

# Emotional Well-Being of Living Kidney Donors: Findings From the RELIVE Study

S. G. Jowsey<sup>1,2,\*</sup>, C. Jacobs<sup>3</sup>, C. R. Gross<sup>3</sup>,  
B. A. Hong<sup>4</sup>, E. E. Messersmith<sup>5</sup>,  
B. W. Gillespie<sup>6</sup>, T. J. Beebe<sup>7</sup>, C. Kew<sup>8</sup>,  
A. Matas<sup>9</sup>, R. D. Yusen<sup>4</sup>, M. Hill-Callahan<sup>5</sup>,  
J. Odum<sup>10</sup>, S. J. Taler<sup>2,11</sup>, and the RELIVE  
Study Group

<sup>1</sup>Department of Psychiatry and Psychology, Mayo Clinic, Rochester, MN

<sup>2</sup>The William J. von Liebig Transplant Center, Mayo Clinic, Rochester, MN

<sup>3</sup>College of Pharmacy and School of Nursing, University of Minnesota, Minneapolis, MN

<sup>4</sup>Washington University School of Medicine, St. Louis, MO

<sup>5</sup>Arbor Research Collaborative for Health, Ann Arbor, MI

<sup>6</sup>Department of Biostatistics, University of Michigan, Ann Arbor, MI

<sup>7</sup>Department of Health Sciences Research, Mayo Clinic, Rochester, MN

<sup>8</sup>Division of Nephrology, University of Alabama at Birmingham, Birmingham, AL

<sup>9</sup>Department of Surgery, School of Medicine, University of Minnesota, Minneapolis, MN

<sup>10</sup>National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD

<sup>11</sup>Division of Nephrology and Hypertension, Mayo Clinic, Rochester, MN

\*Corresponding author: Sheila G. Jowsey, jowsey.sheila@mayo.edu

**Following kidney donation, short-term quality of life outcomes compare favorably to US normative data but long-term effects on mood are not known. In the Renal and Lung Living Donors Evaluation Study (RELIVE), records from donations performed 1963–2005 were reviewed for depression and antidepressant use pre-donation. Postdonation, in a cross-sectional cohort design 2010–2012, donors completed the Patient Health Questionnaire (PHQ-9) depression screening instrument, the Life Orientation Test-Revised, 36-Item Short Form Health Survey and donation experience questions. Of 6909 eligible donors, 3470 were contacted and 2455 participated (71%). The percent with depressive symptoms (8%; PHQ-9 > 10) was similar to National Health and Nutrition Examination Survey participants (7%,  $p = 0.30$ ). Predonation psychiatric disorders were more common in unrelated than related donors ( $p = 0.05$ ). Postdonation predictors of depressive symptoms included nonwhite race OR = 2.00,  $p = 0.020$ ), younger age at donation**

(OR = 1.33 per 10 years,  $p = 0.002$ ), longer recovery time from donation (OR = 1.74,  $p = 0.0009$ ), greater financial burden (OR = 1.32,  $p = 0.013$ ) and feeling morally obligated to donate (OR = 1.23,  $p = 0.003$ ). While cross-sectional prevalence of depression is comparable to population normative data, some factors identifiable around time of donation, including longer recovery, financial stressors, younger age and moral obligation to donate may identify donors more likely to develop future depression, providing an opportunity for intervention.

**Abbreviations:** DCC, Data Coordinating Center; HRSA, Health Resources and Services Administration; LOT-R, The Life Orientation Test-Revised; Mayo, Mayo Clinic, Rochester, MN; MCS, Mental Component Score; NHANES, National Health and Nutrition Examination Survey; NHLBI, National Heart Lung and Blood Institute; NIAID, National Institute of Allergy, Immunology and Infectious Diseases; PCS, Physical Component Score; PHQ-9, Patient Health Questionnaire; QOL, quality of life; RELIVE, Renal and Lung Living Donors Evaluation Study; SF-36, 36-Item Short Form Health Survey; UAB, University of Alabama at Birmingham, AL; UMN, University of Minnesota, Minneapolis, MN

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## Introduction

Existing guidelines for donor selection aim to select donors at low risk for adverse mental health outcomes (1). Yet donors experience multiple stressors including surgery and postoperative pain, need for opiate pain medications, social disruption, time off work with potential financial strain and decreased exercise while recuperating. In addition, when recipient and donor rely on the same family members for assistance during their postoperative recovery, support for the donor may be attenuated. Each of these factors may contribute to risk for depression, and numerous studies have reported that kidney donors may experience short-term mood changes after kidney donation (1–13). The risk for developing depression may be mitigated by preexisting dispositional traits such as an optimistic perception of outcomes. Optimism has been reported to impact long-term medical outcomes and is associated with less depression (14–20). Whether donors with higher optimism are better equipped to withstand the rigors of donation with less distress is unknown.

The Renal and Lung Living Donors Evaluation Study (RELIVE) is a research consortium funded by the National Institute of Allergy, Immunology and Infectious Diseases, the Health Resources and Services Administration and the National Heart Lung and Blood Institute to evaluate intermediate to long-term medical and psychosocial outcomes of live kidney donors. The study cohort consisted of 6909 donors who donated between 1963 and 2005, with follow-up by mailed survey in 2010–2012. In this cross-sectional study, we aimed to estimate the proportion of donors with current depressive symptoms, and test potential predictors of depressive symptoms after donation.

## Methods

The RELIVE study has been described in detail (21,22). This cross-sectional cohort study specifically addressed risk for depression in donors who underwent kidney donation between 1963 and 2005 at one of three large US centers: Mayo Clinic, Rochester, MN (Mayo); University of Alabama at Birmingham, AL (UAB); and University of Minnesota, Minneapolis, MN (UMN), with a Data Coordinating Center (DCC) at the University of Michigan and Arbor Research Collaborative for Health, Ann Arbor, MI.

Trained study staff abstracted data from medical records of all living kidney donors at the three sites ( $n = 8951$ ) including predonation psychiatric history, use of psychotropic medications, presence of chronic pain and history of chemical dependency. The data came from standardized chart abstraction performed at each site, however the actual donor evaluations were not standardized and occurred prior to our study. Starting with the last available mailing address, an attempt was made to contact each donor by mail. If the potential study participant did not respond to the initial letter of invitation within 2–4 weeks, a second mailing was sent, followed by two to three telephone calls. Donors who consented to participate completed a short questionnaire and were invited to complete more in-depth questionnaires on medical and psychosocial health status. Survey procedures and characteristics of RELIVE donors have been reported (21).

### **Use of validated instruments**

The Patient Health Questionnaire (PHQ-9) Depression Scale (23) is widely used to screen for depression in the medical and general population. The questionnaire contains nine items including questions on loss of interest, depressed mood, sleep, appetite and energy changes, low self-worth, difficulty concentrating, psychomotor activity changes and suicidal ideation. For each item, responses are scored between 0 and 3, ranging from “not at all” to “nearly every day”; overall scores can range from 0 to 27. Construct validity and criterion validity have been tested in primary care populations, with a PHQ-9 score  $\geq 10$  found to have 88% sensitivity and 88% specificity for clinical depression (23). Scores of 5, 10, 15 and 20 represent cutpoints for mild, moderate, moderately severe and severe depression. Any donor revealing potentially worrisome psychological responses was contacted by a clinician from the relevant center and referred for additional help if deemed necessary.

The Life Orientation Test-Revised (24) (LOT-R) identifies individuals who maintain positive expectations in adversity. This measure utilizes six items representing an optimistic trait or disposition toward optimism. Respondents indicate their agreement with items on a 0–4 scale (“strongly disagree” to “strongly agree”), with overall scores ranging from 0 to 24 and higher scores indicating optimism. Previous studies have demonstrated

acceptable internal consistency, convergent and discriminant validity (24). Normative data were available for both medical and nonmedical populations.

The 36-Item Short Form Health Survey (SF-36, version 2) (25), is a validated and extensively used measure of quality of life (QOL) reflecting perceptions over the previous 4 weeks. It is divided into two broad scales of behavioral functioning, the Physical Component Score (PCS) and the Mental Component Score (MCS). MCS was not included in the analysis because of its strong correlation ( $r = -0.77$ ) with the depression screening instrument, the PHQ-9. Normative scores exist for the general population and patients with medical conditions.

### **RELIVE study donation-specific questions**

Utilizing questions described and used in the kidney donor literature (26), members of the RELIVE consortium developed a set of questions on the donation experience, attitudes about donation and donation-related relationships. Specific topics included, donor recovery time (e.g., “How long after donation surgery did it take you to return to your usual daily activities, such as walking, driving a car or shopping for groceries?” Less than 3 months, 3–6 months, more than 6 months or I never returned to my usual daily activities), psychological care before and since donation, family support, relationship with the recipient and recipient outcome and motivation for donation including moral obligation which has been described as a three step process that includes awareness of the effect of one’s actions on the welfare of another person, ascribing responsibility to oneself rather than others and accepting the moral norm at issue (26) (study questions available on request). In a pilot study, the questionnaire was administered to 23 donors who donated within the previous 1–4 years at two sites (Mayo and UAB) to evaluate comprehension, flow and order of questions; modifications were made prior to beginning the full study.

Control subjects for comparison with RELIVE donors with respect to depression outcomes were derived from the publicly available National Health and Nutrition Examination Survey (NHANES) 2009–2010 data (27). NHANES participants were matched to RELIVE donors based on sex, race/ethnicity, marital status, educational attainment, using an iteratively relaxed match on age at the time of completing the survey (donors) or participating in NHANES (up to  $\pm 5$  years) until at least one match was identified.

### **Statistical analysis**

Descriptive information is reported as frequencies and percentages for sample characteristics, and means and standard deviations for the PHQ-9, LOT-R and PCS distributions. Scale scores were calculated if less than half of the items were missing. Pearson correlations were calculated between depression severity and optimism.

For regression analyses, all missing data were multiply imputed using IVEware (<http://www.isr.umich.edu/src/smp/ive/>) to generate 10 imputation sets. Thirty-eight donors had imputed values for the LOT-R, and 68 for the PHQ-9. We also imputed missing values in educational attainment at donation ( $n = 474$ ), relationship to recipient ( $n = 7$ ), BMI at donation ( $n = 49$ ), history of psychological difficulties ( $n = 72$ ) and marital status ( $n = 46$ ).

We used logistic regression to examine differences between donors who were depressed at the time of questionnaire completion and those who were not, using PHQ-9 scores at or above 10 as the threshold for clinically relevant depression. Logistic regression was also used to examine differences between donors who reported experiencing emotional, psychological or substance abuse difficulties that they perceived to be a result of donation and those who did not, and to examine differences between donors who sought help for such difficulties and those who did not.

For each of these three outcomes, models were identified using a best subsets approach, selecting the model with the highest likelihood score statistic in which all covariates were statistically significant at  $p < 0.05$ . A comparison of study participants to nonparticipating donors was also performed using logistic regression.

Our study received approval by the following institutional review boards: UAB, IRB approval number X070604010; UMN, IRB approval number 0905M66501; Mayo, IRB approval number 09-001345) and DCCs, IRB approval number CR00032674 and protocol number HUM00004345. Informed consent was provided by each participant.

## Results

### **Cohort demographics and psychiatric characteristics at the time of donation**

The study cohort has previously been described (21). Of 6909 donors eligible for the study, 3470 acknowledged contact. Of these, 2455 agreed to participate. Thus, of the original cohort of potentially eligible subjects the response rate was 36% and for those who acknowledged contact (2455 of 3470) 71% completed the questionnaire. There were 3439 who did not acknowledge contact due to nonreceipt of communications or nonresponse to contact efforts. Of those contacted, 931 declined to participate, 5 had language barriers and 79 withdrew consent or did not return the questionnaire. RELIVE donors who were eligible but did not participate ( $n = 4454$ ) had lower educational attainment at donation, donated more recently, were younger at donation, were less likely to have a history of depression before donation, and were more likely to be black or another nonwhite race, male, separated, divorced or widowed, and related to their recipient (all  $p < 0.05$ ) compared to donors who did participate.

Of the 2455 participants who completed the psychosocial questionnaire (Table 1a, Table 1b; Supplemental Table S1): 93% were white, 61% were women and 52% were 40 years of age or older at donation. Over 41% were siblings and 87% were related either genetically or by marriage to their recipient. Of note, all categories of biologically related or spousal donors were less likely to have a predonation history of psychiatric difficulties than donors who were not related to their recipients (such as friends, coworkers or anonymous donors; 23% among unrelated donors compared to 8% of parents, 7% of children, 7% of siblings, 11% of spouses and 12% of other related donors) based on medical record review (all  $p < 0.05$ ).

At donation, medical records indicated that over 90% of the sample had never been on antidepressant or anti-anxiety medication and had no history of alcoholism; 11% had past or current pain problems (Table 1a). Depression (8%) was the most common preexisting psychiatric condition followed by anxiety (3%), but notably, subjects with bipolar disorder (0.4%) had also donated (Table 1a). On the questionnaire, 11% reported that they had been treated for psychological problems prior to donation.

### **Psychiatric characteristics following donation**

On the questionnaire, 4% noted psychiatric problems at some time after donation; 2% sought treatment, and 1% were in active treatment (Table 2a). Based on scores of 10 or greater on the PHQ-9, 8% of donors reported depressive symptoms at the time of the survey (Table 2b) with few reporting severe symptoms (Figure 1). The distributions of responses to PHQ-9 items are reported in Supplemental Figure S1. RELIVE donors were less likely to be taking medications for psychiatric issues including depression or anxiety (12%) at the time of the survey compared to 15% among matched NHANES controls ( $p = 0.011$ ) (Table 2b).

### **Optimism**

As a group, donor responses (LOT-R mean ( $M$ ) = 17.8, standard deviation ( $SD$ ) = 4.1) were similar to predonation liver donors ( $M = 17.8$ ,  $SD = 3.1$ ) and more optimistic than normative data from both a college-based sample ( $M = 14.3$ ) and medically ill sample ( $M = 15.2$ ) (Supplemental Figure S2) (24). The LOT-R was negatively correlated with depression, with those more optimistic less likely to report depression ( $r = -0.54$ ,  $p < 0.001$ ).

### **Donor characteristics associated with self-report of depression at the time of survey**

Based on logistic regression (Table 3), depression in donors ( $PHQ-9 \geq 10$ ) was associated with a predonation history of depression ( $p < 0.001$ ), longer postdonation recovery time ( $p = 0.009$ ), greater financial burden ( $p = 0.013$ ), stronger agreement with the statement "It was my moral obligation to donate" ( $p = 0.003$ ), and emotional, psychological or substance abuse problems following donation ( $p = 0.010$ ). After excluding donors who had a predonation history of depression, many of the same characteristics remained predictive of depression on the questionnaire.

The absence of depression symptoms ( $PHQ-9 \leq 9$ ) was associated with better physical health (measured as the age- and sex-adjusted PCS from the SF-36,  $p < 0.001$ ), older age at donation ( $p = 0.002$ ), higher optimism (measured as higher scores on the LOT-R,  $p < 0.001$ ), being employed either full-time or part-time at the time of survey ( $p < 0.001$ ) and being of white or European American race ( $p = 0.020$ ). Among donors without a history of depression before donation, absence of depression symptoms was associated with better physical health ( $p < 0.001$ ), higher optimism ( $p < 0.001$ ) and being employed ( $p = 0.033$ ).

In a separate analysis examining donation-specific questions, donors indicated whether they had experienced emotional, psychological or substance abuse concerns as a result of donation. Donors seeking help for these issues after donation were more likely to have a predonation history of depression ( $p = 0.022$ ), and/or to have felt depressed after surgery ( $p < 0.001$ ) (Table 3), and were more likely to report that their recipient's graft had failed

**Table 1a:** Characteristics of donors at the time of donation

	Number of participants	Percent of participants	Number of nonparticipants	Percent of nonparticipants
All donors	2455	100.0	4454	100.0
Age at donation				
Less than 30 years old	505	20.6	1242	27.9
30–39 years old	671	27.3	1484	33.3
40–49 years old	756	30.8	1129	25.3
50–59 years old	424	17.3	475	10.7
60 years old or older	99	4.0	117	2.6
Unknown or missing	0	0.0	7	0.2
Ethnicity				
Non-Hispanic/non-Latino	2416	98.4	3608	81.0
Hispanic/Latino	31	1.3	88	2.0
Unknown or missing	8	0.3	758	17.0
Race				
American Indian	16	0.7	46	1.0
Asian American	11	0.4	47	1.1
Black or African American	113	4.6	548	12.3
White or European American	2282	93.0	3703	83.1
Multi-racial	20	0.8	15	0.3
Unknown race	13	0.5	95	2.1
Gender				
Female	1505	61.3	2421	54.4
Male	950	38.7	2033	45.6
Relationship of living donor to recipient				
Biological, parent	450	18.3	930	20.9
Biological, child	316	12.9	672	15.1
Sibling	1011	41.2	1951	43.8
Biological, other relative	130	5.3	240	5.4
Nonbiological, spouse/partner	219	8.9	285	6.4
Nonbiological, friend	173	7.0	197	4.4
Nonbiological, other unrelated	149	6.1	163	3.7
Unknown	7	0.3	16	0.4
Surgical procedure				
Open	1630	66.4	3244	72.8
Laparoscopic	822	33.5	1207	27.1
Unknown	3	0.1	3	0.1
Predonation historical measures				
History of antidepressant use				
Current	145	5.9	189	4.2
Previous	39	1.6	39	0.9
Never	2220	90.4	4147	93.1
Unknown	51	2.1	79	1.8
History of antianxiety drug use				
Current	54	2.2	94	2.1
Previous	22	0.9	10	0.2
Never	2321	94.5	4263	95.7
Unknown	58	2.4	87	2.0
History of alcoholism or alcohol abuse				
Yes	88	3.6	169	3.8
No	2275	92.7	4088	91.8
Unknown	92	3.7	197	4.4
History of illicit drug use				
Yes	76	3.1	214	4.8
No	2124	86.5	3819	85.7
Unknown	255	10.4	421	9.5
History of chronic pain				
Current	175	7.1	211	4.7
Previous	85	3.5	112	2.5
Never	2099	85.5	3940	88.5
Unknown	96	3.9	191	4.3

Table 1: Continued

	Number of participants	Percent of participants	Number of nonparticipants	Percent of nonparticipants
History of psychiatric difficulties				
Unknown	72	2.9	111	2.5
None of the following	2141	87.2	4022	90.3
Depression	199	8.1	244	5.5
Anxiety	71	2.9	115	2.6
Bipolar	9	0.4	7	0.2
PTSD	0	0.0	7	0.2
Other psychiatric difficulties	26	1.1	48	1.1
Before your donation, had you ever been treated for emotional, psychological or substance abuse difficulties? (Collected on self-report QOL questionnaire)				
Yes	264	10.8	n/a	–
No	2149	87.5	–	–
Missing	42	1.7	–	–

PTSD, post traumatic stress disorder; QOL, quality of life.

( $p = 0.007$ ). Donors who reported emotional, psychological or substance abuse concerns after donation were more likely to have reported history of drug use at the predonation evaluation ( $p = 0.010$ ), history of chronic pain prior to donation ( $p = 0.014$ ), feeling that once the surgery was over they did not receive attention ( $p < 0.001$ ), and were

more likely to encounter postdonation re-hospitalization ( $p < 0.001$ ) or medical complications not requiring hospitalization ( $p < 0.001$ ). Nonsignificant findings for all models are provided in Supplemental Table S2.

Overall, most donors did not have a history of depression, did not report emotional, psychological or substance abuse difficulties after donation, and did not report depression (PHQ-9  $< 9$ ) at follow-up (Figure 2). However, donors who did report depression at the postdonation survey tended to report having difficulties after donation, and also tended to have a history of depression before donation.

Table 1b: Characteristics of donors at quality of life questionnaire completion (5–48 years after donation)

	n	%
All donors	2455	100.0
Age at survey completion		
Less than 30 years old	20	0.8
30–39 years old	125	5.1
40–49 years old	433	17.6
50–59 years old	865	35.2
60–69 years old	673	27.4
70–79 years old	274	11.2
80 years old or older	65	2.6
Educational attainment at survey completion		
Unknown or missing	13	0.5
Less than high school	66	2.7
High school	497	20.2
Some college, vo-tech or associate degree	920	37.5
Bachelor's degree	510	20.8
Graduate degree	449	18.3
Marital status at survey completion		
Missing	13	0.5
Married or living together	1852	75.4
Separated, divorced or widowed	449	18.3
Never married	141	5.7
Work status at survey completion		
Missing	34	1.4
Working full-time for pay	1272	51.8
Working part-time for pay	299	12.2
Not working for pay at present (not unemployed)	770	31.4
Unemployed	80	3.3

## Discussion

This study presents results from a cross-sectional survey of kidney donors' self-reports of depressive symptoms, combined with predonation data on history of depression, use of psychiatric medications and other characteristics. We also tested potential predictors of depressive symptoms. For most donors, we were able to affirm that kidney donation did not confer an increased prevalence of depression. We did identify a small subset of donors who

Table 2a: Psychological difficulties at quality of life questionnaire completion (n = 2455, 5–48 years after donation)

Donor-reported perception of complications because of donation	Donors	
	n	%
Emotional, psychological or substance abuse difficulties	98	4.0
Sought professional help for emotional, psychological or substance abuse difficulties	60	2.4
Currently treated for emotional, psychological or substance abuse difficulties	28	1.1

**Table 2b:** Depression outcomes at QOL questionnaire completion (5–48 years after donation)

	Donors		NHANES matches
	n	%	%
Depression ( $\geq 10$ PHQ-9)	190	7.8	7.0
Major depression based on PHQ criteria <sup>1</sup>	100	4.1	3.8
On medication for depression, anxiety or other psychological disorders <sup>2</sup>	298	12.1	14.6

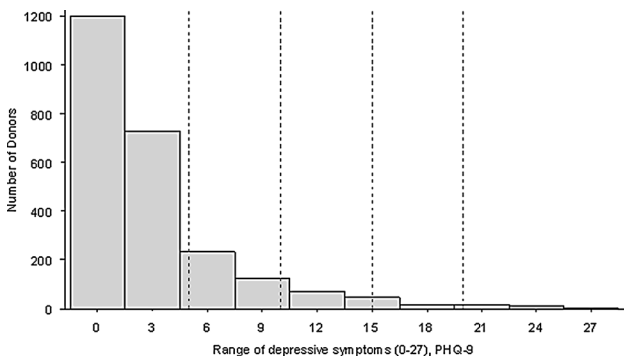
Reported percentages are percentages of donors with nonmissing data; 23 donors were missing PHQ-9 scores. Percentages of matched NHANES participants were calculated using NHANES 2009–2010, imputing PHQ-9 items among participants who were missing less than half of the 9 items.

NHANES, National Health and Nutrition Examination Survey; PHQ, Patient Health Questionnaire; QOL, quality of life.

<sup>1</sup>Major depression was defined as a depressive response to at least five items, at least one of which is in the first two items.

<sup>2</sup>Measure was significantly different between RELIVE donors and age, sex, race, ethnicity and education matched NHANES sample. RELIVE donors were significantly less likely to be on antidepressant medication than similar individuals who participated in NHANES 2009–2010 (chi-square = 6.5,  $p = 0.011$ ). RELIVE, Renal and Lung Living Donors Evaluation Study.

reported an increase of depressive symptoms. Thus our findings from the RELIVE study suggest that long-term psychiatric morbidity following kidney donation occurs, but affects a minority of donors. Factors that contributed to an increased report of depressive symptoms following kidney donation included longer recovery time, increased financial burden, feeling a moral obligation to donate, being younger at donation, being of nonwhite race, lower physical QOL and having lower self-reported optimism. A history of depression at the time of donation was also associated with later depression, which might be expected given the potential for relapse in individuals from the general population with a history of depression. Additionally, reports of rehospitalization and medical complications were asso-



**Figure 1: Histogram of Patient Health Questionnaire-9 Depression Scores in kidney donors 5–48 years after donation.**

ciated with donor perception of increased emotional, psychological or substance abuse problems related to donation. Not surprisingly, current unemployed or non-employed status was associated with current depression.

Depression risk factors have been reported for donors (28). Unlike our findings, Lentine et al, utilizing donor billing data to identify antidepressant use as an indicator of depressive symptomatology (6), reported higher rates of depression in US white donors. Qualitative research and retrospective studies note an association between recipient outcomes and adverse emotional outcomes from donation (12). Although RELIVE donors whose recipients lost their grafts or died were more likely to have obtained professional help for emotional, psychological or substance abuse concerns, we did not find that graft failure led to increased reports of depressive symptoms long-term.

In concurrence with our results, other studies suggest that donors experience less depression or a nonsignificant increase in depression symptoms (7,29,30), better social function, less bodily pain and more vitality than controls or patients undergoing nephrectomy for medical reasons (31). Stable psychiatric conditions were not associated with significant worsening of symptoms at the time of donor surgery (32). Our research supports the existing literature that suggests a high score for optimism sets the stage for better overall outcomes in medical populations (19,20).

The characteristics of nonrelated donors have been the focus of increased attention by the medical community (1) and increased rates of donation by nonbiologically related donors over the last five decades have been reported (22). Interestingly, the higher proportions of preexisting psychiatric disorders in nonrelated donors highlights the need for increased monitoring for depressive symptoms both pre- and postdonor surgery in nonrelated donors.

Based on these findings, social workers, psychologists and psychiatrists evaluating donors may wish to provide increased support to donors who have the potential for a higher prevalence of depression or have a lower threshold for advising these donors about potential adverse psychiatric outcomes. Thus far, interventions to increase the resilience of donors has not been the focus of research. New modalities including mindfulness-based stress reduction interventions, more frequent monitoring of mood symptoms postdonation, and problem-solving strategies to address financial stressors potentially could help alleviate the stress of undergoing donor surgery. Additionally, interventions such as motivational interviewing to explore donor ambivalence, possibly related to social obligation as a motivation to donate, has resulted in improved outcomes in other donor populations (33). This may be especially valuable for donor advocates wishing to assist donors in assessing whether they have sufficiently considered the risks and benefits of donation, to balance feeling compelled to donate by societal values.

**Table 3:** Results of logistic regression predicting psychological difficulties and depression 5–48 years after donation

Outcome	Predictor	OR	Low CI	High CI	p-Value
Depression at QOL questionnaire (PHQ-9 $\geq$ 10; c-statistic = 0.90)					
	History of depression: yes (ref: no)	2.55	1.53	4.26	<0.001
	Emotional, psychological or substance abuse difficulties as a result of donation	2.36	1.23	4.54	0.010
	Race: nonwhite (ref: white)	2.00	1.11	3.59	0.020
	Postdonation recovery time for daily activities (<3 months to never <sup>1</sup> )	1.74	1.15	2.64	0.009
	Donation caused a financial burden	1.32	1.06	1.65	0.013
	It was my moral obligation to donate	1.23	1.07	1.41	0.003
	PCS, age and sex adjusted, per 1/2 standard deviation	0.79	0.72	0.87	<0.001
	Age at donation, per 10 years	0.75	0.62	0.89	0.002
	LOT-R	0.73	0.70	0.77	<0.001
	Employed full- or part-time at survey completion (ref: not employed, unemployed)	0.48	0.32	0.72	<0.001
Depression at QOL questionnaire (PHQ-9 $\geq$ 10) among donors without a history of depression (c-statistic = 0.90)					
	Emotional, psychological or substance abuse difficulties as a result of donation	2.21	1.05	4.66	0.037
	Postdonation recovery time for daily activities (<3 months to never <sup>1</sup> )	1.90	1.21	2.98	0.005
	Donation caused a financial burden	1.41	1.12	1.78	0.004
	It was my moral obligation to donate	1.35	1.16	1.58	<0.001
	PCS, age and sex adjusted, per 1/2 standard deviation	0.74	0.67	0.82	<0.001
	LOT-R	0.73	0.69	0.77	<0.001
	Employed full- or part-time at survey completion (ref: not employed, unemployed)	0.63	0.41	0.96	0.033
“Did you obtain professional help for emotional, psychological or substance abuse concerns that were a result of your donation?” (c-statistic = 0.86)					
	I felt depressed for a while after the surgery (strongly disagree to strongly agree)	2.83	2.32	3.46	<0.001
	History of depression: yes (ref: no, unknown)	2.33	1.13	4.82	0.022
	Graft failure (including recipient death)	2.25	1.25	4.06	0.007
“Did you have any emotional, psychological or substance abuse difficulties that were the result of your donation?” (c-statistic = 0.79)					
	Rehospitalization or additional hospitalization days	3.23	1.90	5.48	<0.001
	History of drug use: yes (ref: no, unknown)	3.02	1.31	6.98	0.010
	Medical complication not requiring hospitalization	2.81	1.77	4.43	<0.001
	Race: nonwhite (ref: white)	2.01	1.01	4.02	0.047
	History of chronic pain predonation: yes (ref: no, unknown)	2.00	1.15	3.48	0.014
	Once the surgery was over, no one really paid much attention to me (strongly disagree to strongly agree)	1.46	1.23	1.75	<0.001
	My family or friends supported me throughout the donor surgery	0.78	0.63	0.96	0.020

Only covariates that were significant ( $p < 0.05$ ) were included in the final models.

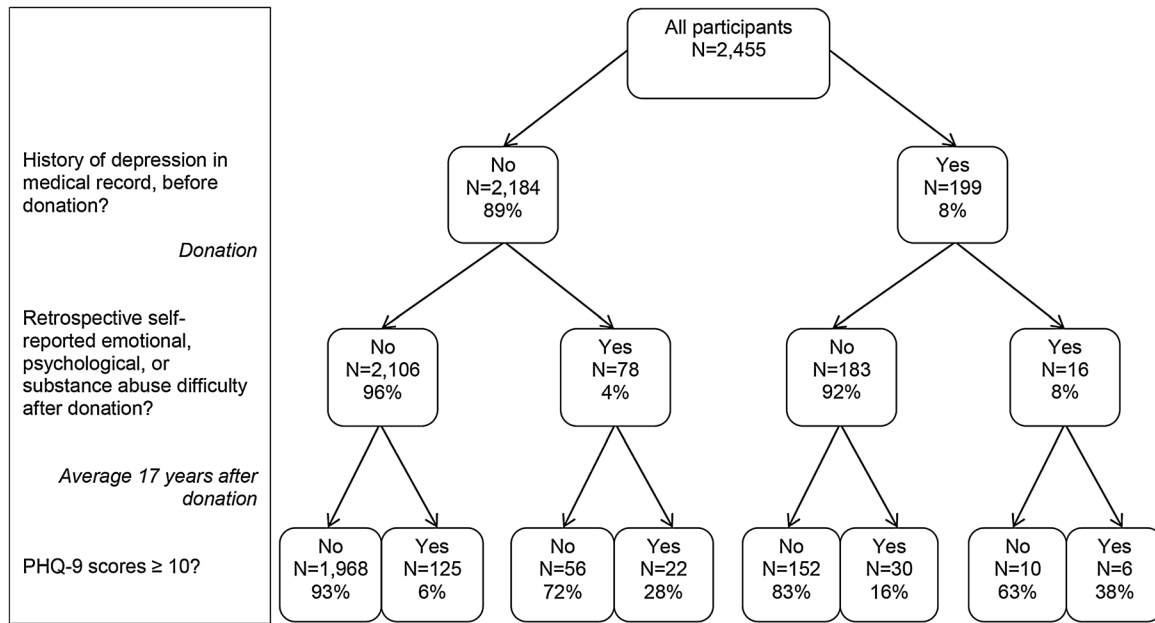
CI, confidence interval; LOT-R, Life Orientation Test-Revised; OR, odds ratio; PHQ, Patient Health Questionnaire; PCS, Physical Component Score (higher score is better); QOL, quality of life.

<sup>1</sup>Response categories for postdonation recovery included: “less than 3 months”; “3–6 months”; “more than 6 months”; and “I never returned to my usual daily activities.”

The main strengths of our study are the long interval from donation to postdonation survey, the large sample size and the diverse geographic and multicenter population. This study addressed the frequency of donor self-reported depression using a standardized rating scale widely used to screen for depression and donors’ self-report of adverse psychological sequelae of donation. Further, we investigated donors’ reports of the attribute of optimism, which may

be an important protective factor against the future development of depressive symptoms.

The challenge of contacting eligible donors up to 50 years after their surgery was formidable; in spite of multiple attempts, only 50% of those identified through medical records could be contacted by study staff. Differences in characteristics between respondents and nonrespondents



**Figure 2: History of depression at donation from medical record review and self-reported depression based on the Patient Health Questionnaire-9 survey an average of 17 years after donation.** Seventy-two donors with unknown history of depression at donation and 14 donors with missing Patient Health Questionnaire-9 scores are not shown in this figure.

might have biased our estimated prevalence of depression, although regression-based predicted probabilities estimated the bias at only 1%.

The RELIVE sample was not as racially and ethnically diverse as the complete living kidney donor population in the United States during the same time period, and tended to be older, more likely to be biologically related to their recipient (21,34) and likely to be employed. We did not have standardized pre-donation data for depressive symptoms or in-person subject interviews post-donation. We used standardized instruments to evaluate for depression and QOL, and used donation specific questions drawn from prior studies (26), and tested for flow of instruments in a separate limited sample of donors. Cognitive interviewing identified a few minor wording improvements and was deemed complete (reaching saturation) after 23 donor interviews. Our study did not collect pre-donation data prospectively and relied in part on recall by study subjects of psychosocial complications that potentially occurred years earlier, around the time of donation. The reliability of retrospective assessments of psychological difficulties shortly after donation is unclear as it is possible that these reports could be conditioned by psychological difficulties that are present at the time of survey completion. In the survey research and cognitive psychology literature, this phenomenon is referred to as retroactive interference (35). The possibility of this type of recall error does undermine somewhat, the defensibility of our statements relating to the temporality of baseline versus current psychological

stress. Readers should interpret and act upon our study findings with this potential limitation in mind.

### Conclusions

This study provides a valuable window into the donor experience using validated instruments to examine the factors contributing to risk for depression years following donation. We believe these data will provide reassurance to donors and clinicians that the experience of donation, often in the setting of a loved one’s illness, does not increase long-term depressive symptoms for most donors. Donors who had good mental health pre-donation were unlikely to develop depression in the years following donation. Specific historical features did predict risk for long-term adverse outcomes and identification pre-donation may facilitate interventions that can improve donor recovery. We found that donors as a group were more likely to be optimistic in disposition which may further protect them from future depression. Further studies to address whether interventions would enhance the experience of higher risk donors and studies on the impact of recipient outcomes on donors could ultimately improve the donor experience.

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## Disclosure

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

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## **Supporting Information**

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

**Figure S1: Individual questions on the Patient Health Questionnaire-9 survey.**

**Figure S2: Life Orientation Test—Revised compared to normative data.**

**Table S1:** List of variables.

**Table S2:** Nonsignificant findings in three predictive logistic models.