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Psychological Outcomes of Living Liver Donors From a Multicenter Prospective Study: Results From the Adult-to-Adult Living Donor Liver Transplantation Cohort Study2 (A2ALL-2)

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Although single-center and cross-sectional studies have suggested a modest impact of liver donation on donor psychological well-being, few studies have assessed these outcomes prospectively among a large cohort. We conducted one of the largest, prospective, multicenter studies of psychological outcomes in living liver donors within the Adult-to-Adult Living Donor Liver Transplantation Cohort Study2 (A2ALL-2) consortium. In total, 271 (91%) of 297 eligible donors were interviewed at least once before donation and at 3, 6, 12, and 24 mo after donation using validated measures. We found that living liver donors reported low rates of major depressive (0–3%), alcohol abuse (2–5%), and anxiety syndromes (2–3%) at any given assessment in their first 2 years after donation. Between 4.7% and 9.6% of donors reported impaired mental well-being at various time points. We identified significant predictors for donors' perceptions of being better people and experiencing psychological growth following donation, including age, sex, relationship to recipient, ambivalence and motivation regarding donation, and feeling that donation would make life more worthwhile. Our results highlight the need for close psychosocial monitoring for those donors whose recipients died (n=27); some of those donors experienced guilt and concerns about responsibility. Careful screening and targeted, data-driven follow-up hold promise for optimizing psychological outcomes following this procedure for potentially vulnerable donors.

Abbreviations: A2ALL2, Adult-to-Adult Living Donor Liver Transplantation Cohort Study2; CI, confidence interval; GEE, generalized estimating equation; HCC, hepatocellular carcinoma; HRQOL, health-related quality of life; LLD, living liver donor; M, months; MCS, mental component summary; PHQ-9, Patient Health Questionnaire 9; Pre, before donation; PRIME-MD, Primary Care Evaluation of Mental Disorders; PTGI-SF, Posttraumatic Growth Inventory–Short Form; SD, standard deviation; SF-36, 36-item Short Form Health Survey; Y, years

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Introduction

The use of living liver donation has been a critical strategy in response to the shortage of deceased donor liver grafts for patients needing this life-saving intervention; however, living liver donors (LLDs) undergo a major

surgical operation with no medical benefit for themselves. The procedure is not only physically demanding for LLDs (1,2) but also can involve a psychological burden (3,4). For this reason, adults chosen as LLDs are typically healthy, both physically and emotionally (5). Given these burdens, it is imperative to have a comprehensive understanding of the psychological effects of living liver donation and to ensure that long-term harm is not caused by donation.

The longitudinal effects of donation on LLDs' psychological well-being have not been well characterized beyond several single-center studies (6–8). At 6–12 mo after donation, most LLDs report their overall psychological well-being to be equivalent to or better than a normative general population or a control population of healthy adults (6), but prior studies have not systematically assessed predonation psychological status. Despite the overall stability in donor well-being after donation, not all donors fare equally well (6,9–11).

From small, single-center studies, we know that LLDs who donate to recipients with hepatocellular carcinoma (HCC) and those who urgently donated to recipients with acute liver failure have significantly worse mental well-being prior to donation than normative populations (6). At 3 mo after donation, however, the mental well-being of these LLDs is not significantly different from normative populations (12). Some reports have suggested worse psychological outcomes among donors whose recipients suffered complications after transplant (3,9), whereas other reports have not found this association (12). In a larger cross-sectional study, past or present psychiatric history, holding a graduate degree, and concerns about the donor's own well-being prior to donation were all associated with poorer psychological outcomes compared with population norms (13).

In a single-institution Japanese study, the rate of new-onset psychiatric complications was <5% among LLDs (14). Furthermore, in a longer term cross-sectional analysis of LLDs in the Adult-to-Adult Living Donor Transplant Cohort Study (A2ALL), most donors maintained above-average health-related quality of life (HRQOL) up to 11 years after donation (10,15). In a recent study (16), almost all (97%) LLDs indicated they would donate again, regardless of complications, and similar results were found in donors 3–9 years after donation in A2ALL (15). Although the existing literature provides a snapshot of the typical trajectory of psychological outcomes for LLDs, current prospective studies of donor psychological outcomes have not rigorously addressed potential predictors of psychological outcomes (6,11,17).

Understanding the impact of liver donation surgery not only on clinical outcomes but also on donors' psychological well-being is critical for several reasons. Having a data-driven understanding of psychological outcomes is critical for donor informed consent and helps set expectations for postdonation recovery. An improved understanding of psychological outcomes may include identification of potential psychological benefits of donation. In addition, identification of donors at higher risk for poor psychological outcomes would allow transplant centers to monitor and treat potentially vulnerable donors during their recovery and aid in the development of targeted interventions. The purpose of this study was to evaluate trends in psychological outcomes over time and potential predictors of these outcomes in a prospective multicenter study of LLDs up to 2 years after donation.

Methods

Patients and study design

The A2ALL-2 consortium consists of eight U.S. transplant centers and one transplant center in Toronto, Canada. Centers began enrolling LLDs and their recipients between February and July 2011, and all centers ended enrollment January 31, 2014. All centers followed the medical and psychosocial evaluation and exclusion criteria for selecting LLDs now included in the current U.S. national policy (18). Because our study was observational, screening protocols were not standardized across centers. Donors in the current prospective study of HRQOL were enrolled on or before their scheduled donation date. Study participants were also required to be English-speaking to participate in telephone interviews. The study was approved by the institutional review boards and privacy boards of the University of Michigan Data Coordinating Center and each of the nine participating transplant centers. All donors provided written informed consent.

Procedure

The A2ALL HRQOL study survey was implemented using computer-assisted telephone interview methods, which ensure consistent wording and reduce missing data by requiring a response (or reason for no response) before advancing to subsequent questions (19–21). Interviewers were trained in computer-assisted telephone interview methods. Predonation interviews were conducted <1 mo prior to donation, and postdonation interviews were conducted at 3, 6, 12, and 24 mo after donation. Participants were interviewed for 35–45 min each time and were compensated $20 (U.S. dollars) for each completed interview. Data collection ended July 15, 2014, after which donors who did not complete all postdonation interviews were administratively censored (n = 29 at 1 year plus another 66 at 2 years after donation). Clinical information, including donor hospitalizations, complications, and recipient indication for transplantation, was abstracted from medical records.

Measures

Psychological outcomes: The major depressive, anxiety, and alcohol abuse modules of the Primary Care Evaluation of Mental Disorders (PRIME-MD) were assessed. Alcohol abuse was defined as any endorsement of the following items more than once in the preceding 6 mo: drinking alcohol despite health problems, drinking alcohol during responsibilities, missed obligations because of drinking, problems getting along with other people because of drinking, or driving after drinking. The PRIME-MD is a validated tool that is designed to identify clinically significant mental health problems in primary care but that has also been implemented successfully in other patient populations (22–24). The modules are useful for identifying syndromes likely to meet diagnostic criteria (25–27).

The mental component summary (MCS) of the 36-item Short Form Health Survey (SF-36), version 2, summarizes the mental well-being of respondents. General population–norm-based scoring of the MCS was used to allow comparison to the U.S. population, which is calibrated to have a mean score of 50 and a standard deviation of 10. The SF-36 is one of the most widely used HRQOL outcome measures in the biomedical literature (28,29).

The Posttraumatic Growth Inventory–Short Form (PTGI-SF; Cronbach's $\alpha = 0.93$ in the present sample) is a 10-item measure used to assess positive outcomes reported by individuals who have experienced traumatic events. In the present study, it was asked with reference to the donation experience. Higher scores indicate a greater degree of perceived positive change following donation. Prior research suggests that the PTGI-SF is a useful scale for determining how well patients are able to reconstruct or strengthen their perceptions of self, others, and the meaning of events (30). The PTGI-SF was administered only at 1 and 2 years after donation.

The Simmons "better person" scale (Cronbach's $\alpha = 0.78$ in the present sample) is a 10-item scale that assesses whether respondents perceive themselves to be better people for having donated. A sample item is, "Since the donation, I think more highly of myself." Ratings range from 1 (not at all true) to 10 (very true). Items are averaged, with higher scores indicating greater perceptions of being a better person (31).

LLDs were also asked a single question about whether they would make the same decision to donate again. If their recipients died, LLDs were asked a single question about whether they felt guilty about the death and whether they felt responsible for the death (both on 1–10 scales with 1 indicating not at all guilty or responsible and 10 indicating very guilty or responsible) (31). Guilt and responsibility were defined as scores of ≥6 on the 10-point scale.

Potential predictors of psychological outcomes: We examined donor demographics (age, sex, race/ethnicity, education, and marital status), clinical characteristics (length of donation hospital stay, postdonation rehospitalizations within the first month, and postoperative complications within the first month), donor–recipient relationship (first-degree relatives, spouse or partner, other biological or nonbiological relatives, and unrelated people including friends and others), whether the donor knew of recipient death prior to the survey time point, and predonation survey items representing donors' physical and mental health and perceptions about donation.

Several predonation survey items included in the current study were based on instruments developed to assess donor experiences during the predonation process (31). These instruments included items that asked about (a) other donation behavior (e.g. blood donation); (b) decision-making items, including whether there were other possible donors for the transplant candidate; (c) a seven-item scale that assessed ambivalence about donating (Cronbach's $\alpha = 0.57$ in this sample); (d) whether someone encouraged or discouraged the donor to donate; (e) anticipated long-term health effects of donation; (f) feeling life would be more worthwhile if the donor donated; and (g) a two-item measure that assessed whether donors had a history of family disapproval of their behavior in the past ("black sheep donors"). Simmons' (31) 11 items pertaining to motivations to donate were averaged to summarize the motivation to donate (Cronbach's $\alpha = 0.77$ in the present sample). The scale ranged from 1 (weak motivation to donate) to 7 (strong motivation to donate). Other potential predonation predictors included the Campbell global life satisfaction item (32), which captures how donors feel about life as a whole, the MCS and physical component summary scores from the SF-36 (29), and the Patient Health Questionnaire 9 (PHQ-9) (33) depression score (Cronbach's $\alpha = 0.73$ in the present sample).

Statistical analysis

Descriptive statistics were used to summarize demographic characteristics of LLDs. We compared those who responded to the A2ALL HRQOL survey with those who did not respond (did not consent or were not interviewed) using t-tests for continuous variables and Pearson chi-square or Fisher exact tests for categorical variables.

Among LLDs who responded to the survey, we also examined psychological characteristics over time. At each assessment time point, we calculated means and standard deviations for continuous variables and percentages for dichotomous variables. For dichotomous outcomes, we also estimated endorsement cumulatively by calculating the percentage who endorsed the outcome at any time after donation. PRIME-MD factors were evaluated as three separate outcomes (major depressive alcohol abuse, and nonpanic generalized anxiety syndromes) and as a group of syndromes at each time point. Lasagna plots were used to illustrate subject-specific changes over time in PRIME-MD syndromes and willingness to donate again for those donors who had each outcome at any time point (34). We hypothesized that willingness to donate again could differ based on whether the recipient died, the length of donation hospital stay, and whether the donor had postdonation complications. Because only 30 donors ever reported an unwillingness to donate again during the study period, we were not adequately powered to do multivariable modeling. Instead, we used unadjusted repeated measures logistic regression models with a generalized estimating equation (GEE) to test for these associations.

We were interested in identifying predonation predictors of donation-related outcomes; however, because several outcomes had low endorsement, we made an *a priori* decision to model only binary outcomes with endorsement >10% at a given time to help ensure reliability and generalizability of model results. To identify predonation predictors of two continuous donation-related outcome measures—the Simmons better person scale and PTGI-SF—GEE models with sandwich standard error estimators were fit among donors who completed the predonation survey and at least one postdonation survey. Predictor variable selection was guided by the method of best subsets (35), adjusted for time. Predictors were retained in models if p-values from overall tests (across all levels for categorical variables) were <0.05 or if Bonferroni-corrected pairwise tests against the reference category were significant for categorical variables.

Recipient indications for liver transplant were missing for some donors. Consequently, to evaluate the impact of recipient diagnosis on donors' psychological outcomes, a subgroup analysis was conducted among donors with such information using modeling methods similar to those in the main analysis. Recipient indications tested in this cohort included hepatitis C virus cirrhosis, HCC and other primary hepatic malignancy, alcohol-related cirrhosis, cryptogenic cirrhosis, primary biliary cirrhosis, primary sclerosing cholangitis, and other liver disease or cirrhosis.

Because there could be differences in screening protocols and other factors across centers, we assessed both the magnitude of center effects and the effect of center adjustment on other covariate coefficients (reflecting possible confounding). To do so, we conducted a sensitivity analysis including center indicators in final models. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc, Cary, NC). Lasagna plots were generated using R version 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Among 297 donors who consented to the study, 271 (91.2%) were interviewed at least once, with 245 interviewed both before and after donation, eight interviewed only before donation, and 18 interviewed only at postdonation time points (Figure 1).

We compared demographic characteristics of respondents (n = 271) and nonrespondents (n = 26, including 19 potential donors who did not consent and seven actual donors who were not interviewed), and no significant differences were found for sex, age, or race/ethnicity (p = 0.74, p = 0.36, and p = 0.11, respectively). Respondents were predominantly female (57%), white

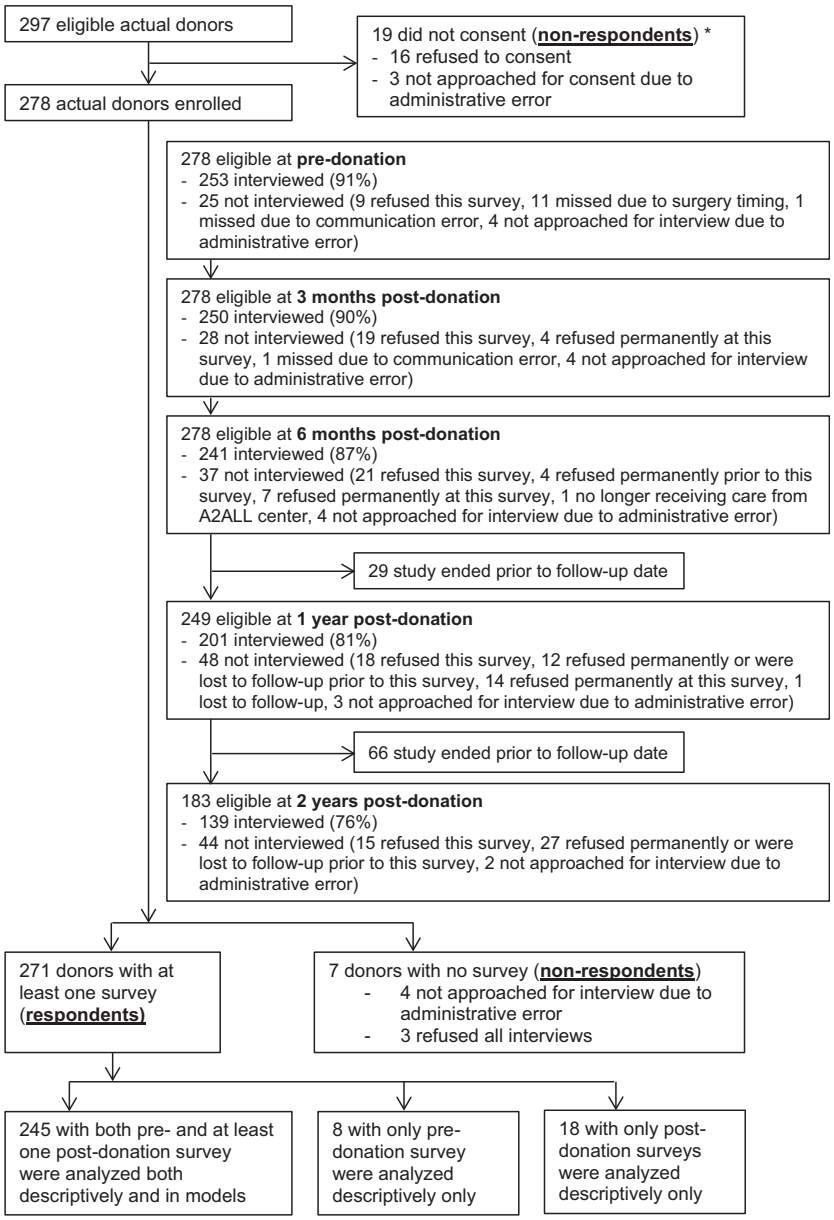

Figure 1: Participant flow diagram. This diagram shows the number of eligible actual donors who consented to the study, were interviewed by the survey center, and were included in descriptive analyses and models. Donors were eligible at each time point if they reached that time point before being administratively censored at the end of study on July 15, 2014. Note: 30 potential donors consented to the study but did not donate and were not included in this flow chart. *Donation status for these 19 donor candidates was unknown because they did not consent to this study. A2ALL, Adult-to-Adult Living Donor Liver Transplantation Cohort Study.

(80%), married (63%), and employed full time (61%) (Table 1). Most had education beyond the high school level (83%), and more than half donated to a first-degree relative (53%). Only 10% (n = 27) of respondents learned about their recipient's death during the study follow-up period.

Psychological characteristics

Table 2 shows the psychological characteristics by pre- and postdonation time points. On average, donors' responses on the better person scale and the PTGI-SF were at about the midpoints of both scales across all time points in which they were administered. On the better person scale, ranging from 1 (low) to 10 (high), donors' 3- and 6-mo postdonation scores were about half a point and a third of a point higher relative to 2 years after donation, respectively. Although decreasing, this magnitude of change is unlikely to be clinically meaningful; nevertheless, it suggests that feelings of self-worth persist over time (33).

Only 8% of donors reported they would not make the same decision to donate again at 3 mo after donation; this decreased to ≈5% at subsequent follow-up assessments. Overall, 11% (n = 30) reported they would not donate again at some point during the study follow-up. Although a few of these donors indicated they would not donate again consistently across all postdonation time points, most indicated only once or twice during follow-up that they would not donate again (Figure 2). Based on unadjusted repeated measures regression models, donors whose recipients died were 8.0 times more likely to report unwillingness to donate again than donors whose recipients did not die (95% confidence interval [CI] 2.9–22.3, p = 0.047); postdonation complications and length of hospital stay were not associated with a donor's unwillingness to donate again (p = 0.95 and p = 0.90, respectively).

With respect to PRIME-MD syndromes, 4–9.5% of donors had at least one syndrome at any given time point, with little change over time observed (Table 2). The most common syndrome was alcohol abuse (2–5%), followed by anxiety syndrome (2–3%) and major depressive syndrome (0–3%). Among donors with any type of syndrome at any time point (n = 43) (Figure 3 right panel), 30 had a syndrome at only one time point; eight had a syndrome at two time points; two had a syndrome at three time points; two had a syndrome at four time points; and one had a syndrome at all five time points. Regarding the individual syndromes, 37 had only one syndrome (yellow, red, and blue in Figure 3) at any time, six had two syndromes (orange and purple) during at least one time point, and no one had all three syndromes at the same time. In addition, 26 of 43 had no syndromes before donation but developed them during postdonation follow-up.

On average, donors' MCS scores were similar across all pre- and postdonation time points and were about 8 to 9.5 points higher than those of the U.S. general population (Table 2). Before donation, 4.7% of donors were considered impaired on the MCS (defined as 0.5 standard deviations below the U.S. normative mean); this percentage increased to 9.6% at 3 mo after donation but then decreased back to 5% at 2 years after donation.

Of donors reporting recipient death during the study follow-up (n = 27), nine (33%) had ever felt guilty and six (22%) had ever felt responsible for the recipient death at some point after their recipient died.

Predictors of psychological outcomes

No binary outcomes were modeled because no outcomes had endorsement >10% for at least one time point to help ensure reliability of model results.

Significant predictors of the Simmons better person scale included time since donation, relationship to recipient, sex, recipient death, and several predonation psychological factors (Table 3). Scores on the better person scale were decreasing over time until 1 year after donation. Donors donating to a first-degree relative had higher scores compared with those donating to unrelated recipients ($\beta = 0.84$, 95% CI 0.19–1.49), on average, whereas female donors ($\beta = -0.70$, 95% CI −1.21 to −0.18) and donors whose recipients died ($\beta = -1.24$, 95% CI −1.89 to −0.59) had lower scores. Higher predonation ambivalence, anticipation that life would be more worthwhile after donation, higher average of donation motivations, and history of other donation behavior (actual or intended) were all associated with higher scores on the Simmons better person scale.

The PTGI-SF average scores were not significantly different between 1 and 2 years after donation (Table 4). Older donors experienced less growth ($\beta = -1.58$ per 10-year increase in age, 95% CI −2.98 to −0.17), on average, as did those who were discouraged to donate ($\beta = -3.56$, 95% CI −6.68 to −0.45). In contrast, donors who anticipated before donation that their life would be more worthwhile after donation had significantly more growth, as measured by the PTGI-SF.

For both modeled outcomes, sensitivity analyses including center indicators in models showed similar results for the identified predictors. Center was significant in predicting the Simmons better person scale (overall p = 0.03) but was not significant in predicting PTGI-SF (p = 0.09). For the Simmons better person scale, using the center with the largest number of donors (n = 90) as the reference category, the differences from the other eight centers ranged from −0.24 (p = 0.61) to 1.41 points (p < 0.001). Only the center with the 1.41-point difference was found to be significantly different from the reference center.

Table 1: Demographic and donation-related characteristics of respondents (n = 271)

Characteristic	Result
Female	57.2% (155)
Age at donation, mean (SD)	36.79 (10.51)
Race/ethnicity[1]	
Non-Hispanic white	80.4% (218)
Hispanic	9.2% (25)
Native American or Alaskan Native	1.8% (5)
Asian	3.0% (8)
Black or African American	2.6% (7)
Native Hawaiian or other Pacific Islander	2.6% (7)
Other	0.4% (1)
Education at survey	
High school or less	17.3% (47)
Vocational or some college	29.2% (79)
College graduate	28.8% (78)
Postgraduate	18.1% (49)
Unknown	6.6% (18)
Married or had long-term partner	63.1% (171)
Relation to transplant recipient	
First-degree relative	53.1% (144)
Parent	2.2% (6)
Child	36.2% (98)
Sibling	14.8% (40)
Spouse or partner	6.3% (17)
Other biological or nonbiological relative	19.2% (52)
Unrelated[4]	21.4% (58)
Postdonation length of hospital stay (days), mean (SD)	5.50 (1.99)
Range	1–24
Number of postoperative complications during the first month after donation[2]	
0	80.4% (218)
≥1	19.2% (52)
Number of hospitalizations during the first month after donation[2]	
0	91.5% (248)
≥1	7.7% (21)
Postdonation recipient vital status from donor reported survey data (n = 263)	
Donor ever aware of recipient death[3]	10.3% (27)
Weeks after donation that recipient death occurred (n = 27), mean (SD)	16.11 (18.22)
Predonation predictors from survey data (n = 253)	
History of other donation behavior (e.g. blood donation)	71.5% (181)
There were other possible donors for the transplant candidate	41.9% (106)
Ambivalence to donate (0 = no ambivalence, 7 = highest ambivalence), mean (SD)	1.97 (1.58)
Someone encouraged the donor to donate	13.4% (34)
Someone discouraged the donor to donate	46.6% (118)
Anticipated long-term health effects of donation	51.0% (129)
Feeling life would be more worthwhile if the donor donated (1 = very unlikely, 10 = very likely),[2] mean (SD)	6.80 (2.79)
History of family disapproval of donor's behavior, % yes	28.5% (72)
Average of motivations to donate (scale of 1–7 with higher score indicating stronger motivation), mean (SD)	4.97 (0.94)
Feeling about life as a whole (1 = complete dissatisfaction, 7 = complete satisfaction), mean (SD)	6.11 (0.90)
SF-36 mental component summary, mean (SD)	58.37 (7.19)
SF-36 physical component summary, mean (SD)	56.20 (3.88)
PHQ-9 depression score (scale of 0–27), mean (SD)	1.45 (2.30)
Range	0–16

Data are shown as % (n) or mean (SD). PHQ-9, Patient Health Questionnaire-9; SD, standard deviation; SF-36, 36-item Short Form Health Survey.

[1]Race/ethnicity: Native American or Alaskan Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, and Other were collapsed into one category in the modeling and in the comparison of respondents versus nonrespondents.

[2]Missing <1%.

[3]Five participants reported that they did not know recipient vital status for at least one time point.

[4]Nine donors were anonymous in this unrelated group. These unrelated donors included both directed and nondirected donors.

Table 2: Psychological outcome characteristics over time

Outcome	Predonation (n = 253)	Postdonation, 3 mo (n = 250)	Postdonation, 6 mo (n = 241)	Postdonation, 1 year (n = 201)	Postdonation, 2 years (n = 139)	Endorsement at any postdonation time point (n = 263)[8]
Better person scale (1 = low, 10 = high)	–	5.02 (2.46)	4.71 (2.54)	4.62 (2.75)	4.57 (2.57)	–
PTGI-SF (0 = low, 50 = high)[1]	–	–	–	25.23 (13.13)	24.92 (13.69)	–
Would not make the same decision to donate again[2]	–	8.0% (20)	4.2% (10)	5.0% (10)	5.8% (8)	11.4% (30)
Any PRIME-MD syndrome[3]	5.5% (14)	4.0% (10)	5.9% (14)	9.5% (19)	5.8% (8)	14.1% (37)
Major depressive syndrome[4]	0.4% (1)	0.4% (1)	0.0% (0)	2.5% (5)	0.0% (0)	2.3% (6)
Alcohol abuse syndrome[5]	4.0% (10)	2.4% (6)	4.2% (10)	5.5% (11)	3.6% (5)	8.4% (22)
Nonpanic general anxiety syndrome[6]	2.0% (5)	1.6% (4)	1.7% (4)	3.5% (7)	2.2% (3)	5.3% (14)
Donor whose recipient was no longer alive[7]	–	n = 13	n = 18	n = 14	n = 14	n = 27
Feel guilty about death (≥6 on scale of 1 [not at all guilty] to 10 [very guilty])	–	7.7% (1)	33.3% (6)	21.4% (3)	0.0% (0)	33.3% (9)
Feel responsible for death (≥6 on scale of 1 [not at all responsible] to 10 [very responsible])	–	0.0% (0)	22.2% (4)	21.4% (3)	7.1% (1)	22.2% (6)
General HRQOL						
SF-36 MCS (U.S. mean = 50, SD = 10, higher is better)[7]	58.37 (7.19)	58.16 (9.46)	58.67 (8.32)	57.95 (10.92)	59.52 (7.53)	–
SF-36 MCS impaired (<0.5 SD of the mean)[7]	4.7% (12)	9.6% (24)	7.9% (19)	9.5% (19)	5.0% (7)	18.6% (49)

Data are shown as % (n) or mean (SD). HRQOL, health-related quality of life; MCS, mental component summary; PHQ-9, Patient Health Questionnaire 9; PRIME-MD, Primary Care Evaluation of Mental Disorders; PTGI-SF, Posttraumatic Growth Inventory–Short Form; SD, standard deviation; SF-36, 36-item Short Form Health Survey.
[1]Missing n = 1 at 1 year.
[2]Missing n = 5 at 6 mo.
[3]Missing n = 2 at 3 mo, n = 3 at 6 mo, and n = 1 at 1 year.
[4]Missing n = 1 at 3 mo, n = 2 at 6 mo, and n = 1 at 1 year.
[5]Missing n = 3 at 6 mo.
[6]Missing n = 1 at 3 mo and n = 3 at 6 mo.
[7]Missing n = 1 at 6 mo.
[8]This may be underestimated, given that not all respondents responded at all time points.

The subgroup analysis (n = 226) examining the effects of recipient indications for liver transplant on donors' psychological outcomes did not reveal any recipient indication or diagnosis significantly associated with the better person scale or the PTGI-SF, except for cryptogenic cirrhosis. Donors whose recipients had an indication for transplant of cryptogenic cirrhosis had an average of 7.5 points (95% CI 0.67–14.4) more posttraumatic growth compared with donors whose recipients' indication for transplant did not include cryptogenic cirrhosis.

Discussion

We conducted one of the largest multicenter prospective studies of LLDs' psychological well-being to date. At 2 years after donation, nearly 95% of donors interviewed reported they would make the decision to donate again if they could. It is useful to note, however, that up to 11% of our sample indicated at some point during the postdonation study period that they would not donate again, and this rate is somewhat higher than reported in prior studies of LLDs (9,36). The slight discrepancy may be due to the fact that our participants were reporting their experience to a survey center that was not directly associated with the donation team.

In our cohort, we found that LLDs reported low rates of major depressive, alcohol abuse, and anxiety syndromes at any given time point in their first 2 years following donation (generally <5% for any individual syndrome at any given time point). This finding is compatible with

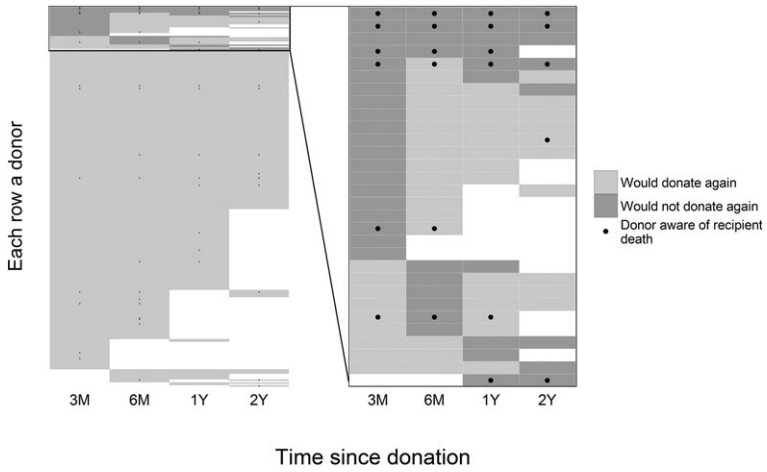

Figure 2: Donor-specific willingness to donate again (light gray) or not (dark gray) is shown for each survey: 3 mo, 6 mo, 1 year, and 2 years. Each row in the graph represents a donor, and white boxes indicate missing surveys. Recipient deaths that were known to the donor are shown with black dots, with the first dot in each row representing the time point when the donor first reported awareness of recipient death. The left side includes all donors with postdonation surveys (n = 263), and the right side shows only donors who reported they would not donate again at one time point or more (n = 30). M, months; Y, years.

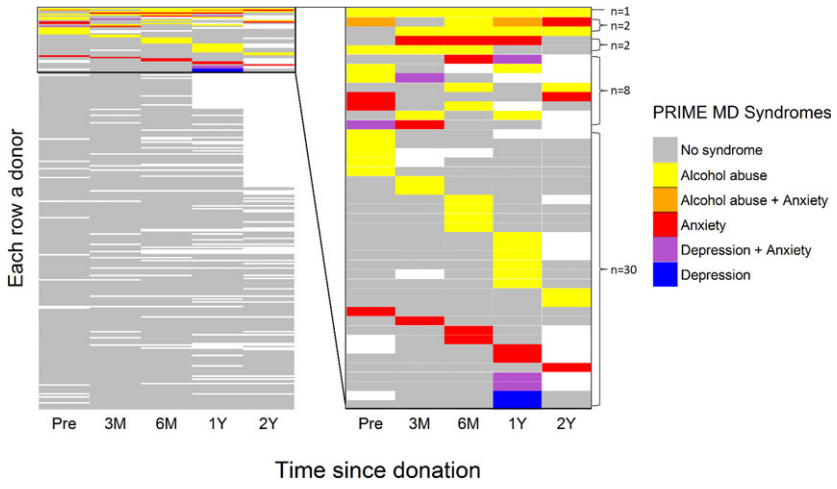

Figure 3: Donor-specific Primary Care Evaluation of Mental Disorders (PRIME-MD) syndromes by time point: predonation, 3 mo, 6 mo, 1 year, and 2 years. In the graph, each row represents a donor, and white boxes indicate missing surveys. The left side includes all donors (n = 271), and the right side shows only donors who had any syndrome at one time point or more (n = 43). M, months; Pre, before donation; Y, years.

earlier A2ALL cohort research (1) and other prospective studies (12) that have investigated rates of LLD psychiatric symptoms. Furthermore, our donors reported mental well-being that is consistent with or better than that of the general population and other LLD populations, on average (6,10,11,16). That said, a minority of patients describe impairment in this domain, even before donation (10).

Although it is generally good news that few donors experience these psychiatric syndromes or impaired mental well-being, the fact that alcohol abuse was endorsed at all among liver donors is worrisome. To explore a *post hoc* hypothesis, we examined whether PRIME-MD–measured alcohol abuse syndrome in donors was associated with recipient alcohol cirrhosis diagnosis—a "birds of a feather flock together" hypothesis—but found no association across all time points (p = 0.26). We are aware of no prior research that has looked at drinking behavior among LLDs. At the predonation survey, however, 4% of our sample endorsed alcohol abuse syndrome in the previous 6 mo. Some donors also endorsed

Table 3: Predictors of Simmons better person scale (0 = low, 10 = high) from repeated measures linear regression models (n = 245)

		95% CI		
	Regression coefficient	Lower	Upper	p-value
Postdonation time point				<.001
3 mo versus 2 years	0.58	0.30	0.86	<.001
6 mo versus 2 years	0.34	0.07	0.61	.01
1 year versus 2 years	0.12	−0.14	0.37	.36
Donor–recipient relationship				.054
First-degree relative versus unrelated	0.84	0.19	1.49	.012
Spouse/partner versus unrelated	−0.15	−1.49	1.19	.82
Other biological or nonbiological relative versus unrelated	0.46	−0.32	1.24	.25
Female versus male	−0.70	−1.21	−0.18	.008
Recipient death (time-dependent)	−1.24	−1.89	−0.59	<.001
Predonation predictors				
Ambivalence scale (0 = no ambivalence, 7 = ambivalence)	0.24	0.07	0.40	.005
If I donate, I will feel my life is more worthwhile (1 = very unlikely, 10 = very likely)	0.27	0.17	0.37	<.001
Average of motivations to donate (scale of 1–7 with higher score meaning stronger motivation)	0.61	0.31	0.91	<.001
History of other donation behavior	0.79	0.21	1.37	.008

Variables tested for inclusion but not significant: donor demographics (age at donation, race/ethnicity, education, marital status), clinical characteristics (length of hospital stay, whether donor was rehospitalized or had complication during the first month after donation), whether there were other possible donors for the transplant candidate, whether someone encouraged or discouraged the donor to donate, whether donor anticipated long-term health effects of donation, "black sheep" donor, how donor felt about life as a whole, predonation 36-item Short Form Health Survey mental and physical component summaries, and Patient Health Questionnaire 9 depression score. CI, confidence interval.

Table 4: Predictors of Posttraumatic Growth Inventory (0 = low, 50 = high) from repeated measures linear regression models (n = 192)

	Regression	95% CI		
Predictor	coefficient	Lower	Upper	p-value
Postdonation time point 1 versus 2 years	0.22	−1.57	2.02	.81
Age at donation (per 10-year increase)	−1.58	−2.98	−0.17	.03
If I donate, I will feel my life is more worthwhile (1 = very unlikely, 10 = very likely)	2.06	1.51	2.61	<.001
Anyone discouraged to donate	−3.56	−6.68	−0.45	.03

Variables tested for inclusion but not significant: donor demographics (sex, race/ethnicity, education, marital status), clinical characteristics (length of hospital stay, whether donor was rehospitalized or had complication during the first month after donation), donor–recipient relationship, recipient death, history of other donation behavior, whether there were other possible donors for the transplant candidate, ambivalence to donate, whether someone encouraged the donor to donate, whether donor anticipated long-term health effects of donation, "black sheep" donor, average of motivations to donate, how donor felt about life as a whole, 36-item Short Form Health Survey mental and physical component summaries, and Patient Health Questionnaire 9 depression score. CI, confidence interval.

symptoms of alcohol abuse syndrome at 3- and 6-mo postdonation surveys. Especially given the time frame for liver regeneration in donors, it would be prudent for LLDs to be monitored more closely for their alcohol use both before and after donation (37).

Donors whose recipients had died were more likely to report unwillingness to donate again compared with donors whose recipients did not die. Furthermore, a third of those donors whose recipients died felt guilty and 22% felt responsible at some point for the recipient's death. Our findings highlight that these donors may benefit from additional monitoring to ensure they receive adequate psychosocial support and treatment, if necessary (10,38,39).

Our study has several strengths, including the large multicenter prospective design and the use of standardized patient-reported outcomes to describe the sample over time. A recent review highlighted the need for exactly this type of prospective living donor outcomes study and stronger evidence-based psychosocial screening criteria (17). Consistent with prior research, we found that many donors experienced positive psychological outcomes as a result of their donation, including feelings of self-worth and personal growth. Although low levels of endorsement for many of the outcomes did not allow for statistical modeling, our observational findings are worth

highlighting in and of themselves. Future research of longer term psychological outcomes is warranted because some key psychological sequelae to donation may not become apparent until much later after the donation experience (15).

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Disclosure

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