)	Systematic review of qualitative studies	
This table excludes: Janki 2015⁶ and Organspende-info.de¹¹ which were included only for their descriptive characteristics; Chen 2019³, IQTIC 2018⁵ and Thiel 2005¹³ are based on registry data and Bundesgesetzblatt Verlag 2019² which is a web site;. HRQoL = health-related quality of life; NA = not applicable; NR = not reported					

4. DISCUSSION

4.1 STRENGTHS, LIMITATIONS AND UNCERTAINTIES

The evidence presented in this report has been based, where possible, on rigorous systematic reviews. There is only a small amount of high-quality evidence on long term risks of living donor kidney donation, an issue highlighted in a previous review of outcomes relating to living kidney donation.²⁵ For long term outcomes, follow up duration may not be adequate as most studies report a follow up period of up to ten years rather than lifetime follow up.^{10, 18} Registry data can be used as evidence sources for treatment uptake and self reported quality of life including fatigue.^{13,600}

The review by O’Keeffe¹⁰ used in this report highlighted further limitations of the data including comparability of donor and non-donor groups. Living kidney donors may be often in better general health than the general population before donation. Donors, unlike the general population, undergo robust evaluation and are highly selected for good baseline health.²⁸ In addition, a more thorough surveillance post-donation may increase disease diagnosis. These are important limitations for patients and clinicians to bear in mind when making decisions about living kidney donation.

A further issue is the results presented are for ‘the average patient’. Patients will need to be informed of specific characteristics that might increase their risk of adverse outcomes. The KDIGO guidelines on living donation include the statement ‘When possible, transplant programs should provide each donor candidate with individualized quantitative estimates of short-term and long-term risks from donation, including recognition of associated uncertainty, in a manner that is easily understood by donor candidates.’¹⁸ However, the extent to which donation-attributable risk varies according to individual health characteristics is not always known.¹⁸

Within aforementioned limitations, we have identified that there is no evidence of an increased risk of cancer, cardiovascular disease, type 2 diabetes or hypertension when assessed between five and 15 years after kidney donation. There is an increased risk of end-stage renal disease. However, in real terms the increase in risk is small.

Similarly, no evidence was found that quality of life is adversely impacted for living donors of kidneys. Indeed, donors tend to have higher quality of life in regard to vitality when compared to non-donors (although this may be an artefact of pre-selection of healthier individuals in the cohort of donors compared to non-donors).

Based on analysis of two studies from a recent well-conducted systematic review (237 donors, 22,299 non-donors), there was inconclusive evidence of increased risk of gestational hypertension, low birthweight or pre-term birth. However women who become pregnant may be at greater risk of preeclampsia (approximately 6% as opposed to 3% in non-donor pregnancies). It would appear that families who are contemplating a future pregnancy would be well advised to consider this evidence prior to deciding whether to volunteer for living kidney donation.

A summary of all evidence is set out in Table 21.

Table 20: Summary of evidence

Evidence	Favours non donation	Favours donation	Notes
FAQ2: What is the impact of kidney donation on long-term donor survival?			
All-cause mortality	-	-	There is no evidence of increased risk of death from any cause at between six and 15 years after kidney donation.
FAQ3: How long does a donor take to recover?			
Length of stay	NA		The average length of stay in hospital is about 5 days.
Duration of convalescence	NA		The average duration of convalescence is about 24 days.
FAQ4: What are the short and long-term risks of kidney donation?			
Postoperative mortality	NA		Deaths in the postoperative period (usually defined as up to 30 days after operation) are rare.
Postoperative complications	NA		Approximately 2% of people may have complications during surgery and about 7% may have complications after surgery. About 3% have complications due to infection.
Reoperations and readmissions to hospital	NA		Less than 1% of people needed a further surgical procedure and approximately 3% had to be readmitted to hospital.
Pain	NA		In a group of just over 1000 donors the average level of pain on day one was about 4 on a scale of 0 to 10 where 0 is no pain and 10 is unbearable pain. This went down on average to just over 2 at the time of discharge and just over 1 at 14 to 30 days after the procedure.
Risk of disease	-	-	There is no evidence of an increased risk of cancer, cardiovascular disease, type 2 diabetes or hypertension between five and 15 years after kidney donation.
Risk of end-stage renal disease	✓		There is an increased risk of end-stage renal disease with living kidney donation. However, in real terms the increase in risk is small. If 1000 kidney donors were followed up for ten years, five might have end-stage renal disease. If 1000 non-donors were followed up for ten years, one might have end-stage renal disease.
FAQ5: What are the long-term implications of kidney donation?			
Satisfaction with cosmetic aspects of surgery	✓		A small proportion of patients may have concerns over the scars left by surgery
Financial implications	-	-	No evidence was found to suggest that donors would be worse off in financial terms compared to

Evidence	Favours non donation	Favours donation	Notes
			non-donors. Scrutiny of insurance details and use of checklists might be helpful.
Quality of Life	-	-	There is no evidence suggesting that quality of life is negatively impacted by donation of a kidney. Indeed, the quality of life of donors is often better than that of non-donors because they tend to be healthier (having undergone rigorous eligibility testing)
Implications of long term medical follow up	-	-	No studies were found which reported the impact of long term medical follow up
Impact on pregnancy	✓		There appears to be an increased risk of pre-eclampsia for kidney donors. It is also possible that there may be increased gestational hypertension, pre term birth and low birthweight (although the evidence has considerable uncertainty). Donors contemplating a future pregnancy will have additional factors to consider prior to donation of a kidney
Impact on future employment	-	-	No results of significance were reported from studies
FAQ6: What are ethical issues involved in kidney donation?			
Donor perspective	NA, this is a personal decision		The donor candidate should be informed of short and long term risks, and evaluated physically and psychosocially in an environment void of non-factual influence
Recipient perspective	NA, this is a personal decision		Education and psychosocial support may help process the recipient’s concerns and feelings towards the kidney receipt
KEY			
-	No noticeable difference		
✓	Noticeably better but not statistically or clinically significant (or subject to probable bias)		
✓	Statistically significantly better or guideline recommendation		
FAQ = frequently asked question; NA = Not applicable			

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APPENDIX 1: SEARCH STRATEGIES

Database	Dates	Results
CDSR	2012 – 2019/05/Iss5	5
DARE	2012 – 2015/05/30	6
HTA	2012 – 2018/05/30	
KSR Evidence	2012 – 2019/05/30	45
Epistemonikos	2012-2019/05/30	119
NHS Evidence	2012/01/01-2019/05/30	67
NICE	up to 2019/05/30	14
GIN	2012-2019/05/30	46
ECRI	up to 2019/05/30	16
Total		318
Total after de-duplication		260

SDM database searches

Database	Dates	Results
Embase	2015-2019 May 29	169
MEDLINE & In-Process	2015-2019 May 29	96
MEDLINE DU & Epub	2015-2019 May 29	4
Total		269
Total after de-duplication		192

CDSR: Issue 5 of 12, May 2019

Searched: 29.5.19

- #1 MeSH descriptor: [Kidney Transplantation] explode all trees 3471
- #2 MeSH descriptor: [Kidney] explode all trees 3787
- #3 MeSH descriptor: [Nephrectomy] explode all trees 301
- #4 MeSH descriptor: [Living Donors] explode all trees 324
- #5 (#1 or #2 or #3) and #4 226
- #6 ((Living or live or alive) NEAR/2 (donor* or organ* or donat* or give* or giving or gift*)):ti,ab,kw 1604
- #7 (kidney* or renal or nephrectomy or nefrectomy):ti,ab,kw 71815
- #8 #6 and #7 1080
- #9 ((Kidney* or renal or nephrectomy or nefrectomy) NEAR/2 (donor* or donat* or give)):ti,ab,kw 1262
- #10 (Living or live or alive):ti,ab,kw 38133
- #11 #9 and #10 720
- #12 ("kidney exchange*" or "kidney swap*" or "kidney paired donation*" or "kidney paired exchange*"):ti,ab,kw 4
- #13 #5 or #8 or #11 or #12 with Cochrane Library publication date Between Jan 2012 and Dec 2019 833

CDSR = 5

CENTRAL = 828

DARE (www.crd.york.ac.uk/): 2012 – March 2015

HTA (www.crd.york.ac.uk/): 2012 – March 2018

Searched: 30.5.19

- 1 MeSH DESCRIPTOR Kidney Transplantation EXPLODE ALL TREES
- 2 MeSH DESCRIPTOR Kidney EXPLODE ALL TREES
- 3 MeSH DESCRIPTOR Nephrectomy EXPLODE ALL TREES
- 4 MeSH DESCRIPTOR Living Donors EXPLODE ALL TREES
- 5 #1 OR #2 OR #3
- 6 #4 AND #5
- 7 (Living or live or alive):TI AND (donor* or organ* or donat* or give* or giving or gift*):TI AND (kidney* or renal or nephrectomy or nefrectomy):TI
- 8 ("kidney exchange*" or "kidney swap*" or "kidney paired donation*" or "kidney paired exchange*"):TI
- 9 #6 OR #7 OR #8
- 10 (#9) IN DARE, HTA FROM 2012 TO 2019

6 results

KSR Evidence (www.ksrevidence.com): up to 30 May 2019

Searched: 30.5.19

#	Query	Results
1	(living or live or alive) and (donor* or organ* or donat* or give* or giving* or gift*) and (kidney* or renal or nephrectomy or nefrectomy) in All text Date published: 2012–2019;	45
2	"kidney exchange*" or "kidney swap*" or "kidney paired donation*" or "kidney paired exchange*" in All text Date published: 2012–2019;	1
3	#1 or #2	45

Epistemonikos (www.epistemonikos.com): up to 30 May 2019

Searched: 30.5.19

(title:((title:((Living OR live OR alive) AND (donor* OR organ* OR donat* OR give* OR giving OR gift*) AND (kidney* OR renal OR nephrectomy OR nefrectomy)) OR abstract:((Living OR live OR alive) AND (donor* OR organ* OR donat* OR give* OR giving OR gift*) AND (kidney* OR renal OR nephrectomy OR nefrectomy))) OR (title:("kidney exchange*" OR "kidney swap*" OR "kidney paired donation*" OR "kidney paired exchange*")) OR abstract:("kidney exchange*" OR "kidney swap*" OR "kidney paired donation*" OR "kidney paired exchange*")))) OR abstract:((title:((Living OR live OR alive) AND (donor* OR organ* OR donat* OR give* OR giving OR gift*) AND (kidney* OR renal OR nephrectomy OR nefrectomy)) OR abstract:((Living OR live OR alive) AND (donor* OR organ* OR donat* OR give* OR giving OR gift*) AND (kidney* OR renal OR nephrectomy OR nefrectomy))) OR (title:("kidney exchange*" OR "kidney swap*" OR "kidney paired donation*" OR "kidney paired exchange*")) OR abstract:("kidney exchange*" OR "kidney swap*" OR "kidney paired donation*" OR "kidney paired exchange*"))))

Filtered: 2012-2019, Systematic Review

119 results

NHS Evidence (www.evidence.nhs.uk): up to 30 May 2019

Searched: 30.5.19

Search terms filtered to Guidance and Policy or Systematic Reviews from 01/01/2012 – 29/05/2019	Hits
"live kidney transplant"	0
"live kidney transplantation"	0
"live donor" "kidney transplantation"	15
"live organ donation" kidney	0
Live "kidney donation"	10
Living "kidney donation"	17
Living "kidney donor"	10
Live "kidney donor"	7
"living donor" kidney	47
"living donor" renal	39
"living donor" nephrectomy	12
"living donation" nephrectomy	4
"living donation" renal	14
"living donation" kidney	17
"kidney exchange"	1
"kidney swap"	0
"kidney paired donation"	2
"living organ donation" kidney	7
Total	202
Total after duplicates removed	67

NICE (www.nice.org.uk): up to 30 May 2019

Searched: 30.5.19

Search filtered to Guidance, 2012 - 2019	Hits
"living donors" kidney	4
"kidney transplantation"	12
"living donation" kidney	1
"living donor" renal	3
Nephrectomy	2
Total	22

Total after de-duplication	14
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International Guideline Library (www.g-i-n.net): up to 30 May 2019

Searched: 30.5.19

Search terms	Hits
Kidney transplantation [MeSH]	24
Living donors [MeSH]	0
"live donor" (kidney* or renal or nephrectomy or nefrectomy)	104
"organ donation"	1
"kidney donation"	2
"kidney exchange"	0
"kidney swap"	0
"kidney paired donation"	0
Total	131
Total filtered by date 2012 – 2019, duplicates removed	46

ECRI Institute (<https://guidelines.ecri.org/>): up to 30 May 2019

Searched: 30.5.19

Search terms	Hits
"kidney transplantation"	10
"living donor"	2
"living kidney donor"	1
"living donation" nephrectomy	1
"live kidney donation"	0
"live kidney donor"	1
"kidney exchange"	0
"kidney swap"	0
"kidney paired"	0
"Live renal donation"	3
"living renal donor"	0
"living organ donor"	0
"living renal donation"	0

Living donor organ transplantation	3
Total	21
Total after duplications removed	16

Embase (Ovid): 1974 – 2019 May 29

Searched: 30.5.19

- 1 kidney/ or nephrectomy/ (281469)
- 2 living donor/ (28289)
- 3 1 and 2 (4051)
- 4 ((Living or live or alive) adj2 (donor\$ or organ\$ or donat\$ or give\$ or giving or gift\$)).ti,ab,ot,dj,dq. (45123)
- 5 (kidney\$ or renal or nephrectomy or nefrectomy).ti,ab,ot,dj,dq. (1081103)
- 6 4 and 5 (16757)
- 7 ((Kidney\$ or renal or nephrectomy or nefrectomy) adj2 (donor\$ or donat\$ or give\$ or giving or gift\$)).ti,ab,ot,dj,dq. (22348)
- 8 (living or live or alive).ti,ab,ot,dj,dq. (646719)
- 9 7 and 8 (11319)
- 10 ("kidney exchange\$" or "kidney swap\$" or "kidney paired donation\$" or "kidney paired exchange\$").ti,ab,ot,dj,dq. (604)
- 11 3 or 6 or 9 or 10 (18365)
- 12 shared decision making/ (4521)
- 13 ((share\$ or sharing\$ or inform\$ or patient\$ or donor\$) adj3 (decision\$ or deciding\$ or choice\$ or preference\$)).ti,ab. (111155)
- 14 sdm.ti,ab. (2759)
- 15 or/12-14 (113938)
- 16 11 and 15 (390)
- 17 limit 16 to yr="2015 -Current" (169)

MEDLINE & In-Process & Other Non-Indexed Citations (Ovid): 1946 – 2019 May 29

Searched: 30.5.19

- 1 kidney transplantation/ (91827)
- 2 kidney/ (264182)
- 3 living donors/ (14357)
- 4 (1 or 2) and 3 (6295)
- 5 ((Living or live or alive) adj2 (donor\$ or organ\$ or donat\$ or give\$ or giving or gift\$)).ti,ab,ot. (29471)
- 6 (kidney\$ or renal or nephrectomy or nefrectomy).ti,ab,ot. (816349)
- 7 5 and 6 (8907)
- 8 ((Kidney\$ or renal or nephrectomy or nefrectomy) adj2 (donor\$ or donat\$ or give\$ or giving or gift\$)).ti,ab,ot. (12667)
- 9 (living or live or alive).ti,ab,ot. (485408)
- 10 8 and 9 (6232)
- 11 ("kidney exchange\$" or "kidney swap\$" or "kidney paired donation\$" or "kidney paired exchange\$").ti,ab,ot. (294)
- 12 or/4,7,10-11 (11611)
- 13 Decision Making/ (88686)
- 14 ((share\$ or sharing\$ or inform\$ or patient\$ or donor\$) adj3 (decision\$ or deciding\$ or choice\$ or preference\$)).ti,ab. (73186)

15 sdm.ti,ab. (2085)
16 or/13-15 (151926)
17 12 and 16 (331)
18 limit 17 to yr="2015 -Current" (96)

MEDLINE Epub Ahead of Print, Daily Update (Ovid): up to 2019 May 29

Searched: 30.5.19

1 kidney transplantation/ (56)
2 kidney/ (59)
3 living donors/ (17)
4 (1 or 2) and 3 (7)
5 ((Living or live or alive) adj2 (donor\$ or organ\$ or donat\$ or give\$ or giving or gift\$)).ti,ab,ot.
(550)
6 (kidney\$ or renal or nephrectomy or nefrectomy).ti,ab,ot. (10199)
7 5 and 6 (168)
8 ((Kidney\$ or renal or nephrectomy or nefrectomy) adj2 (donor\$ or donat\$ or give\$ or giving or
gift\$)).ti,ab,ot. (229)
9 (living or live or alive).ti,ab,ot. (10217)
10 8 and 9 (118)
11 ("kidney exchange\$" or "kidney swap\$" or "kidney paired donation\$" or "kidney paired
exchange\$").ti,ab,ot. (10)
12 or/4,7,10-11 (177)
13 Decision Making/ (92)
14 ((share\$ or sharing\$ or inform\$ or patient\$ or donor\$) adj3 (decision\$ or deciding\$ or choice\$
or preference\$)).ti,ab. (2407)
15 sdm.ti,ab. (75)
16 or/13-15 (2506)
17 12 and 16 (5)
18 limit 17 to yr="2015 -Current" (4)