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Depression Diagnoses after Living Kidney Donation: Linking United States Registry Data and Administrative Claims

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Abstract

Background—Limited data exist on correlates of psychological outcomes after kidney donation.

Methods—We used a database integrating OPTN registrations for 4,650 living kidney donors in 1987–2007 with administrative data of a U.S. private health insurer (2000–2007 claims) to identify depression diagnoses among prior living donors. The burden and demographic correlates of depression after enrollment in the insurance plan were estimated by Cox's regression. Graft failure and death of the donor's recipient were examined as time-varying exposures.

Results—After start of insurance benefits, the cumulative frequency of depression diagnosis was 4.2% at one-year and 11.5% at five years, and was less common than among age-and-gender matched general insurance beneficiaries (rate ratio 0.70, 95% CI 0.60–0.81). Demographic and clinical correlates of increased likelihood of depression diagnoses among the prior donors included female gender, white race and some perioperative complications. After adjustment for donor demographic factors, recipient death (aHR 2.23, 95% CI 1.11–4.48) and death-censored graft failure (aHR 3.30, 95% CI 1.49–7.34) were associated with two-to-three times the relative risk of subsequent depression diagnosis among non-spousal unrelated donors. There were trends towards increased depression diagnoses after recipient death and graft failure among spousal donors, but no evidence of associations of these recipient events with the likelihood of depression diagnosis among related donors.

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Conclusions—Recipient death and graft loss predict increased depression risk among unrelated living donors in this privately-insured sample. Informed consent and post-donation care should consider the potential impact of recipient outcomes on the psychological health of the donor.

Keywords

Administrative claims; Depression; Diagnoses; Kidney transplantation; Living donors; Registries

INTRODUCTION

Depression is a prevalent condition in the general U.S. population, estimated to impact 6.6% of Americans within a given 12-month observation window (1). To date, information on depression after living kidney donation is largely drawn from single-center survey and interview-based studies. A 2006 systematic review by Clemens et al. combining data for more than 5,000 living donors estimated that depression affects 5 to 23% of donors at an average of four years after nephrectomy (2). While quality-of-life-scores that are statistically similar to those of controls have been identified in some prior donor samples (3–5), increased depression rates and exacerbations of pre-existing depression after donor nephrectomy have also been reported(6, 7).

Study findings have varied in how recipient outcomes impact donors psychologically. A small study of 32 living donors surveyed before and at an average of 19 months after donation found a significant decrease in depression index scores in the cases of successful transplants (recipient alive with graft function at assessment) (8). In contrast, evidence from case reports and focused interviews demonstrated links between recipient graft failure or death and the onset of psychological symptoms in donors including depression, “mental paralysis”, “mentally falling apart”, and even suicide (9, 10). Research teams conducting larger surveys suggested that recipient death or graft failure predicted regret about donation and lower donor quality-of-life (4, 11), but a recent multi-national survey reported similar quality-of-life scores among donors whose recipients experienced an adverse outcome and donors whose recipients were alive with function(5).

Surveys and interviews can yield important information about psychological health outcomes, but these designs also may be limited by sampling and response biases. Administrative billing claims track records of provider-reported diagnoses that offer descriptions of conditions identified in the course of clinical practice. To advance understanding of depression among a national sample of prior living kidney donors in the U.S., we examined a unique database that links Organ Procurement and Transplant Network (OPTN) identifiers of prior living kidney donors to billing claims of a private insurer. Provider-reported depression diagnoses were used to examine the burden and correlates of depression among prior donors, with particular attention to associations of recipient clinical outcomes with donor depression.

RESULTS

Demographic and Clinical Correlates of Depression Diagnoses among Prior Living Donors

Among 4,650 prior living donors in the full study sample, 54.6% were female and 76.3% were white race. Eighty one percent of donors were biologically related to their recipient, 7.6% were spouses, and 11.2% were non-spousal unrelated donors (Table 1). The median durations from donation to start and end of captured insurance benefits were 4.9 and 7.7 years, respectively. After start of benefits, the cumulative frequency of depression diagnosis was 4.2% at one-year and 11.5% at five years. Among the donors with depression diagnoses, 83.4% filled a prescription for an anti-depressant medication at some point within the available claims data, with a median time of 9 days between depression diagnosis and prescription fill dates.

In bivariate analysis, clinical correlates of depression diagnoses among the prior donors included donor age, gender and race (Table 1). Specifically, the likelihood of depression diagnosis rose significantly by 2% with each increase in year of donor age at the start of insurance benefits (aHR 1.02, 95% CI 1.01–1.03). Depression after the start of insurance benefits was more than twice as likely among female compared with male prior donors (aHR 2.41, 95% CI 1.89–3.06) and among white compared with non-white donors (aHR 2.07, 95% CI 1.50–2.86). In absolute terms, by five years after the start of insurance enrollment, claims for depression diagnoses occurred among 7% of male and 15.5% of female prior donors ($P<0.0001$). Depression diagnoses were identified among 6.5% of non-white and 13.2% of white prior donors by five years after the start of plan benefits ($P<0.0001$). Similar bivariate associations with donor age, gender and race were observed using depression diagnoses with pharmacological treatment as the outcome measure (SDC Results, Appendix 1).

The likelihood of depression diagnosis among prior donors within the captured insurance data was not significantly associated with the type of donor-recipient relationship or the duration of time from nephrectomy to the start of enrollment in the insurance plan (Table 1). By five years after enrollment, the cumulative frequency of depression among biologically related, spousal, and non-spousal unrelated donors was 11.0%, 12.5% and 16.5%, respectively, but these differences were not statistically significant ($P>0.05$).

The linked data captured 2,264 persons who donated after the start of OPTN collection of information on surgery type, of whom 48.7% underwent donor nephrectomy by laparoscopic techniques including hand-assisted laparoscopy. Surgery type was not associated with the likelihood of post-donation depression ($P=0.31$). The sample included 460 persons who donated during the period of OPTN collection of information on perioperative complications, of whom 0.9% required reoperation, 1.1% had other complications (including the need for percutaneous procedures), 1.8% required readmission, and 5.4% had any reported complication (Table 2). Although these events were infrequent, reoperation was strongly associated with post-donation depression diagnoses (aHR 7.73, 95% CI 1.05–58.33, $P=0.04$) in bivariate analyses, and other complications showed a nearly significant association (aHR 4.27, 95% CI 0.98–18.48, $P=0.05$). The association of reoperation with post-donation depression remained significant after adjustment for baseline donor

demographic factors (aHR 9.73, 95% CI 1.02–99.15, $P=0.048$). Finally, patterns were similar using depression with pharmacological treatment as the outcome measure, such that reoperation and other complications were significantly associated with these outcomes after adjustment for baseline demographic traits.

Depression Burden among Living Donors Compared to Non-Donor Controls

In the matched-pairs comparisons, depression diagnoses occurred at a rate of 5.0 per 100 person-years in the living donor sample compared with 7.1 per 100 person-years among age- and-gender matched beneficiaries in the insurance plan (rate ratio 0.70, 95% CI 0.61–0.80) (Table 2). While depression diagnoses were more common among women than men, donor-to-control rate ratios were similar across genders. Point estimates for depression diagnosis rate ratios in the living donors compared with age- and sex-matched non-donors were less than 1.0 across donor relationship categories (rate ratios 0.68 to 0.85), although the confidence interval excluded 1.0 only in the largest donor relationship category of biologically related. We also stratified the living donor sample according to those with time from donation to insurance enrollment as above or below the sample median. The rate of depression diagnoses in living donors was the same regardless of the timing of insurance enrollment (Table 2).

Associations of Recipient Clinical Events with Subsequent Donor Depression

Prior to donor enrollment in the study insurance plan, 11.4% of donors had lost recipients from death and 11.7% of donated grafts had failed for other reasons. By five years after donor insurance enrollment, recipient death and graft failure affected another 12.0% and 8.7%, respectively (Kaplan-Meier estimate). After adjustment for baseline donor demographic factors in these models, recipient clinical outcomes predicted approximately 2 to 3-fold increases in the relative risks of depression among non-spousal unrelated living donors (Table 3A). Specifically, recipient death was associated with a 123% increase in the relative risk of subsequent depression diagnosis (aHR 2.23, 95% CI 1.11–4.48) among non-spousal unrelated donors. Recipient death-censored graft loss was associated with a 230% increase in the relative risk of subsequent depression diagnosis (aHR 3.30, 95% CI 1.49–7.34) among non-spousal unrelated donors. There were trends toward increased depression risk after recipient death and graft failure among spousal donors (aHR point estimates >2.0), but these associations were not statistically significant. Recipient death (aHR 1.11, $P=0.5$) and graft failure (aHR 1.06, $P=0.8$) did not show evidence of associations with the likelihood of subsequent depression diagnosis among related donors. Consistent findings were observed using depression with pharmacological treatment as the outcome measure (Table 3B).

DISCUSSION

Psychological outcomes after kidney donation are not systematically tracked in national transplant registries. We examined a database integrating U.S. living donor registration information with billing claims from a private health insurer to study depression diagnoses in large national sample of prior donors. The study revealed, first, that depression diagnoses were present in some prior donors, at an estimated rate of approximately 5 per 100 person-

years. When compared to an age- and sex-matched sample of general insurance beneficiaries who were not living donors, however, depression diagnoses were less frequent among prior donors in the same insurance system. Therefore, a “red-flag” of greater depression burden among donors was not demonstrated. Second, the frequency of depression diagnoses in prior living donors varied by demographic and clinical factors, being more common in women compared to men, in white compared to non-white living donors, and among donors who experienced certain perioperative complications. Third, recipient death and graft loss predicted increased risk of depression diagnosis in unrelated living donors, but there was no association between depression and these negative outcomes for biologically related donors.

Depression is not uncommon in the general population, and thus one important question is whether kidney donation increases the risk of depression. We found that the rate of depression diagnoses among prior donors was significantly lower than among age-and-gender matched general insurance beneficiaries in the same insurance system. Consistent with our use of general controls and findings, prior studies reported superior quality of life and health summary scores among prior donors compared with general U.S. population norms (4, 12). It is true that donors and non-donors are different individuals facing different physical and psychological health and external stressors, and that donors undergo selection before donation. A recent multi-national survey also found similar quality-of-life scores among donors and controls screened for baseline good health (5).

While past findings on donor quality-of-life and the overall frequency of depression diagnoses observed in the current study are encouraging, some donors will experience feelings of loss, depression, and reduced mental energy (3, 13). Being a donor often means recovering from surgery while serving as a care-giver, making convalescence stressful (3). Even when this period is over, the relief can result in paradoxical depression (14). Thus, it remains important to identify baseline traits and clinical events that may predict poor psychological outcomes.

Gender-based variation in the frequency of depression is well established in the general population. For example, a nationally representative face-to-face household survey in 48 states estimated that the lifetime odds of depression in American women are 1.7-times the odds in men (95% CI 1.5–2.0) (1). Similarly, we found that depression diagnoses were more than twice as common among female compared with male adult prior donors, and that this pattern was consistent among non-donor beneficiaries of the same insurer. With this clearly established gender difference, it may be that female donors need additional depression screening before donation and psychological support afterwards if depression emerges during follow-up.

We also found that white donors were twice as likely to have depression diagnoses after donation, compared with non-white donors. Significantly lower lifetime prevalences of major depressive disorder were identified among African Americans (adjusted odds ratio 0.51) and Hispanics (adjusted odds ratio 0.38) compared with white persons in the National Health and Nutrition Examination Survey (NHANES) III (15). The mechanism of lower frequencies of clinically detected depression among persons of other racial and ethnic backgrounds compared with white persons appears to be in part due to minorities’ reluctance

in seeking mental healthcare and indirect, or “culture bound”, presentations. In an investigation of the symptomatology of depressed Chinese Americans, Yeung et al. found that 42% of those with major depression initially presented with physical complaints, while none of the subjects reported complaints of mood alteration (16). Manifestation of depression with somatic, rather than mental or emotional, symptoms has been identified in Hispanic and Asian Indian populations (17, 18). Future research should investigate whether demographic differences in depression diagnoses after kidney donation reflect care seeking, clinical ascertainment, or true differences in disease burden.

As collection of perioperative complications data by the OPTN began recently, we examined associations of early complications with depression in a subgroup of recent donors. Despite a small number of complications, we observed significant associations of the requirement for reoperation with post-donation depression, and associations of other complications including percutaneous interventions with depression with pharmacological treatment. While the effect estimates are imprecise (ie, have wide confidence limits) due to the small sub-sample and rarity of perioperative complications, the results suggest that live donors who experience surgical complications may need focused followup of their psychological health. Further study is needed to refine these preliminary findings.

Limited data are available on whether donor-recipient relationship impacts or modifies post-donation psychological outcomes. In a survey of 524 responding prior donors at the University of Minnesota in 1998–1996 that was mostly composed of living related donors (92%), a relationship other than first-degree blood relative was associated with a nearly significant trend towards increased odds of regretting donation or viewing the overall experience as very stressful (odds ratio 3.5, $P=0.06$) (4). Another survey of 167 donors found that the emotional experience was more positive than expected among 51% of first-degree relatives compared with 31% of donors with more distant relationships (19). In the current study, we found trends towards more common depression among unrelated compared with biologically related donors, but this pattern was not statistically significant.

Although donor-recipient relationship itself was not a significant correlate of post-donation depression in our study, we found that relationship modified the impact of adverse recipient events on the risk of depression diagnosis in the donor. Specifically, recipient death and graft loss predicted two-to-three-fold increased risk of subsequent depression among unrelated non-spousal donors. To our knowledge, such variations have not been previously examined, but prior studies suggested that adverse recipient events may have psychological consequences for some living donors. A multi-national cohort of 203 donors in 1970–2007 assessed in 2004–2008 (median of 5.5 years after transplant) reported similar quality-of-life scores among donors whose recipients experienced an adverse outcome and those whose recipients were alive with function (5). In contrast, recipient death within the first year of transplant was associated with three-times the likelihood of regretting donation or finding the experience very stressful (odds ratio 3.3, $P=0.1$) in the University of Minnesota survey (4). A survey that included responses of 39 donors whose recipients died or lost their graft reported that 43% believed their role as a donor made the failure more devastating and 11% had experienced suicidal ideation (19). In another small survey, 50% of donors felt their

experience was not “worth it” when the recipient died (20). Two donor suicides following graft loss or death of the recipient were examined as case reports (10).

Our observation of varying impacts of adverse recipient outcomes according to donor-recipient relationship is hypothesis generating, but cannot be explained with the available data. One hypothesis is that non-related, and thus more altruistic, donors are more psychologically vulnerable to failure of the gift, but further study is needed to assess the impact of recipient events on donor depression using a broader array of measures. At present, we agree with the recommendations of Litwin and Weizer that transplant teams should assess and attend to the mental health of all donors after recipient death or death failure, even if the transplant was years ago (10, 21). If the donor’s care has transitioned to a primary care provider, this may require communication and assessment through the current provider.

Limitations of this study include factors related to the sample and outcome measures. The claims data are derived from a private insurance plan, and uninsured living donors are not captured. Claims are surrogate measures for diagnoses and coding errors are possible. Clinical recognition of depression in particular is impacted by the willingness of the patient to seek care and directly present symptoms (15, 17, 18), and because depression codes may be differently interpreted by clinicians, claims do not offer severity information that can be obtained through surveys and interviews (22). The available data limit the capture of diagnoses to benefits periods of the linked health insurance and thus we focused on diagnoses during available observation windows of benefits under the insurer, which began at a median of five years after donation. Pre-donation benefits were captured for only a minority of the donors (14.4%), and thus information on pre-donation depression diagnoses was not available for inclusion. Of note, the depression diagnosis rate among donors was similar regardless of time from nephrectomy to plan enrollment in this analysis. Further, given that psychological outcomes are not systematically tracked after donation, even large survey studies frequently employ designs that capture donors at varying times after donation (4, 5). Given the duration of available insurance benefits, we did not have sufficient data to screen controls, and thus the donor-control comparison must be interpreted with the limitations of other general comparisons (4, 12).

In conclusion, in this privately insured sample of prior donors, we found that depression diagnoses were more common in women, in white donors, and in unrelated donors after recipient graft failure or death. While the study design and available data are inherently impacted by care seeking patterns and patient-provider communication, these data offer an additional perspective on post-donation mental health outcomes diagnosed in real practice that supplement information obtained through surveys, interviews and case reports. Additional studies should investigate whether demographic differences in depression diagnoses after kidney donation reflect care seeking, clinical ascertainment, or true differences in disease burden. Although most donors appear to experience good or stable psychological health (2, 4, 5), it is incumbent on the transplant community to seek to identify those at risk for depression and other mental illnesses. At this time, we believe that informed consent and post-donation care should attend to the potential impact of perioperative complications and recipient outcomes on the donor’s psychological health.

METHODS

Data Source and Sample

Study data were assembled by linking OPTN records for prior living kidney donors with administrative data from a national private health insurer. OPTN records include information on all donors and transplant recipients in the U.S. as submitted by OPTN member centers. After approval by the Health Resources and Services Administration (HRSA) and the Saint Louis University Institutional Review Board, beneficiary identifier numbers from the insurer's electronic databases were linked using names and birthdates to unique OPTN identifiers for living kidney donors. Analyses were performed using Health Information Portability and Accountability Act-compliant, limited datasets with all direct identifiers removed.

People were eligible if they had OPTN records of serving as a living kidney donor sometime between October 1987 and July 2007 and benefits under the participating insurer after donor nephrectomy at some point in May 2000–December 2007 (the period of available claims data). All study participants were simultaneously enrolled in medical and pharmacy benefits with this insurer exclusively during the study window. Because of the large sample size, the anonymity of the patients studied, and the non-intrusive nature of the research, a waiver of informed consent was granted per the Department of Health and Human Services Code of Federal Regulations (Title 45, Part 46, Paragraph 46.116).

Definitions of Outcomes and Covariates

Living Donor Characteristics and Recipient Clinical Events—Demographic data from the OPTN at donor nephrectomy included age, gender, race and donor-recipient relationship status as reported by the transplant center. Time from donation to the start of captured insurance benefits (at or after donation) and age at benefits start were computed for use in “time-to-depression diagnosis” models. The relationship of the donor to the recipient was defined by OPTN report as biologically related, spouse or partner, or other. Recipient graft failure and associated dates were drawn from OPTN reports based on indication of the permanent return of the transplant patient to dialysis or re-transplantation. Recipient death events were identified by OPTN reporting and supplemented with the Social Security Death Master File. As OPTN collection of descriptive information on the donation procedure has evolved over time, we performed sub-analyses considering type of donor nephrectomy surgery (open versus laparoscopic, collection starting 1998) and peri-operative complications reported to the OPTN within 6 weeks of donation (collection starting 2004) among sub-samples who donated during the period of collection of the relevant variables.

Depression Diagnoses and At-Risk Periods—Depression diagnoses were defined by identification of billing claims with a corresponding diagnosis (International Classification of Diseases Code 9th Edition Clinical Modification (ICD9-CM)) code for major depression or depression NOS (296.2, 296.3, 311) in the primary analyses. In secondary analyses, we defined depression as a provider-reported depression diagnosis on a billing claim with concomitant or subsequent pharmacy claims for antidepressant medications Appendix (SDC, Materials and Methods – Appendix 2). A schematic of the study design, constructed

to assess associations of donor demographic traits and recipient clinical outcomes with the burden of depression in this sample, is shown in Figure 1. The available data capture insurance enrollment windows for health outcomes assessment at varying times in relation to nephrectomy across the study sample. Time to depression diagnosis was computed as the time from the start of captured post-donation benefits to submission of the first depression claim, adjusted for the time from nephrectomy to the start of benefits. At-risk time was right censored at the end of insurance benefits or December 2007.

Statistical Analyses

Correlates of Depression after Donation—Datasets were merged and analyzed with SAS for Windows software, version 9.2 (SAS Institute Inc., Cary, NC). Bivariate associations (hazards ratio, HR) of factors reported before the index date, including donor demographics, time from donation to the index date, and donor-recipient relationship, were assessed by Cox's regression. Cox's regression was also used to estimate a probability distribution function for depression diagnosis after the start of benefits under the insurer, adjusted for time from nephrectomy to enrollment in the insurance plan.

Associations (adjusted hazards ratio, aHR) of recipient post-transplant graft failure and death with donor depression were examined by time-varying Cox's regression. The time-varying regression considers the recipient events that occurred before donor insurance enrollment and post-enrollment recipient events as potential predictors of subsequent donor depression diagnoses. Recipient graft failure and death events were further characterized by the donor-recipient relationship. Stratification by relationship was used to establish donors in a given relationship category who remained without depression diagnosis as reference groups. This allowed estimation of all time-dependent variables within a single model, facilitating comparison of effect estimates, as illustrated in previous studies (23). The time-varying covariates were included in all final models, and stepwise selection was performed across other factors with a P-value for retention of <0.05 .

Comparison of Depression Frequency to Non-Donor Controls—To compare the burden of depression among the donors to a non-donor sample, donors were matched one-to-one with general insurance beneficiaries (non-donors) by gender and age when benefits began. Maximum observation time defined by benefits duration in each matched pair was limited to the shortest available in the pair. We compared the individual cases of depression per observation time among the donors versus age- and gender-matched controls as rate ratios. Comparisons were stratified according to donor traits of interest.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Schematic of the design for integration of recipient clinical event information with donor depression diagnoses ascertained during insurance benefits periods.

Dx, diagnosis; LKD, living kidney donor; OPTN, Organ Procurement and Transplantation Network

Table 1

Distribution of living donor traits and bivariate associations with depression diagnoses after enrollment in the captured insurance system.

Full Sample (N=4,650)	Trait Distributions in Sample	Bivariate Associations with Living Donor Depression HR (95% CI)
Living Donor Demographic Traits		
Mean ± SD		
Age at Donation	37.2 ± 10.0	1.02 (1.01–1.03) [‡]
Age at Start of Benefits in Study Plan	42.7 ± 10.5	1.02 (1.01–1.03) [‡]
Percentages		
Female Gender	54.6%	2.41 (1.89–3.06) [§]
White, Non-Hispanic	76.3%	2.07 (1.50–2.86) [§]
Relationship to Recipient		
Biologically Related	81.3%	Reference
Spouse/Partner	7.6%	1.16 (0.79–1.71)
Not Biologically Related or Spouse	11.2%	1.30 (0.93–1.81)
Median(IQR)		
Years from Donation to Start of Insurance Benefits	4.9 (1.7–8.7)	1.02 (0.99–1.05)
Sub-Sample who Donated after Start of OPTN Collection of Surgical Complications (2004 or later, N= 460)	Percentages	Bivariate Associations with Living Donor Depression HR (95% CI)
Reoperation	0.9%	7.73 (1.03–55.33) [‡]
Other Complication (including Percutaneous Intervention)	1.1%	4.27 (0.98 – 18.48) [*]
Readmission	1.8%	--
Any Complication (Composite)	5.4%	2.46 (0.57–10.66)

IQR, inter-quartile range

P values:

^{*} 0.05;

[‡] P 0.04–0.0001;

[§] P < 0.0001

--Not evaluable

Table 2

Depression diagnosis rate ratios among prior living donors compared with age- and gender-matched general insurance beneficiaries.

Full Sample	Living Donors Diagnoses per 100 person-yr	Controls Diagnoses per 100 person-yr	Rate Ratio, Living Donors vs. Controls (95% CI)
Both Genders	5.0	7.1	0.70 (0.61–0.80) [†]
Female	6.6	9.2	0.72 (0.61–0.85) [†]
Male	3.1	4.7	0.65 (0.50–0.84) [†]
By Donor-Recipient Relationship			
Biologically Related	4.9	7.1	0.68 (0.58–0.80) [†]
Spouse/Partner	5.0	5.9	0.85 (0.51–1.40)
Not Biologically Related or Spouse	5.8	8.3	0.69 (0.47–1.04)
By Insurance Plan Enrollment Time after Donation*			
Early	5.0	7.0	0.71 (0.58–0.86) [†]
Later	5.0	7.3	0.69 (0.56–0.84) [†]

* Sub-samples defined by enrollment in the study insurance plan before or after median sample time from nephrectomy to plan enrollment

[†] P<0.05

Table 3

Associations of recipient death and graft failure with subsequent living donor depression, according to donor-recipient relationship in the study sample (N=4,650).

A. Outcome: Living Donor Depression Diagnosis		
	Model 1 –Recipient Graft Failure as Predictor aHR (95% CI) for Living Donor Depression	Model 2 –Recipient Death as Predictor aHR (95% CI) for Living Donor Depression
Time-Varying Recipient Event, by Relationship to Donor*		
If Recipient Biologically Related to Donor	1.06 (0.76–1.49)	1.11 (0.84–1.45)
If Recipient Spouse of Donor	2.04 (0.76–5.50)	2.00 (0.86–4.64)
If Recipient Not Biologically Related or Spouse of Donor	3.30 (1.49–7.34) [†]	2.23 (1.11–4.48) [†]
Donor Demographic Traits		
Female Gender	2.44 (1.91–3.11) [§]	2.43 (1.90–3.10) [§]
White, Non-Hispanic	2.11 (1.53–2.92) [§]	2.12 (1.53–2.94) [§]

B. Living Donor Depression Diagnosis with Pharmacological Treatment		
	Model 1 –Recipient Graft Failure as Predictor aHR (95% CI) for Living Donor Depression	Model 2 –Recipient Death as Predictor aHR (95% CI) for Living Donor Depression
Time-Varying Recipient Event, by Relationship to Donor*		
If Recipient Biologically Related to Donor	1.08 (0.74–1.57)	1.00 (0.69–1.45)
If Recipient Spouse of Donor	1.45 (0.42–4.96)	1.76 (0.57–5.44)
If Recipient Not Biologically Related or Spouse of Donor	3.16 (1.28–7.80) [†]	2.86 (1.29–6.37) [†]
Donor Demographic Traits		
Female Gender	2.57 (1.74–3.79) [§]	2.57 (1.74–3.78) [§]
White, Non-Hispanic	2.51 (1.91–3.30) [§]	2.50 (1.90–3.28) [§]

* Recipient event was Graft Failure in Model 1, and Death in Model 2

Pvalues:

[†] P 0.02–0.0001;

[§] P < 0.0001