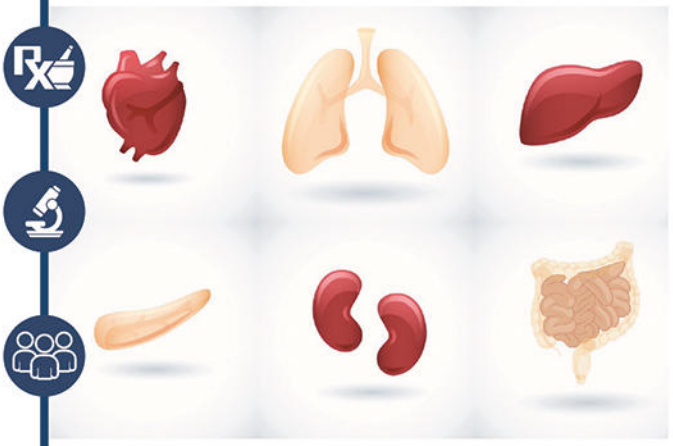
AMERICAN SOCIETY OF® TRANSPLANTATION

COMPREHENSIVE TRAINEE CURRICULUM



COMPREHENSIVE TRAINEE CURRICULUM

WATCH 52 ONLINE LESSONS INCLUDING:

- *Adult and Pediatric Liver*
- *Adult Cardiac and Pulmonary*
- *Abdominal Transplant Surgery*
- *Cardiothoracic Transplant Surgery*
- *Adult and Pediatric Kidney*
- *Transplant Pharmacy*

Solid organ transplantation is a multidisciplinary field, leading to a diverse community of professionals within the AST. As a result, it is often necessary for trainees to have extensive knowledge of all areas of transplantation—not just their specialty.

Check out this brand new resource, meant to supplement the training trainees and fellows receive at their university or hospital.

$50 members / $200 non-members

AMERICAN SOCIETY OF TRANSPLANTATION

American Journal of Transplantation 2015; 15: 3041–3054
Wiley Periodicals Inc.

doi: 10.1111/ajt.13453

Minireview

The Course and Predictors of Health-Related Quality of Life in Living Kidney Donors: A Systematic Review and Meta-Analysis

L. Wirken[1,2,*], H. van Middendorp[1,2], C. W. Hooghof[3], M. M. Rovers[4], A. J. Hoitsma[3], L. B. Hilbrands[3] and A. W. M. Evers[1,2]

[1]Leiden University, Institute of Psychology, Health, Medical and Neuropsychology Unit, Leiden, The Netherlands
[2]Department of Medical Psychology, Radboud university medical center, Nijmegen, The Netherlands
[3]Department of Nephrology, Radboud university medical center, Nijmegen, The Netherlands
[4]Radboud Institute of Health Sciences, Radboud university medical center, Nijmegen, The Netherlands
[*]Corresponding author: Lieke Wirken, l.wirken@fsw.leidenuniv.nl

A better understanding of the course and risk factors for impaired long-term health-related quality of life (HRQoL; ie, physical, psychological, and social–relational functioning) after kidney donation might help clinicians improve the care of live kidney donors. This systematic review and meta-analysis summarizes prospective studies about the course and predictors of HRQoL in living kidney donors. Studies indicate that shortly after donation, donors have lower HRQoL, with minor to moderate changes in psychological and social–relational functioning and major changes in physical functioning. At 3–12 months after donation, HRQoL returned to baseline or was slightly reduced, particularly for fatigue, but scores were still comparable to general population norms. Results were mainly robust across surgery techniques. A limited number of studies examined risk factors for impaired HRQoL, with low psychological functioning before donation as the most consistent predictor. Based on these results, clinicians can inform potential donors that, on average, kidney donors have high long-term HRQoL; however, donors with low psychological functioning at baseline are those most at risk of impaired long-term HRQoL. Future studies should focus on other potentially relevant predictors of postdonation HRQoL, including donor eligibility criteria and donor–recipient relationships, to optimize screening and interventions for donors at risk.

Abbreviations: BDI, Beck Depression Inventory; BMI, body mass index; CI, confidence interval; EQ-5D, EuroQol 5D; ES, effect size; HADS, Hospital Anxiety and Depression Scale; HALN, hand-assisted transperitoneal laparoscopic donor nephrectomy; HARP, hand-assisted retroperitoneoscopic donor nephrectomy; HRQoL, health-related quality of life; LDN, laparoscopic donor nephrectomy; MFI-20, Multidimensional Fatigue Inventory; MIDN, mini-incision donor nephrectomy; NA, data not available; NS, not significant; ODN, open donor nephrectomy; SAS, Zung Self-rating Anxiety Scale; SCL-90, Symptom Checklist-90; SDS, Zung Self-rating Depression Scale; SF-36, Short Form-36 Health Survey; SF-36 MCS, Short Form-36 mental component summary score; SF-36 PCS, Short Form-36 physical component summary score; SSQ, Social Support Questionnaire; STAI, State-Trait Anxiety Inventory; TERS, Transplant Evaluation Rating Scale; VAS, visual analog scale; WHO QoL-Bref, World Health Organization Quality of Life Brief Questionnaire

Received 17 July 2014, revised 05 July 2015 and accepted for publication 06 July 2015

Introduction

The high percentages of living donor kidney transplantations worldwide have prompted research into kidney donors' health-related quality of life (HRQoL), consisting of physical, psychological and social–relational functioning (1). Donors have been found to have high HRQoL before donation (2–4), often better than that of the general population, probably because of the stringent medical screening for kidney donor eligibility. After donation, however, approximately 5%–25% of donors experience problems with physical or psychosocial functioning, such as depressed mood, fatigue or pain (5–7). A previous systematic review of mostly cross-sectional and a few prospective studies concluded that most donors experienced no change or improvement in psychosocial functioning on average at 4 years after donation but that a small group of donors reported adverse psychosocial outcomes (5).

After this previous review, new prospective studies and randomized controlled trials were published addressing the HRQoL of living kidney donors (8–14). Moreover, advances in surgery techniques, such as minimally invasive techniques, and expansion of donor eligibility criteria (eg, acceptance of donors at higher ages, body mass index

[BMI], or blood pressure), may have affected HRQoL (15–17). In addition, because impaired HRQoL after donation has been found, it is relevant to know potential predictors to guide screening and interventions for donors at risk to prevent impaired functioning after donation. Currently, guidelines to select eligible living kidney donors are based mainly on physical and not on psychosocial criteria (2,15,18–22). Consequently, we conducted an updated systematic review and meta-analysis of the current literature (1) on the course of HRQoL of living kidney donors from before to after donation and (2) on predictors of postdonation HRQoL.

Methods

Literature search strategy and inclusion criteria

PubMed, Embase, Cinahl, and PsycINFO databases from 1990 until February 2014 were systematically searched, using *living kidney donors, psychological factors*, and *quality of life* as keywords. In addition, the reference lists of included studies and review articles were examined for other potentially relevant articles. All prospective studies published in English peer-reviewed journals investigating HRQoL before and after donation and using validated self-report questionnaires were included. Details of the protocol for this systematic review and meta-analysis were registered on PROSPERO (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42013006517).

HRQoL domains

The questionnaires used to assess different HRQoL domains are reported in Table 1. Physical functioning was assessed as *physical disability*, defined as physical limitations in daily activities due to health; *pain*, defined as the frequency and interference of pain and discomfort in performing daily activities; and *fatigue*, defined as a lack of energy and different fatigue dimensions (physical and mental fatigue, reduced activities and motivation). *Psychological functioning* included feelings of anxiety, nervousness or depression. *Social–relational functioning* concerned limitations of social activities due to health.

Data extraction and study quality assessment

The following data were extracted from the included studies: data collection period and country, number of living donors, demographic variables, donor–recipient relationship, surgery techniques, questionnaires, assessment points and HRQoL outcome measures. Short Form-36 Health Survey (SF-36) physical and mental component summary scores were categorized as physical disability and psychological functioning, respectively (11,23). When surgery techniques were not mentioned, study authors were contacted.

For the course analyses, postdonation assessments were classified into three periods: the early postoperative period (months 1–2), short-term functioning (months 3–6), and long-term functioning ($\geq$12 months).

Two authors (L.W. and H.v.M.) independently assessed the risk of bias of included studies using the Cochrane risk of bias criteria (24). Potential differences were discussed until consensus was reached. Two domains were scored: (1) attrition bias, based on incomplete outcome data (low risk: donors with and without missing data were compared on outcomes; high risk: no reasons for dropout mentioned or data missing potentially related to outcomes; unclear risk: insufficient information) and (2) other potential sources of bias, namely, range of postdonation assessment period (low risk: standardized timing; high risk: very broad standard deviation of timing; unclear risk: broad variation of timing but within one period) and the use of validated questionnaires (low risk: validated questionnaires; high risk: no validated questionnaires; unclear risk: potentially biased assessment). Initially, studies with either a high or low risk of bias (study quality) were all included to assess the course of HRQoL. Subsequently, sensitivity analyses were used to explore the robustness of the main findings using high- and low-quality studies separately.

Data synthesis and analyses

The generic inverse variance analysis methodology for meta-analysis of within-subject designs was applied to analyze HRQoL changes from predonation to the three postdonation assessment periods, using standardized mean differences (SMDs or Hedges' g) and standard errors or standard deviations of the SMDs to calculate effect sizes (ESs). An ES of 0.2 represented a small effect, 0.5 represented a medium effect, and 0.8 represented a large effect (25). If data to calculate ESs were not reported, study authors were contacted; some studies had to be excluded because of authors' nonresponse (18,26) or data not being provided (4,27). Because of repeated assessments within donors, an average correlation of $r = 0.5$ was imputed between pre- and postdonation HRQoL. Because correlations were generally not reported, correlation coefficients of 0.1 and 0.9 were also examined to explore the robustness of the effects. All HRQoL scores were scaled in the direction of negative SMDs representing a decline of HRQoL over time. In case of between-study heterogeneity (I^2) $<$70%, fixed-effects models were used; otherwise, random-effects models were used (28). Analyses were conducted using Review Manager version 5.3 (29). To frame the results, the clinical significance of the pre- to postdonation assessment changes was examined by comparing change scores with clinical relevance norms of the psychometric instruments applied in the included studies. The SF-36, for example, was the most used instrument to assess HRQoL, with manuals reporting a 5-point difference as clinically relevant (30–34).

To explore the impact of surgery techniques on HRQoL course, they were categorized as *laparoscopic donor nephrectomy* (LDN; standard laparoscopic and hand-assisted laparoscopic donor nephrectomy [HALN]), *mini-incision donor nephrectomy* (MIDN; incisions $<$15 cm), and *open donor nephrectomy* (ODN; with or without rib resection). When data were reported on two surgery techniques within one category (eg, HALN and LDN), the data of the overall most frequently used technique was included for meta-analysis, after which it was explored whether results changed when the other technique was included. If multiple questionnaires within one HRQoL domain were assessed, the overall most frequently used questionnaire across all studies was initially included in the meta-analysis. Subsequently, sensitivity analyses were conducted to test the robustness of the main findings when using the other questionnaires.

Results

Literature search

Our search yielded 2845 publications, of which 57 full-text articles were reviewed for eligibility; 23 were excluded (Figure 1). The 34 remaining studies had at least one assessment before and after donation: 25 (74%) on HRQoL course, five (15%) on predictors, and four (12%) on course and predictors.

Table 2 describes characteristics of the 34 included studies, which were published between 2002 and 2014. In total, 3201 living kidney donors participated in the included

Table 1: Questionnaires and timing of predonation and postdonation health-related quality of life (HRQoL) assessments of the studies assessing the course of HRQoL

Study (year)	HRQoL questionnaires	Timing of predonation HRQoL assessment (time to donation)	Timing of postdonation HRQoL assessments (time after donation)
Aguiar et al (2007) (50)	SF-36	NA	1 and 3 mo
Andersen et al (2007) (9)	SF-36	1–2 days	1 and 12 mo
Bahler et al (2013) (52)	SF-36	NA	1, 4, and 7 mo
Bergman et al (2005) (47)	SF-36	NA	4 weeks (M = 29 days)
Chien et al (2010) (56)	SF-36	92.9 ± 5.0 days	3 mo (80.4 ± 16.6 days)
Dols et al (2010) (10)	SF-36 MFI-20	NA	6 years (range 1–8)
Dols et al (2014) (14)	SF-36	NA	1, 3,[1] 6,[1] and 12 mo
Frade et al (2008) (59)	SF-36 SAS SDS	NA	18.8 ± 12.8 mo
Garcia et al (2013) (23)	SF-36	20 ± 27 days	3 mo (126 ± 89 days) and 12 mo (445 ± 164 days)
Guleria et al (2011) (57)	WHO QoL-Bref HADS	2 weeks	6 mo
Klop et al (2013a) (4)	SF-36	NA	1, 3, 6, and 12 mo[1]
Klop et al (2013b) (53)	SF-36	1 day	1 and 12 mo
Kok et al (2006a) (27)	SF-36 MFI-20	1 day	1, 3, 6, and 12 mo
Kok et al (2006b) (49)	SF-36 MFI-20 EQ-5D	1 day	1, 3, 6, and 12 mo[1]
Kroencke et al (2012) (3)	SF-36 HADS	126 ± 112 days	3 mo (96 ± 22 days) and 12 mo (381 ± 31 days)
Kurien et al (2011) (11)	SF-36	1 mo	6 mo
Lopes et al (2011) (18)	SAS SDS	NA	≥12 mo[1]
Lopes et al (2013) (46)	SF-36	NA	≥12 mo
Lumsdaine et al (2005) (48)	WHO QoL-Bref	NA	6 weeks and 12 mo
Massey et al (2010) (61)	SCL-90	NA	2.3 years (3–97 mo)
Minnee et al (2008) (51)	SF-36 MFI-20 VAS Pain	NA	SF-36: 1, 3, 6, and 12 mo MFI-20: 1, 3, 6, and 12 mo VAS pain: 28 days
Minz et al (2005) (60)	BDI STAI SSQ	NA	3 mo
Nicholson et al (2011) (12)	SF-36	1 day	6 weeks
Smith et al (2003) (54)	SF-36	NA	4 mo
Smith et al (2004) (2)	SF-36	NA	4 and 12 mo
Timmerman et al (2013) (62)	SCL-90	9 mo (range 2–13)	19 mo (range 3–36)
Vemuru Reddy et al (2011) (58)	WHO QoL-Bref	2 weeks	6 mo
Virzi et al (2007) (55)	SF-36	1 mo	4 mo
Walton-Moss et al (2007) (26)	SF-36	NA	6 and 12 mo[1]

BDI, Beck Depression Inventory (35); EQ-5D, EuroQol 5D (36); HADS, Hospital Anxiety and Depression Scale (37); MFI-20, Multidimensional Fatigue Inventory (38); NA, data not available; SAS, Zung Self-rating Anxiety Scale (39); SCL-90, Symptom Checklist-90 (40); SDS, Zung Self-rating Depression Scale (41); SF-36, Short Form-36 Health Survey (32); SSQ, Social Support Questionnaire (42); STAI, State-Trait Anxiety Inventory (43); VAS, visual analog scale (44); WHO QoL-Bref, World Health Organization quality of life brief questionnaire (45).
[1]Data not available for meta-analysis.

studies, with sample sizes varying from 14 to 501 (median sample size: n = 97). Two studies assessed the same cohort of donors (18,46). Donors had a median age of 47.4 years (range 18–94 years), and an average of 60% of donors were female (range 43%–100%). The largest percentage of studies was conducted in the Netherlands (29%), followed by the United States (15%) and India (12%). Response rates at the first assessment varied between 37% and 100%, and dropout rates at the follow-up assessment varied between 0% and 81%.

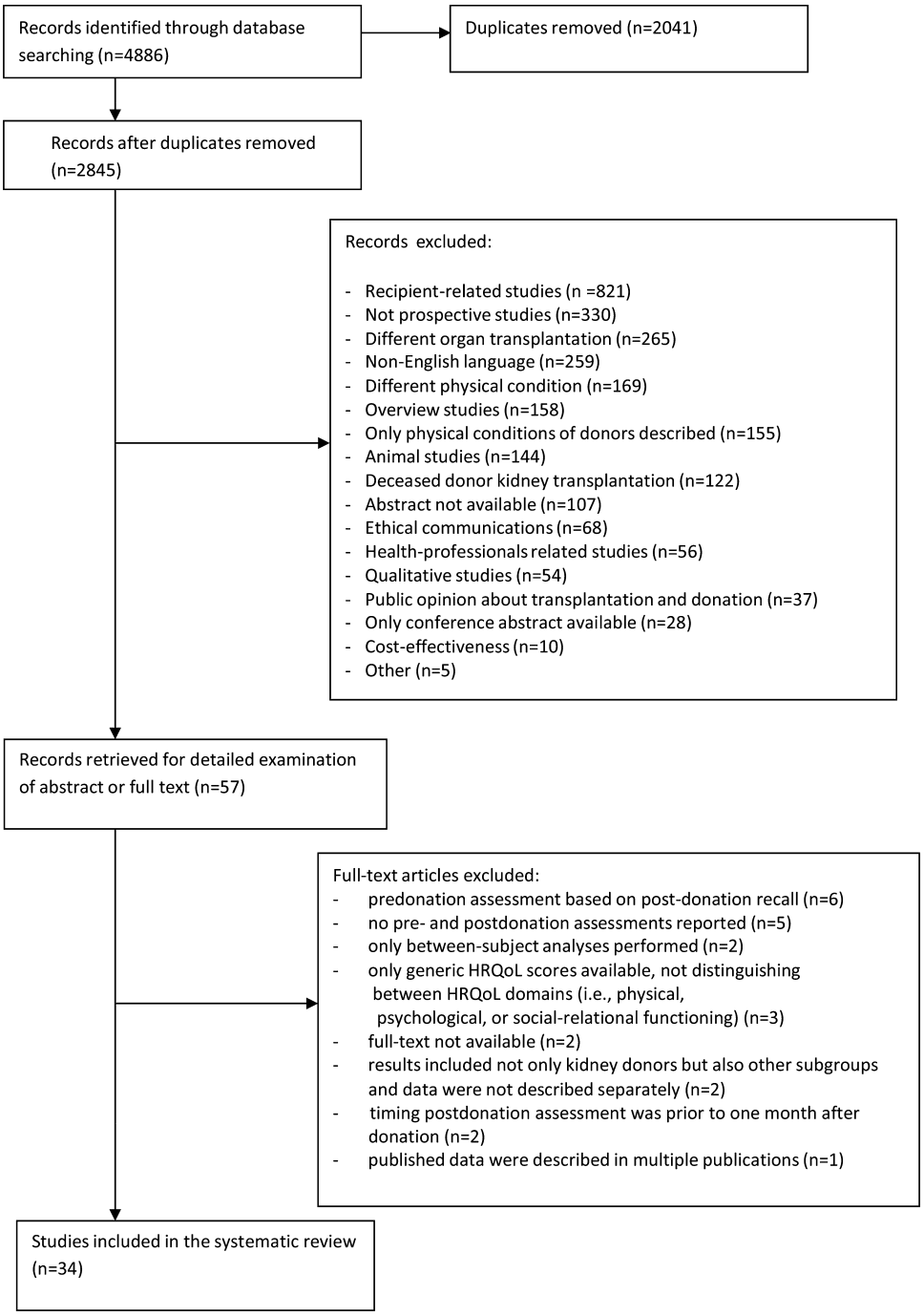


Figure 1: Flow chart.

Study quality assessment

The response rates of the included studies were generally high, with a mean response rate across all studies of 89%. The mean of percentage of dropouts on the last assessment point was 20%. The attrition bias was low in 47% of studies, unclear in 38% of studies, and high in 15% of studies. Other sources of bias (ie, range of postdonation assessment period and the use of validated questionnaires) were low in 70% of studies, unclear in 9% of studies, and high in 21% of studies (Figures S1 and S2).

Study results

Course of HRQoL: The timing of predonation HRQoL assessments was not specified in 16 studies (55%) and varied between 1 day and 9 months before donation in the

Table 2: Characteristics of studies included in the systematic review and meta-analysis for both course and prediction of health-related quality of life

Study (year)	Study purpose	Course data available for meta-analysis	Country	No. of donors	Year data collection	Female sex	Donor age (range)	Surgery technique	Donor type	Multicenter	Response rate	Dropout last assessment
Aguiar et al (2007) (50)	1	Yes	Brazil	60	2003	68%	41.6 ± 8.9	MIDN: 100%	Related: 92% Unrelated: 8%	No	NA	10%
Andersen et al (2007) (9)	1	Yes	Norway	122	2001–2004	55%	45.5	ODN: 48% LDN: 52%	Related: 80% Unrelated: 20%	No	51%	21%
Bahler et al (2013) (52)	1 + 2	Yes	United States	101	2006–2010	56%	38 (19–62)	LDN: 100%	Related: 76% Unrelated: 24%	No	NA	76%
Bergman et al (2005) (47)	1	Yes	Canada	35	2001–2004	57%	40 (31–49)	LDN: 100%	NA	No	97%	8%
Chien et al (2010) (56)	1 + 2	Yes	Taiwan	14	2005–2008	50%	45.3 (28–62)	LDN: 100%	Related: 100%	No	NA	26%
Dols et al (2010) (10)	1	Yes	The Netherlands	100	2001–2004	47%	52.5	MIDN: 50% LDN: 50%	Related: 74% Unrelated: 26%	Yes	88%	11%
Dols et al (2014) (14)	1	Yes	The Netherlands	190	2008–2010	52%	52.6	LDN: 50% HARP: 50%	NA	Yes	91%	14%
Frade et al (2008) (59)	1	Yes	Portugal	32	NA	53%	41 (21–64)	MIDN: 100%	Related: 100%	No	NA	NA
Fukunishi et al (2002) (65)	2	–	Japan	65	NA	54%	53.1 (31–64)	NA	NA	No	NA	NA
Garcia et al (2013) (23)	1	Yes	Brazil	50	2007–2009	62%	41 (25–68)	MIDN: 100%	Related: 92% Unrelated: 8%	No	100%	0%
Glotzer et al (2013) (64)	2	–	United States	83	2000–2010	69%	42.8 (18–60)	NA	NA	No	37%	0%
De Groot et al (2012) (21)	2	–	The Netherlands	316	1997–2009	65%	52.6 (25–77)	ODN: 0.3% MIDN: 96.7% LDN: 3%	Related: 54% Unrelated: 46%	No	74%	0%
Gross et al (2013) (63)	2	–	United States	233	1963–2005	61%	58 (24–94)	ODN: 66% LDN: 33% Unknown: 1%	Related: 78% Unrelated: 22%	Yes	73%	0%
Guleria et al (2011) (57)	1	Yes	India	73	NA	100%	42.6 ± 10.5	MIDN: 84%. LDN: 16%	Related: 100%	No	100%	NA
Klop et al (2013a) (4)	1	No	The Netherlands	501	2001–2010	54%	<40: 20%; 40–60: 53%; 60–70: 21%; 70< 6%	MIDN: 24%, LDN: 57%, HARP:19%	Related: 55% Unrelated: 45%	Yes	NA	16%
Klop et al (2013b) (53)	1	Yes	The Netherlands	40	2011–2012	58%	48.0 (21–77)	LDN: 50% HARP: 50%	NA	No	98%	37%
Kok et al (2006a) (27)	1	Yes	The Netherlands	100	2001–2004	47%	48.8	MIDN: 50% LDN: 50%	Related: 74% Unrelated: 26%	Yes	88%	11%
Kok et al (2006b) (49)	1	No	The Netherlands	100	2001–2005	61%	52.1 (20–90)	MIDN: 45% LDN: 55%	Related: 52% Unrelated: 48%	No	80%	11%
Kroencke et al (2012) (3)	1	Yes	Germany	79	2005–2009	61%	53.6 ± 11.3	ODN: 37%, MIDN: 52%, LDN: 11%	Related: 59% Unrelated: 41%	No	93%	25%
Kurien et al (2011) (11)	1	Yes	India	50	2009–2010	70%	45.8	LDN: 50% LESS: 50%	NA	No	NA	NA
Lopes et al (2011) (18)	1	No	Portugal	45	2002–2008	58%	41.2 (20–60)	MIDN: 100%	Related: 100%	No	100%	60%
Lopes et al (2013) (46)	1	Yes	Portugal	45	2002–2008	58%	41.2 (20–60)	MIDN: 100%	Related: 100%	No	100%	60%
Lumsdaine et al (2005) (48)	1	Yes	United Kingdom	40	2000–2004	63%	49 (24–71)	ODN:100%	Related: 65% Unrelated: 35%	Yes	95%	23%
Massey et al (2010) (61)	1 + 2	Yes	The Netherlands	24	2000–2008	54%	58.5 (33–84)	LDN: 100%	Unrelated: 100%	No	96%	NA
Minnee et al (2008) (51)	1	Yes	The Netherlands	105	2002–2006	58%	<35: 12%; 35–44: 26%; 45–54: 29%; 55–64: 26%; 65–74: 6%; >74: 1%	HALN: 100%	Related: 62% Unrelated: 38%	No	100%	2%
Minz et al (2005) (60)	1	Yes	India	75	2003	72%	42.8 ± 11.6	NA	Related: 75% Unrelated: 25%	No	NA	NA
Nicholson et al (2011) (12)	1	Yes	United Kingdom	84	2000–2004	60%	46.3	MIDN: 33% LDN: 67%	NA	No	89%	NA
Rodrigue et al (2013) (66)	2	–	United States	133	2002–2012	57%	43.1 ± 11.2	LDN: 100%	Related: 54% Unrelated: 46%	Yes	92%	16%
Smith et al (2003) (54)	1	Yes	Australia	48	1997–2001	52%	48 (26–72)	ODN: 100%	Related: 61% Unrelated: 39%	No	98%	8%

(*Continued*)

Table 2: Continued

Study (year)	Study purpose	Course data available for meta-analysis	Country	No. of donors	Year data collection	Female sex	Donor age (range)	Surgery technique	Donor type	Multicenter	Response rate	Dropout last assessment
Smith et al (2004) (2)	1+2	Yes	Australia	48	1998–2002	54%	48.7 (26–72)	ODN: 85% LDN 15%	NA	No	94%	6%
Timmerman et al (2013) (62)	1	Yes	The Netherlands	49	2000–2011	43%	59 (31–84)	LDN: 100%	Unrelated: 100%	No	99%	29%
Vemuru Reddy et al (2011) (58)	1	Yes	India	106	NA	73%	43.2 (22–65)	MIDN: 86% LDN: 14%	Related:76% Unrelated: 24%	No	94%	6%
Virzi et al (2007) (55)	1	Yes	Italy	48	2002–2004	79%	54.2 (33–81)	ODN: 100%	Related: 75% Unrelated: 25%	No	NA	NA
Walton-Moss et al (2007) (26)	1	No	United States	52	NA	67%	41.5 ± 11.8	LDN: 100%	Related: 100%	No	100%	81%

Study purpose 1 indicates health-related quality of life course study, and study purpose 2 indicates a prediction study. Response rate indicates the percentage of donors that agreed to participate.
HALN, hand-assisted transperitoneal laparoscopic donor nephrectomy; HARP, hand-assisted retroperitoneoscopic donor nephrectomy; LESS, laparo-endoscopic single-site donor nephrectomy; LDN, laparoscopic donor nephrectomy; MIDN, mini-incision donor nephrectomy; NA, data not available; ODN, open donor nephrectomy.

other studies. The timing of postdonation assessments varied between 1 month and 6 years after donation (Table 1).

Table 3 summarizes the meta-analytical findings on the course of the physical, psychological and social–relational HRQoL domains.

Physical functioning

Physical disability: During the first 2 months after donation, physical disability was higher than at baseline, with a large ES (−1.03 [95% confidence interval (CI) −1.12 to −0.93]) (9,12,14,47–53). At 3–6 months after donation, physical disability was comparable to baseline (small ES −0.16 [95% CI −0.39 to 0.07]) (2,3,11,23,49–52,54–58); however, long-term physical disability was higher again (small ES −0.12 [95% CI −0.20 to −0.05]) (2,3,9,10,14,23,46,48,49,51,53,59) (see forest plot in Figure S3). Clinically significant changes between pre- and postdonation assessments were found during the early postoperative recovery period in all studies but in only 17% of studies long term. Long-term physical disability was comparable to general population norms.

Pain: During all postdonation periods, higher pain levels were found than at baseline, with a large ES during the first two postdonation months, and small ESs at the other assessments (ES range: −1.05 to −0.10 [95% CI range (−1.31 to −0.80) to (−0.18 to −0.02)]) (2,3,9,10,12,14,46,47,49–53,55,56,59) (Figure S4). Clinically significant changes between pre- and postdonation assessments were found in the early postoperative recovery period in all studies but in only 20% of studies long term. Pain levels long term were comparable to general population norms.

Fatigue: During the first 2 months after donation, higher fatigue levels were found than at baseline, with a large ES (−0.93 [95% CI −1.03 to −0.83]) (9,12,14,47,49–53). At 3–6 months after donation, fatigue was comparable to baseline (−0.22 [95% CI −0.49 to 0.05]) (3,49–52,55,56); however, long-term fatigue was higher again (small ES −0.26 [95% CI −0.35 to −0.18]) (2,3,9,10,14,46,49,51,53,59) (Figure S5). Clinically significant changes between pre- and postdonation assessments were found in the early postoperative recovery period in all studies and in 50% of studies long term after donation; however, long-term fatigue levels were also comparable to general population norms.

Psychological functioning

During the first 2 months after donation, psychological functioning was reduced in comparison to that before donation (small ES −0.22 [95% CI −0.38 to −0.06]) (9,12,14,47–53). At 3–6 months after donation, psychological functioning was comparable to baseline (ES 0.18 [95% CI −0.10 to 0.47]) (2,3,11,23,49–52,54–58,60).

Table 3: Meta-analytic results of studies assessing the change in health-related quality of life of living kidney donors at different postdonation assessment periods compared with predonation functioning

	Sample size		Heterogeneity[1]		Effect sizes			
Timing of postdonation HRQoL assessment	k[2]	n[3]	I^2 (%)[4]	p[5]	SMD[6]	95% CI	z[7]	p[8]
1–2 mo								
Physical disability	13	625	49	0.02	−1.03	−1.12 to −0.93	20.65	<0.001
ODN	3	121	6	0.35	−1.20	−1.44 to −0.97	10.09	<0.001
MIDN	2	79	0	0.97	−1.26	−1.55 to −0.96	8.43	<0.001
LDN	8	425	54	0.03	−0.95	−1.06 to −0.83	16.12	<0.001
Pain	12	588	83	<0.001	−1.05	−1.31 to −0.80	8.16	<0.001
ODN	2	83	93	<0.001	−1.40	−2.55 to −0.26	2.40	0.02
MIDN	2	79	0	0.39	−0.89	−1.15 to −0.63	6.73	<0.001
LDN	8	426	84	<0.001	−1.02	−1.32 to −0.71	6.58	<0.001
Fatigue	12	586	49	0.03	−0.93	−1.03 to −0.83	18.69	<0.001
ODN	2	81	0	0.67	−1.04	−1.31 to −0.77	7.59	<0.001
MIDN	2	79	36	0.21	−0.66	−0.90 to −0.42	5.40	<0.001
LDN	8	426	50	0.05	−0.97	−1.09 to −0.86	16.39	<0.001
Psychological functioning	13	626	73	<0.001	−0.22	−0.38 to −0.06	2.72	0.007
ODN	3	121	73	0.02	−0.38	−0.75 to 0.00	1.97	0.05
MIDN	2	79	0	0.56	−0.40	−0.63 to −0.17	3.37	<0.001
LDN	8	426	75	<0.001	−0.13	−0.33 to 0.07	1.27	0.20
Social–relational functioning	13	628	67	<0.001	−0.69	−0.78 to −0.61	15.42	<0.001
ODN	3	123	89	<0.001	−0.48	−0.67 to −0.28	4.84	<0.001
MIDN	2	79	0	0.85	−0.62	−0.86 to −0.37	4.96	<0.001
LDN	8	426	29	0.20	−0.78	−0.89 to −0.67	14.05	<0.001
3–6 mo								
Physical disability	14	683	87	<0.001	−0.16	−0.39 to 0.07	1.38	0.17
ODN	3	140	76	0.02	−0.13	−0.48 to 0.22	0.73	0.46
MIDN	6	360	94	<0.001	−0.15	−0.64 to 0.33	0.63	0.53
LDN	5	183	0	0.44	−0.17	−0.31 to −0.02	2.25	0.02
Pain	8	345	58	0.02	−0.36	−0.47 to −0.25	6.48	<0.001
ODN	1	48	–	–	−0.69	−1.00 to −0.38	4.31	<0.001
MIDN	3	139	61	0.08	−0.36	−0.53 to −0.19	4.13	<0.001
LDN	4	158	51	0.10	−0.28	−0.44 to −0.12	3.41	<0.001
Fatigue	8	346	82	<0.001	−0.22	−0.49 to 0.05	1.63	0.10
ODN	1	48	–	–	0.56	0.25 to 0.87	3.50	<0.001
MIDN	3	139	71	0.03	−0.20	−0.52 to 0.13	1.19	0.23
LDN	4	159	0	0.65	−0.43	−0.60 to −0.27	5.27	<0.001
Psychological functioning	15	684	93	<0.001	0.18	−0.10 to 0.47	1.26	0.21
ODN	3	140	85	0.002	−0.30	−0.73 to 0.13	1.37	0.17
MIDN	6	360	96	<0.001	0.35	−0.22 to 0.91	1.20	0.23
LDN	5	184	85	<0.001	0.32	−0.09 to 0.73	1.51	0.13
Social–relational functioning	11	519	80	<0.001	0.03	−0.16 to 0.22	0.34	0.73
ODN	1	48	–	–	0.81	0.48 to 1.14	4.76	<0.001
MIDN	5	312	57	0.05	−0.02	−0.20 to 0.16	0.21	0.84
LDN	4	159	9	0.35	−0.14	−0.31 to 0.03	1.64	0.10
≥12 mo								
Physical disability	15	703	65	<0.001	−0.12	−0.20 to −0.05	3.17	0.002
ODN	3	141	60	0.08	−0.30	−0.48 to −0.13	3.46	<0.001
MIDN	6	270	80	<0.001	−0.13	−0.25 to −0.01	2.09	0.04
LDN	6	292	0	0.61	−0.03	−0.15 to 0.08	0.57	0.57
Pain	13	617	0	0.50	−0.10	−0.18 to −0.02	2.54	0.01
ODN	2	103	0	0.41	−0.24	−0.44 to −0.04	2.34	0.02
MIDN	5	220	0	0.82	−0.06	−0.19 to 0.08	0.84	0.40
LDN	6	294	27	0.23	−0.09	−0.21 to 0.02	1.59	0.11
Fatigue	13	615	19	0.26	−0.26	−0.35 to −0.18	6.41	<0.001
ODN	2	101	13	0.28	−0.39	−0.59 to −0.19	3.83	<0.001
MIDN	5	220	15	0.32	−0.19	−0.32 to −0.05	2.76	0.006
LDN	6	294	18	0.30	−0.28	−0.40 to −0.16	4.64	<0.001

(*Continued*)

Table 3: Continued

Timing of postdonation HRQoL assessment	Sample size		Heterogeneity[1]		Effect sizes			
	k[2]	n[3]	I^2 (%)[4]	p[5]	SMD[6]	95% CI	z[7]	p[8]
Psychological functioning	17	778	49	0.01	−0.11	−0.18 to −0.04	2.95	0.003
ODN	3	141	0	0.42	−0.24	−0.41 to −0.07	2.76	0.006
MIDN	6	270	56	0.05	−0.08	−0.20 to 0.04	1.27	0.21
LDN	8	367	54	0.03	−0.08	−0.18 to 0.03	1.49	0.14
Social–relational functioning	16	730	35	0.09	0.04	−0.03 to 0.12	1.17	0.24
ODN	3	143	3	0.35	−0.13	−0.30 to 0.04	1.50	0.13
MIDN	5	220	44	0.13	0.14	0.00 to 0.28	1.99	0.05
LDN	8	367	10	0.35	0.05	−0.05 to 0.15	1.03	0.30

Estimated correlation between predonation and postdonation assessment of HRQoL was 0.5.
HRQoL, health-related quality of life; LDN, laparoscopic donor nephrectomy; MIDN, mini-incision donor nephrectomy; ODN, open donor nephrectomy.
[1]Variation in study outcomes between studies.
[2]Number of comparisons.
[3]Number of donors included in analysis.
[4]Percentage of variation across studies that is due to heterogeneity rather than to chance.
[5]Significance level of heterogeneity.
[6]Standardized mean difference before versus after donation (effect size).
[7]Test for overall effect.
[8]Significance level of effect assessment.

Long-term psychological functioning was reduced again (small ES −0.11 [95% CI −0.18 to −0.04]) (2,3,9,10,14,23,46,48,49,51,53,59,61,62) (Figure S6). Clinically significant changes between pre- and postdonation assessments were found in 50% of studies during the early recovery period and in 7% of studies long term after donation. Long-term psychological functioning was comparable to general population norms.

Social–relational functioning

During the first 2 months after donation, social–relational functioning was reduced compared with baseline, with a moderate ES (−0.69 [95% CI −0.78 to −0.61]) (9,12,14,47–53), but similar to baseline for the later periods (ES 0.03 [95% CI −0.16 to 0.22] and 0.04 [95% CI −0.03 to 0.12], respectively) (2,3,9,10,14,46,48–53,55–62) (Figure S7). Clinically significant differences were found during the early postoperative recovery period in 90% of studies but in only 8% of studies long term after donation. Long-term social functioning was comparable to that of the general population.

In summary, results show that shortly after donation, as expected, donors have an HRQoL reduction in comparison to the level before donation, with small to moderate ESs for psychological and social functioning and large ESs for physical functioning, with scores that correspond with norms for clinically relevant changes. In the short term, HRQoL returned to baseline on all domains except pain, which was still slightly reduced (small ES). In the long term, donors on average showed somewhat reduced physical and psychological functioning compared with functioning before donation (small ES), but levels were comparable to general population norms, and differences between pre- and postdonation assessments were not clinically relevant. In the longer term, slightly elevated scores of fatigue were found in 50% of studies, but fatigue scores were still comparable to general population norms. The individual results of studies that had to be excluded due to missing data were overall in the same line (see Table S1).

Secondary analyses

Subgroup analyses were conducted to study differences in pre- and postdonation HRQoL changes for different surgery techniques. Results were generally comparable for the different surgery techniques, with a few exceptions that did not show a consistent pattern of better or worse functioning for one surgery technique compared with others (Table 3).

Because of the heterogeneity between studies, sensitivity analyses were conducted on the use of different questionnaires within one HRQoL domain and study quality assessment. Studies could not be compared with regard to applying more or less stringent donor eligibility criteria because these criteria were not reported in most studies. Results were mainly robust across the use of different questionnaires and study quality. Finally, HRQoL outcomes were similar for imputing low ($r = 0.1$) or high ($r = 0.9$) correlation coefficients instead of the average ($r = 0.5$) correlation coefficients between pre- and postdonation assessments.

Prediction of HRQoL

Nine studies investigated pre- or postdonation predictors for long-term HRQoL after kidney donation, with each predictor being included in up to five studies at most (Table 4). Reduced postdonation physical functioning was related to nonwhite race (63), smoking (21) and a history of psychiatric difficulties (63), whereas it was not related to age (63,64), predonation creatinine levels (21,64), blood pressure and cardiovascular events (21). Inconsistent results were found for BMI, which was related to physical functioning in one (63) of three studies (21,63,64).

Reduced postdonation psychological functioning was related to worse self-reported physical functioning 4 months after donation and to worse psychological functioning before and 4 months after donation (2). Reduced psychological functioning was not related to predonation self-rated health (61), marital status (2,52), nonwhite race (63), predonation BMI (21,52,56,63,64), creatinine level (64), smoking, blood pressure, cardiovascular events (21), surgery technique (2,52) or duration (52), nephrectomy side, use of a hand-assistance port (52), length of hospital stay (2), inability to distinguish and verbalize emotions (alexithymia) (65), the donor–recipient relationship or recipient length of hospital stay (2,52,56). Inconsistent results were found for recipient complications (related in two [52,66] of three studies [2,52,66]), lower age (related in one [63] of five studies [2,52,56,63,64]), female sex (related in one [52] of three studies [2,52,56]) and psychiatric history (related in two [52,63] of four studies [2,52,61,63]). No predictors were examined for postdonation social–relational functioning.

Discussion

This systematic review and meta-analysis investigated prospective studies on the course and predictors of HRQoL (ie, physical, psychological and social–relational functioning) after living kidney donation. Results indicated that shortly after donation, donors have lower HRQoL than before donation on all domains, with small to moderate changes in psychological and social functioning and large changes in physical functioning. At 3–12 months after donation, HRQoL returned to baseline or was slightly reduced compared with that before donation, particularly for fatigue; however, levels were comparable to those of the general population. Results were mainly robust across surgery techniques, questionnaires used and study quality. The limited number of prediction studies have provided only some rudimentary ideas on potential risk factors for developing longer term HRQoL problems; however, results indicated that donors with low psychological functioning at baseline were those most at risk of impaired longer term HRQoL.

The current review extended the findings from the 2006 review on psychosocial HRQoL (5) by distinguishing different HRQoL domains, using quantifiable meta-analytic techniques, addressing the influence of surgery techniques and methodological bias, and including the prospective results of recent and large cohort studies. Results of current meta-analysis were generally in line with the previous review, showing that HRQoL was comparable with general population norms during the long-term postdonation period, with slightly reduced scores for physical and psychological functioning (5).

The short-term reduction of postdonation physical HRQoL is not unexpected because of the invasive surgical intervention performed in a healthy body. Previous research indicated that donors experienced more postoperative pain than expected before surgery (67–69), and this underscores the importance of providing appropriate presurgery information about possible short-term and long-term health outcomes. The invasive surgery and resulting short-term physical disabilities may explain, at least in part, the early reduction of psychological and social–relational functioning, which could also be the result of psychological factors (eg, anxiety) and social–relational factors (eg, concerns about the recipient's health) (5).

The results of the current meta-analysis can support guidelines for future donor decision making, which can be used in donor counseling in clinical practice. Clinicians can inform potential donors that although HRQoL scores decrease shortly after donation, HRQoL recovers to population norms within several months after donation. Only fatigue scores could remain somewhat higher in the long term, but findings are also comparable to general population norms. The possible continuation of higher fatigue levels long term is a new finding that requires further investigation. It is not yet clear whether these findings might be a consequence of donation; however, it could potentially be the consequence of a combination of multiple factors (eg, aging, living with one kidney, or because donors are not familiar with physical limitations and may be inclined to resume their daily activities too early after surgery). Although fatigue has been found to correlate with worse psychological functioning in the general population (34,70) and in patients with chronic somatic conditions (71,72), the comparison of donors' HRQoL with general population norms in this meta-analysis indicated that postdonation HRQoL scores were comparable to the general population for all dimensions. The description of a valid comparison group remains important in future donor research.

From the limited and inconclusive results on prospective predictors of long-term HRQoL, no firm conclusions can be drawn, but the most consistent evidence points to low psychological functioning as a predictor for impaired long-term HRQoL and underscores the relevance of screening of psychological functioning and psychiatric history. Consequently, additional counseling might be beneficial for donors with HRQoL scores that differ from general population norms in terms of clinically relevant differences; however,

Table 4: Physical and psychological predictors of long-term health-related quality of life of living kidney donors

Study (year)	Predictors	Psychological outcome assessment	Significance psychosocial outcomes	Physical outcome assessment	Significance physical outcomes
Bahler et al (2013) (52)	**Physical:**				
	Predonation BMI	SF-36 MCS 1 mo after donation	NS		
	Nephrectomy side		NS		
	Use of a hand-assistance port		NS		
	Surgery duration		NS		
	Length of hospital stay		NS		
	Psychological:				
	Psychiatric history		$p < 0.05$		
	Social–relational:				
	Relation to the recipient		NS		
	Recipient complications		$p < 0.05$		
	Other:				
	Age		NS		
	Female sex		$p < 0.05$		
	Marital status		NS		
Chien et al (2010) (56)	**Physical:**				
	Predonation body weight	Change in SF-36 MH before to 3 mo after donation	NS		
	Predonation BMI		NS		
	Serum creatinine 2 days after donation		NS		
	24-h creatinine clearance		$p < 0.01$		
	Hospital stay		NS		
	Social–relational:				
	Relationship with recipient		NS		
	Other:				
	Age		NS		
	Sex		NS		
Fukunishi et al (2002) (65)	**Psychological:**	Postdonation psychiatric syndrome	NS		
	Predonation alexithymia				
Glotzer et al (2013) (64)	**Physical:**				
	Predonation BMI	SF-36 MCS after donation	NS	SF-36 PCS after donation	NS
	Predonation creatinine level		NS		NS
	Other:				
	Age		NS		NS
de Groot et al (2012) (21)	**Physical:**				
	Predonation BMI	SF-36 MCS after donation	NS	SF-36 PCS after donation	NS
	Predonation smoking		NS		$p < 0.01$
	Predonation blood pressure		NS		NS
	Predonation renal clearance		NS		NS
	Predonation cardiovascular events		NS		NS
Gross et al (2013) (63)	**Physical:**				
	Predonation BMI[1]	SF-36 MCS after donation	NS	SF-36 PCS after donation	$p < 0.001$
	Psychological:				
	History of psychiatric difficulties[1]		$p < 0.001$		$p < 0.001$
	Other:				
	Age[2]		$p < 0.001$		NS
	Nonwhite race		NS		$p < 0.01$
Massey et al (2010) (61)	**Physical:**				
	Self-rated health scores	Satisfaction with donation afterward	NS		
	Psychological:				
	Inadequacy in thought and action		$p < 0.05$		
	Mental health history		NS		
	Physical:				
	Self-rated health scores	Perceived impact of donation on psychological well-being after donation	NS		
	Psychological:				
	Predonation psychological complaints		NS		
	Mental health history		NS		
	Psychological:				
	Predonation phobic anxiety	Worse satisfaction with supervision during admittance to the hospital after donation	$p < 0.05$		
	Predonation depression		$p < 0.05$		
	Predonation hostility		$p < 0.01$		
Rodrigue et al (2013) (66)	**Social–relational:**				
	Recipient graft failure	Overestimated expectations of personal growth	$p < 0.05$		
		Overestimated expectations of interpersonal benefit	NS		
		Overestimated expectations of spiritual growth	NS		
Smith et al (2004) (2)	**Physical:**				
	Surgery technique	Psychiatric caseness 12 mo after donation	NS		
	Length of hospital stay		NS		
	Predonation SF-36 PCS		NS		
	SF-36 PCS 4 mo after donation		$p < 0.01$		

Table 4: Continued

Study (year)	Predictors	Psychological outcome assessment	Significance psychosocial outcomes	Physical outcome assessment	Significance physical outcomes
	Psychological:				
	Psychiatric caseness lifetime		NS		
	Psychiatric caseness previous 12 mo		NS		
	Predonation SF36 MCS		$p < 0.05$		
	SF-36 MCS 4 mo after donation		$p < 0.01$		
	Psychiatric caseness 4 mo after donation		$p < 0.01$		
	Social–relational:				
	Recipient hospital stay		NS		
	Recipient graft failure		NS		
	Donor–recipient relationship		NS		
	Other:				
	Age		NS		
	Sex		NS		
	Marital status		NS		
	Physical:				
	Surgery technique	SF36 MCS 12 mo postoperatively	NS		
	Psychological:				
	Predonation TERS scores[1]		$p < 0.05$		
	SF-36 MCS 4 mo after donation[2]		$p < 0.01$		

BMI, body mass index; NS not significant; SF-36 MCS, Short Form-36 mental component summary score; SF-36 PCS, Short Form-36 physical component summary score; TERS, Transplant Evaluation Rating Scale.
[1]Negative correlation coefficient.
[2]Positive correlation coefficient.

this systematic review clearly indicates that more prospective research in sufficiently sized samples is required to identify relevant HRQoL risk factors at an early stage that may be used to develop and offer interventions to prevent longer term HRQoL problems in living kidney donors.

A number of studies could not be included because of methodological constraints, such as recall bias, and because only generic HRQoL scores were provided. Moreover, the studies that were included had some limitations. First, the impact of the currently applied, more liberal criteria for donor selection on postdonation HRQoL could not be examined because studies did not clearly distinguish between the use of strict versus more lenient donor eligibility criteria. Second, the timing of predonation assessments varied from months to a few days before surgery, with 55% of studies not specifying the timing of the predonation assessment, making it difficult to compare baseline findings and preventing the assessment of the impact of timing on HRQoL changes. Because predonation assessments are often part of the donor-selection procedure, elevated predonation HRQoL scores could be reported out of fear not to pass the screening procedure when problems would be reported. In contrast, predonation assessments a few days before surgery may lead to higher-than-normal distress levels because of the upcoming surgery. Third, although response rates for first assessments were generally high, response rates for repeated assessments were often not reported and may have affected the results. Fourth, some potentially relevant predictors of postdonation HRQoL have not been examined yet, including donor complications during or after surgery, the donor–recipient relationship type (eg, directed versus nondirected donation), more lenient eligibility criteria for donors, cultural differences (eg, with regard to health care systems and screening procedures), recipient and graft survival, and pretransplant health status of the recipient (eg, on dialysis or not). Finally, although it cannot be totally excluded that the results after donation are possibly influenced by the phenomenon of regression to the mean (73,74), this seems unlikely because repeated measures of HRQoL after donation do not show a consistent decrease in HRQoL scores over time, and the large number of studies included did not show a similar regression to the mean individually.

In conclusion, this systematic review and meta-analysis showed that HRQoL returned to baseline or was only slightly reduced on longer term assessments, although HRQoL scores decreased shortly after donation; however, HRQoL levels were comparable to general population norms. On the basis of these results, clinicians can inform potential donors that there is generally no risk involved with the donation. Results of prediction studies indicate that donors with low psychological functioning at baseline are those most at risk of impaired long-term HRQoL.

Future research is required to quantify the extent and identify the reasons for the small reduction of long-term HRQoL to estimate the need for future interventions for this group. Predonation psychological functioning was the most consistent predictor for long-term HRQoL after living kidney donation; however, more systematic prospective research on predictors of the HRQoL of living kidney donors is required to identify possible risk factors for longer term HRQoL problems more reliably. This knowledge could provide valid selection criteria in the psychosocial screening of living kidney donors and could be used to focus psychosocial interventions before and after donation on donors at risk of developing long-term HRQoL problems.

Acknowledgments

Funding of this study was provided by a grant of the Dutch Kidney Foundation. The authors thank A.R. Donders from the Department for Health Evidence of the Radboud University Medical Center for statistical support.

Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

References

1. WHOQOL: Measuring quality of life. Geneva, Switzerland: World Health Organization; 1997. http://www.who.int/mental_health/media/68.pdf.
2. Smith GC, Trauer T, Kerr PG, Chadban SJ. Prospective psychosocial monitoring of living kidney donors using the Short Form-36 Health Survey: Results at 12 months. Transplantation 2004; 78: 1384–1389.
3. Kroencke S, Fischer L, Nashan B, Herich L, Schulz KH. A prospective study on living related kidney donors' quality of life in the first year: Choosing appropriate reference data. Clin Transplant 2012; 26: 418–427.
4. Klop KW, Dols LF, Weimar W, Dooper IM, Ijzermans JN, Kok NF. Quality of life of elderly live kidney donors. Transplantation 2013; 96: 644–648.
5. Clemens KK, Thiessen-Philbrook H, Parikh CR, et al. Psychosocial health of living kidney donors: A systematic review. Am J Transplant 2006; 6: 2965–2977.
6. Reimer J, Rensing A, Haasen C, Philipp T, Pietruck F, Franke GH. The impact of living-related kidney transplantation on the donor's life. Transplantation 2006; 81: 1268–1273.
7. Wiedebusch S, Reiermann S, Steinke C, et al. Quality of life, coping, and mental health status after living kidney donation. Transplant Proc 2009; 41: 1483–1488.
8. Bargman V, Sundaram CP, Bernie J, Goggins W. Randomized trial of laparoscopic donor nephrectomy with and without hand assistance. J Endourol 2006; 20: 717–722.
9. Andersen MH, Mathisen L, Veenstra M, et al. Quality of life after randomization to laparoscopic versus open living donor nephrectomy: Long-term follow-up. Transplantation 2007; 84: 64–69.
10. Dols LFC, Ijzermans JNM, Wentink N, et al. Long-term follow-up of a randomized trial comparing laparoscopic and mini-incision open live donor nephrectomy. Am J Transplant 2010; 10: 2481–2487.
11. Kurien A, Rajapurkar S, Sinha L, et al. First prize: Standard laparoscopic donor nephrectomy versus laparoendoscopic single-site donor nephrectomy: A randomized comparative study. J Endourol 2011; 25: 365–370.
12. Nicholson ML, Elwell R, Kaushik M, Bagul A, Hosgood SA. Health-related quality of life after living donor nephrectomy: A randomized controlled trial of laparoscopic versus open nephrectomy. Transplantation 2011; 91: 457–461.
13. Hofker HS, Nijboer WN, Niesing J, et al. A randomized clinical trial of living donor nephrectomy: A plea for a differentiated appraisal of mini-open muscle splitting incision and hand-assisted laparoscopic donor nephrectomy. Transpl Int 2012; 25: 976–986.
14. Dols LF, Kok NF, d'Ancona FC, et al. Randomized controlled trial comparing hand-assisted retroperitoneoscopic versus standard laparoscopic donor nephrectomy. Transplantation 2014; 97: 161–167.
15. Mandelbrot DA, Pavlakis M, Danovitch GM, et al. The medical evaluation of living kidney donors: A survey of US transplant centers. Am J Transplant 2007; 7: 2333–2343.
16. Kaisar MO, Nicol DL, Hawley CM, et al. Change in live donor characteristics over the last 25 years: A single centre experience. Nephrology 2008; 13: 646–650.
17. Wilson CH, Sanni A, Rix DA, Soomro NA. Laparoscopic versus open nephrectomy for live kidney donors. Cochrane Database Syst Rev 2011: CD006124.
18. Lopes A, Frade IC, Teixeira L, et al. Depression and anxiety in living kidney donation: Evaluation of donors and recipients. Transplant Proc 2011; 43: 131–136.
19. Tong A, Chapman JR, Wong G, De Bruijn J, Craig JC. Screening and follow-up of living kidney donors: A systematic review of clinical practice guidelines. Transplantation 2011; 92: 962–972.
20. Andrews PA, Burnapp L, Manas D, et al. Summary of the British Transplantation Society/Renal Association U.K. guidelines for living donor kidney transplantation. Transplantation 2012; 93: 666–673.
21. De Groot IB, Stiggelbout AM, Van Der Boog PJM, Baranski AG, Marang-Van De Mheen PJ. Reduced quality of life in living kidney donors: Association with fatigue, societal participation and pre-donation variables. Transpl Int 2012; 25: 967–975.
22. Duerinckx N, Timmerman L, Van Gogh J, et al. Predonation psychosocial evaluation of living kidney and liver donor candidates: A systematic literature review. Transpl Int 2014; 27: 2–18.
23. Garcia MFFM, Andrade LGM, Carvalho MFC. Living kidney donors—a prospective study of quality of life before and after kidney donation. Clin Transplant 2013; 27: 9–14.
24. Higgings JPT, Green S, eds. *Cochrane handbook for systematic reviews of interventions version 5.1.0 [updated March 2011]*. The Cochrane Collaboration; 2011. http://handbook.cochrane.org
25. Cohen J. *Statistical power analysis for the behavioral sciences*, 2nd ed. London, UK: Routledge; 1988.
26. Walton-Moss B, Boulware LE, Cooper M, Taylor L, Dane K, Nolan MT. Prospective pilot study of living kidney donor decision-making and outcomes. Clin Transplant 2007; 21: 86–93.
27. Kok NFM, Alwayn IPJ, Tran KTC, Hop WCJ, Weimar W, Ijzermans JNM. Psychosocial and physical impairment after mini-incision open and laparoscopic donor nephrectomy: A prospective study. Transplantation 2006; 82: 1291–1297.
28. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986; 7: 177–188.
29. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre TCC, 2014. Version 53 Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.
30. Fisher PL, Durham RC. Recovery rates in generalized anxiety disorder following psychological therapy: An analysis of clinically significant change in the STAI-T across outcome studies since 1990. Psychol Med 1999; 29: 1425–1434.
31. Den Oudsten BL, Zijlstra WP, De Vries J. The minimal clinical important difference in the World Health Organization Quality of Life instrument-100. Support Care 2013; 21: 1295–1301.
32. Ware JE. SF-36 health survey: Manual and interpretation guide, 1993.
33. Hiroe T, Kojima M, Yamamoto I, et al. Gradations of clinical severity and sensitivity to change assessed with the Beck Depression Inventory-II in Japanese patients with depression. Psychiat Res 2005; 135: 229–235.

34. Lin JM, Brimmer DJ, Maloney EM, Nyarko E, Belue R, Reeves WC. Further validation of the Multidimensional Fatigue Inventory in a US adult population sample. Popul Health Mmetrics 2009; 7: 18.
35. Beck AT, Ward CH, Mendelson MM, Mock JJ, Erbaugh JJ. AN inventory for measuring depression. Arch Gen Psych 1961; 4: 561–571.
36. The EuroQol Group. EuroQol - a new facility for the measurement of health-related quality of life. Health Pol 1990; 16: 199–208.
37. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatrica Scandinavica 1983; 67: 361–370.
38. Smets EMA, Garssen B, Bonke B, De Haes JCJM. The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. J Psychosom Res 1995; 39: 315–325.
39. Zung WWK. A rating instrument for anxiety disorders. Psychosomatics 1971; 12: 371–379.
40. Derogatis LR, Lipman RS, Covi L. SCL-90: An outpatient psychiatric rating scale- preliminary report. Psychopharmacol Bull 1973; 9: 13–28.
41. Zung WK. A self-rating depression scale. Arch Gen Psych 1965; 12: 63–70.
42. Sarason IG, Levine HM, Basham RB, Sarason BR. Assessing social support: The social support questionnaire. J Appl Soc Psychol 1983; 44: 127–139.
43. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press, 1983.
44. Freyd M. The graphic rating scale. J Educ Psychol 1923; 14: 83–102.
45. WHOQOL Group. Development of the WHOQOL: Rationale and current status. Int J Ment Health 1994; 23: 24–56.
46. Lopes A, Frade IC, Teixeira L, Almeida M, Dias L, Henriques AC. Quality of life assessment in a living donor kidney transplantation program: Evaluation of recipients and donors. Transplant Proc 2013; 45: 1106–1109.
47. Bergman S, Feldman LS, Mayo NE, et al. Measuring surgical recovery: The study of laparoscopic live donor nephrectomy. Am J Transplant 2005; 5: 2489–2495.
48. Lumsdaine JA, Wray A, Power MJ, et al. Higher quality of life in living donor kidney transplantation: Prospective cohort study. Transpl Int 2005; 18: 975–980.
49. Kok NFM, Lind MY, Hansson BME, et al. Comparison of laparoscopic and mini incision open donor nephrectomy: Single blind, randomised controlled clinical trial. British Med J 2006; 333: 221–224.
50. Aguiar WF, Passerotti CC, Claro JFdA, et al. Mini-incisions by lombotomy or subcostal access in living kidney donors: A randomized trial comparing pain, safety, and quality of life. Clin Transplant 2007; 21: 269–276.
51. Minnee RC, Bemelman WA, Polle SW, et al. Older living kidney donors: Surgical outcome and quality of life. Transplantation 2008; 86: 251–256.
52. Bahler CD, Sundaram CP. Quality of life following laparoscopic living-donor nephrectomy. J Soc Laparoendoscopic Surgeons 2013; 17: 273–278.
53. Klop KW, Kok NF, Dols LF, et al. Can right-sided hand-assisted retroperitoneoscopic donor nephrectomy be advocated above standard laparoscopic donor nephrectomy: A randomized pilot study. Transplant Int 2013; 27: 162–169.
54. Smith GC, Trauer T, Kerr PG, Chadban SJ. Prospective psychosocial monitoring of living kidney donors using the SF-36 health survey. Transplantation 2003; 76: 807–809.
55. Virzi A, Signorelli MS, Veroux M, et al. Depression and quality of life in living related renal transplantation. Transplant Proc 2007; 39: 1791–1793.
56. Chien CH, Wang HH, Chiang YJ, Chu SH, Liu HE, Liu KL. Quality of life after laparoscopic donor nephrectomy. Transplant Proc 2010; 42: 696–698.
57. Guleria S, Reddy VSK, Bora GS, Sagar R, Bhowmik D, Mahajan S. The quality of life of women volunteering as live-related kidney donors in India. Natl Med J India 2011; 24: 342–344.
58. Vemuru Reddy SK, Guleria S, Okechukwu O, Sagar R, Bhowmik D, Mahajan S. Live related donors in India: Their quality of life using world health organization quality of life brief questionnaire. Indian J Urol 2011; 27: 25–29.
59. Frade IC, Fonseca I, Dias L, et al. Impact assessment in living kidney donation: Psychosocial aspects in the donor. Transplant Proc 2008; 40: 677–681.
60. Minz M, Udgiri N, Sharma A, et al. Prospective psychosocial evaluation of related kidney donors: Indian perspective. Transplant Proc 2005; 37: 2001–2003.
61. Massey EK, Kranenburg LW, Zuidema WC, et al. Encouraging psychological outcomes after altruistic donation to a stranger. Am J Transplant 2010; 10: 1445–1452.
62. Timmerman L, Zuidema WC, Erdman RAM, et al. Psychologic functioning of unspecified anonymous living kidney donors before and after donation. Transplantation 2013; 95: 1369–1374.
63. Gross CR, Messersmith EE, Hong BA, et al. Health-related quality of life in kidney donors from the last five decades: Results from the RELIVE study. Am J Transplant 2013; 13: 2924–2934.
64. Glotzer OS, Singh TP, Gallichio MH, Conti DJ, Siparsky NF. Long-term quality of life after living kidney donation. Transplant Proc 2013; 45: 3225–3228.
65. Fukunishi I, Sugawara Y, Takayama T, Makuuchi M, Kawarasaki H, Surman OS. Association between pretransplant psychological assessments and posttransplant psychiatric disorders in living-related transplantation. Psychosomatics 2002; 43: 49–54.
66. Rodrigue JR, Paek M, Whiting J, et al. Trajectories of perceived benefits in living kidney donors: Association with donor characteristics and recipient outcomes. Transplantation 2014; 97: 762–768.
67. Schover LR, Streem SB, Boparai N, Duriak K, Novick AC. The psychosocial impact of donating a kidney: Long-term followup from a urology based center. J Urol 1997; 157: 1596–1601.
68. Karrfelt HME, Berg UB, Lindblad FIE, Tyden GE. To be or not to be a living donor: Questionnaire to parents of children who have undergone renal transplantation. Transplantation 1998; 65: 915–918.
69. Rodrigue JR, Cross NJ, Newman RC, et al. Patient-reported outcomes for open versus laparoscopic living donor nephrectomy. Prog Transplant 2006; 16: 162–169.
70. Schwarz R, Krauss O, Hinz A. Fatigue in the general population. Onkologie 2003; 26: 140–144.
71. Munch TN, Stromgren AS, Pedersen L, Petersen MA, Hoermann L, Groenvold M. Multidimensional measurement of fatigue in advanced cancer patients in palliative care: An application of the multidimensional fatigue inventory. J Pain Symptom Manag 2006; 31: 533–541.
72. Kuhnt S, Ernst J, Singer S, et al. Fatigue in cancer survivors-prevalence and correlates. Onkologie 2009; 32: 312–317.
73. Yudkin PL, Stratton IM. How to deal with regression to the mean in intervention studies. Lancet 1996; 347: 241–243.
74. Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: What it is and how to deal with it. Int J Epidemiol 2005; 34: 215–220.

Supporting Information

Additional Supporting Information may be found in the online version of this article.

Table S1: The course of health-related quality of life from studies that are excluded from meta-analysis.

Figure S1: Risk of bias graph. Review authors' judgments about each risk of bias item presented as percentages across all included studies.

Figure S2: Risk of bias summary. Review authors' judgments about each risk of bias item for each included study.

Figure S3: Forest plot meta-analysis of physical disability.

Figure S4: Forest plot meta-analysis of pain.

Figure S5: Forest plot meta-analysis of fatigue.

Figure S6: Forest plot meta-analysis of psychological functioning.

Figure S7: Forest plot meta-analysis of social–relational functioning.