

# UCSF

## UC San Francisco Previously Published Works

### Title

Fatigue, Pain, and Other Physical Symptoms of Living Liver Donors in the Adult-to-Adult Living Donor Liver Transplantation Cohort Study

### Permalink

<https://escholarship.org/uc/item/06g2d0s4>

### Journal

Liver Transplantation, 24(9)

### ISSN

1527-6465

### Authors

Butt, Zeeshan  
DiMartini, Andrea F  
Liu, Qian  
[et al.](#)

### Publication Date

2018-09-01

### DOI

10.1002/lt.25185

Peer reviewed



Published in final edited form as:

*Liver Transpl.* 2018 September ; 24(9): 1221–1232. doi:10.1002/lt.25185.

## Fatigue, Pain, and other Physical Symptoms of Living Liver Donors in the Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL-2)

Zeeshan Butt, PhD<sup>1</sup>, Andrea F. DiMartini, MD<sup>2</sup>, Qian Liu, MPH<sup>3</sup>, Mary Ann Simpson, PhD<sup>4</sup>, Abigail R. Smith, PhD, MS<sup>3,5</sup>, Jarcy Zee, PhD<sup>3</sup>, Brenda W. Gillespie, PhD<sup>5</sup>, Susan Holtzman, PhD<sup>6</sup>, Daniela Ladner, MD, MPH<sup>1</sup>, Kim Olthoff, MD<sup>7</sup>, Robert A. Fisher, MD<sup>8</sup>, Silvia Hafliger, MD<sup>9</sup>, Chris E. Freise, MD<sup>10</sup>, Mercedes Susan Mandell, MD<sup>11</sup>, Averell H. Sherker, MD<sup>12</sup>, and Mary Amanda Dew, PhD<sup>2</sup>

<sup>1</sup>Departments of Medical Social Sciences, Surgery, & Psychiatry and Behavioral Sciences Northwestern University, Chicago IL

<sup>2</sup>Departments of Psychiatry, Psychology, Epidemiology, Biostatistics, and Clinical and Translational Science, University of Pittsburgh, Pittsburgh PA

<sup>3</sup>Arbor Research Collaborative for Health, Ann Arbor, MI

<sup>4</sup>Department of Transplantation, Lahey Hospital and Medical Center, Burlington, MA

<sup>5</sup>Department of Biostatistics, University of Michigan, Ann Arbor, MI

<sup>6</sup>Department of Psychology, University of British Columbia, Kelowna, BC

<sup>7</sup>Department of Surgery, University of Pennsylvania, Philadelphia, PA

<sup>8</sup>Division of Transplantation, The Transplant Institute Beth Israel Deaconess Medical Center, Harvard University, Boston, MA

<sup>9</sup>Department of Psychiatry, Columbia University, New York, NY

<sup>10</sup>Departments of Medicine and Surgery, University of California at San Francisco, San Francisco, CA

<sup>11</sup>Department of Medicine, University of Colorado, Denver, Aurora, CO

<sup>12</sup>National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD

### Abstract

**Background**—Little is known about living liver donors' perceptions of their physical well-being following the procedure.

---

CORRESPONDING AUTHOR: Zeeshan Butt, PhD, Departments of Medical Social Sciences, Surgery, & Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, 633 N Saint Clair Street, 19<sup>th</sup> Floor, Chicago, Illinois 60611, 312-503-7708, office, z-butt@northwestern.edu.

### CONFLICTS of INTEREST

The authors of this manuscript have no conflicts of interest to disclose.

**Methods**—We collected data on donor fatigue, pain, and other relevant physical outcomes as part of the prospective, multi-center Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL-2) Consortium. A total of 271 (91%) of 297 eligible donors were interviewed at least once at pre-donation and 3, 6, 12, and 24 months after donation using validated measures, when available. Repeated measures regression models were used to identify potential predictors of worse physical outcomes.

**Results**—We found that donors reported more fatigue immediately after surgery that were returning to pre-donation levels by two years post-donation. A similar pattern was seen across a number of other physical outcomes. Abdominal or back pain and interference from their pain were rated relatively low on average at all study points. However, 21% of donors did report clinically significant pain at some point during post-donation study follow-up. Across multiple outcomes, female donors, donors whose recipients died, donors with longer hospital stays after surgery, and those whose families discouraged donation were at risk for worse physical well-being outcomes.

**Conclusions**—While not readily modifiable, we have identified risk factors that may help identify donors at risk for worse physical outcomes for targeted intervention.

### Keywords

Activities; Hepatectomy; Patient-reported outcomes; Quality of life; Worries

---

Liver transplantation is the only life-saving intervention for patients with end stage liver disease and certain patients with hepatocellular carcinoma. However, there is a shortage of available deceased donors for liver transplantation. One strategy to alleviate the shortage of liver grafts has been the introduction of living liver donor (LLD) transplantation. LLDs are typically healthy adults who do not derive any personal medical benefit from the procedure. Therefore, in order to justify exposing LLDs to such an operation, it is imperative to understand not only the clinical outcomes of the surgery, but the physical impact of donation from the donor's perspective.

The potential mortality and morbidity risks of LLD transplantation have been described. (1,2) Donor death is the most serious complication for LLD, with estimated mortality less than 0.5%. (3) Short-term post-operative complications after LLD transplantation have also been well characterized, with Abecassis and colleagues (2) reporting a 39% overall morbidity among right lobe donors, and 2.8% of patients experiencing Clavien grade 3 (i.e. resulting in residual or lasting functional disability) or 4 (i.e. leading to transplant or death) complications, while the remaining reported more minor, grade 1 and 2 complications. Median follow-up period ranged from 1.8 to 3.4 years post-donation, depending on the cohort. (2) Notably, nearly four-fifths of these complications resolved within three months of presentation. Patient perceptions of their physical well-being are also important outcomes of LLD but can be difficult to quantify. (4) In particular, the impact of donation on LLD fatigue, pain, and other physical outcomes is not well understood beyond the first year after donation. (5,6)

The majority of research to date has employed single-center, cross-sectional designs to characterize donor symptoms during the first year after donation. Before donation, LLD

physical well-being is often equal to or significantly higher than normative adult populations.(7,8) Not surprisingly, donors experience the most impact on their physical well-being within the first three months of donation and report returning to near normal levels by one year post-donation.(5) According to Hsu et al,(9) in their sample of donors with median post-surgery follow-up of 25.9 months, the most common physical complaints in donors included throbbing, itching and/or numbness around the surgical site, followed by reduced general physical vigor, sleep disturbance, and slowed reaction ability. The most prominent symptoms within one month of donation in one LLD cohort included bloating and loss of muscle tone.(7) In another cohort, in the 6 to 12 months after donation, the most common complaints were a change in body image, increased tiredness, and fatigue.(8, 10) Few studies have described the timeline of symptom resolution in this population. Additionally, most longitudinal studies follow donors only up to one year, leaving questions regarding the longer-term impact of donation on physical well-being.

To improve our explanation of the risks of surgery to LLDs, we must have better information about the incidence and time course of donors' fatigue, pain, and other relevant physical outcomes. We have previously reported the perceived psychological, social, and economic outcomes in LLDs.(11, 12) The purpose of the present longitudinal study was to evaluate LLD perception of their physical outcomes and potential predictors of these outcomes in a prospective, multi-center observational study.

## **MATERIALS and METHODS**

### **Study design**

The A2ALL-2 consortium consists of nine North American transplant centers with data collected on potential LLDs and their recipients. These centers started study enrollment on a staggered basis from February to July 2011 and ended enrollment on January 31, 2014. As our study was observational, screening protocols or other practices were not standardized across centers. However, all centers followed the medical and psychosocial evaluation and exclusion criteria for selecting LLD that are now included in the current US national policy. (13) Data for this analysis were obtained from eligible LLDs prospectively enrolled in the A2ALL-2 study. Potential donors were considered eligible for the present study if they were English speaking, were scheduled to donate during the study enrollment period, and were approached for participation on or before their scheduled donation date. The study was approved by the institutional review boards/research ethics board and privacy boards of the University of Michigan Data Coordinating Center and each of the nine participating transplant centers.

### **Procedure**

Potential LLDs were approached by transplant center study coordinators to obtain informed consent. Trained survey center interviewers then contacted consented participants within one month prior to donation and at 3, 6, 12, and 24 months post-donation. Donors who didn't reach a post-donation interview time point by the end of the study on July 15, 2014 were administratively censored (n=29 at 1 year plus another 66 at 2 years after donation). Each interview took approximately 45 minutes to complete and was facilitated by use of a

computer-assisted telephone interview to streamline data recording and storage. Participants were compensated with \$20 (USD) for each completed interview. Site and study-wide quality assurance and retraining was implemented for the duration of the study. Clinical information, including donor hospitalizations and complications was collected prospectively within A2ALL-2.

## Measures

### Primary Physical Outcomes

**FACIT-Fatigue scale:** The Functional Assessment of Chronic Illness Therapy – Fatigue subscale (FACIT-F) is a 13-item scale that asks respondents to rate statements regarding their fatigue experience and its impact on their daily lives. Using conventional scoring, the FACIT-F subscale ranges from 0 to 52 with lower scores indicating greater levels of fatigue. Originally developed for use with cancer patients,(14,15) the scale has been successfully tested for use in the general population and other chronic illness populations.(16,17) In the current study, we converted FACIT-F scores to Patient-Reported Outcomes Measurement Information System (PROMIS) T-scores (M=50; SD=10) for modeling to reduce skewness of the score distribution and defined clinically significant fatigue as >0.5 SD above the normative mean.(18,19) This allows for comparison to future studies using PROMIS and the PROMIS general population norms.(18) The converted fatigue scale has a possible range of 30.3 to 83.5 with higher scores indicating greater levels of fatigue.

**Brief Pain Inventory, pain intensity, and interference:** The Brief Pain Inventory (BPI) is a self-reported instrument that assesses the severity of pain and its impact on daily functions. It has been validated in patients with cancer and other chronic illnesses.(20) Donors provided a single-item rating for the level of abdominal or back pain they experienced at the time of assessment, ranging from 0=no pain to 10=pain “as bad as you can imagine.” Pain interference was summarized by the mean of the seven interference items that range from 0 to 10. Patients who reported no pain were assigned 0 on pain interference.

**Number of current physical symptoms attributed to donation:** Donors were asked to identify how many physical symptoms they experienced in the past month that could be attributed to the donation. Specifically, donors were asked about 10 possible clinical signs and symptoms, including bleeding, pain, itching, tension, numbness, and infection at surgical site. They were also asked about abdominal pain, low back pain, abdominal bloating/swelling, and decreased stomach tone. A count was used to quantify these symptoms, ranging from 0–10.

**SF-36 PCS:** The Short Form-36, version 2 (SF-36) is one of the most widely used general measures of health status. The 36-item instrument can be summarized by two aggregated scores – the physical component summary (PCS) and mental component summary (MCS) – which explain 80–85% of the score variance.(21,22) Scores are standardized to a general population (mean=50, standard deviation=10). Higher scores indicate better health-related quality of life. Our focus for the present study was PCS scores.

**Secondary Physical Outcomes**—A number of secondary physical outcomes were explored by donor report, including: the number of post-donation health-related worries endorsed (four items including worries about physical effects of donation, current health, future health, and never feeling 100% well again; Cronbach's alpha 0.75, suggesting adequate internal consistency reliability), ability to do physical activities as well since donation, whether the donor is back to normal physically, whether recovery was slower than expected (vs. as expected or faster than expected), any current donation-related medical problems, a rating of how physically stressful the donation was, and any overall negative feelings about donation (vs. neutral or positive feelings).

**Potential Predictors of Physical Outcomes**—Potential predictors of physical outcomes included pre-donation survey items to assess donor experiences during the pre-donation process.(23) These instruments included psychosocial background, represented by donation history, donation decision-making items including whether there were other possible donors for the candidate, ambivalence to donate (a seven-item scale with Cronbach's alpha 0.57 in the present sample), whether someone encouraged or discouraged the donation, anticipated long-term health effects of donation, feeling life would be more worthwhile, and if the donor felt like a "black sheep" (i.e. experienced any family disapproval for their decision). Simmons' 11 items pertaining to motivations to donate were averaged to summarize the strength of motivation to donate (Cronbach's alpha=0.77). The scale ranged from 1 (weak motivation to donate) to 7 (strong motivation to donate). Other potential predictors included the Campbell global life satisfaction item, which captures how donors feel about life as a whole,(24) the MCS and PCS scores from the SF-36, and the Patient Health Questionnaire-9 (PHQ-9) depression score (Cronbach's alpha = 0.73).

Additional potential predictors included donor demographics (age, sex, race/ethnicity, education, marital status, and household income pre-donation), clinical characteristics (pre-donation body mass index [BMI], length of donation hospital stay, post-donation hospitalizations within the first month, and post-operative complications within the first month), donor relation to the recipient (1<sup>st</sup> degree relative, spouse/partner, other biological or non-biological relative, or unrelated), and whether the donor learned of recipient death prior to a given survey time point.

Surgical variables including the lobe donated and laparoscopic versus open surgery were also examined. However, they were only analyzed descriptively and were not considered as potential covariates in the modeling. In part, this was due to a lack of within center variability on these variables. To help address this, center was included as a predictor in sensitivity analysis models.

### Statistical Analysis

Comparisons of demographic characteristics between respondents and non-respondents have been previously published.(11,12) Non-respondents included potential donors who did not consent to the study and actual donors who were not interviewed.

Descriptive statistics were used to describe physical outcomes at each assessment time point. We calculated means and standard deviations for continuous variables and percentages for

dichotomous variables. For continuous outcomes, we compared three month post-donation vs. pre-donation and two year post-donation vs. pre-donation using paired t-test and adjusted for multiple comparisons using the Bonferroni correction. For dichotomous outcomes, we also estimated endorsement cumulatively by calculating the percentage who endorsed the outcome at any time post-donation.

To investigate changes in physical outcomes following donation and to identify predictors of physical outcomes, repeated measures linear, logistic, or negative binomial regressions were fit among donors who completed a pre-donation survey and at least one post-donation survey. Outcomes endorsed by less than 10% of donors at every time point were not modeled to avoid limited generalizability with sparse outcomes. For each of the models above, generalized estimating equations models with sandwich standard error estimators were used to characterize the correlation among the repeated measures. Post-donation time point was included as a categorical variable (three months, six months, one year, and two years post-donation) and was retained in all regression models to show the outcome trajectories over time, even if it was not statistically significant. Variable selection was guided by the method of best subsets adjusting for time point.<sup>(25)</sup> Predictors were retained in models if p-values were less than 0.05. Categorical predictors were retained if overall tests (over all levels) were less than 0.05, or if Bonferroni-corrected pairwise tests against the reference category were significant. Model assumptions, e.g. functional forms for continuous covariates and residual distributions, were checked and were met in all models.

For descriptive analyses assessing the prevalence of physical outcomes, as a sensitivity analysis, we also performed the analyses only among subjects who completed all interviews to evaluate whether missed or refused surveys had any impact on the results. For modeling, we conducted sensitivity analyses to examine whether center was associated with outcomes by evaluating the overall p-values of center in the final models. We also assessed whether controlling for centers in the final models changed the effects of other predictors.

All analyses were performed using SAS version 9.4 (SAS Institute, Inc, Cary, NC).

## RESULTS

Study attrition as well as the demographics and clinical characteristics of respondents and non-respondents have been published previously.<sup>(11,12)</sup> In brief, out of 297 eligible donors, 271 (91.2%) were interviewed at least once during study follow-up; 19 did not consent; and 7 consented but were not interviewed due to administrative errors or refusals. Among those interviewed, 253, 250, 241, 201 and 139 were interviewed at pre-donation, 3, 6, 12, and 24 months after donation, respectively, making a total of 245 interviewed both before and after donation, 8 interviewed only before donation, and 18 interviewed only after donation.

The 271 donors who were interviewed were mostly female (57%), white (80%), married (63%), and employed full time (61%). Slightly more than half donated to a first-degree relative (53%). The majority (84%) of donors had right lobe hepatectomies and 35% had laparoscopic surgery. During the first month post-donation, 19% had one or more post-operative complications and 8% had one or more hospitalizations. During the study follow

up, 27 (10%) donors reported recipient death. Respondents were similar to the 26 donors who did not consent or were not interviewed on sex, age, and race-ethnicity. Comparisons on clinical variables including recipient death were not possible since we did not have information on those variables for non-respondents.

### Physical Outcome Characteristics

Table 1 shows the outcome characteristics by pre- and post-donation time points. The average FACIT-fatigue (conventional) score ranged from 43.3 to 47.9 over the follow-up period, with 2% to 15% reporting impaired levels of fatigue (defined as 0.5 SD, or 5 points, above the PROMIS normative mean). The average level of abdominal or back pain was low at all study time points, and donors reported minimal interference as measured by the BPI-pain interference scale. Although the mean level of abdominal or back pain was low, 4% to 13% of donors reported moderate to severe pain (defined as 4 or higher on pain scale from 0 to 10) at some point during the study. Across all the post-donation time points, the average number of physical symptoms attributed to donation ranged from 2.3 to 4.6. In addition, the average PCS ranged from 48.2 to 56.2, with 3% to 29% of donors reporting impaired PCS (defined as 0.5 SD below the United States normative mean).

With respect to the trajectories of these primary physical outcomes over time, FACIT-F, level of abdominal or back pain, pain interference, and PCS showed increased impairment from pre-donation to three months post-donation (all significant based on paired t-tests). These physical quality of life measures improved from six months to two years post-donation but still did not reach pre-donation levels by two years post-donation (only statistically significant for pain, based on paired t-tests) (Table 1). These trends were confirmed for FACIT-F and level of abdominal or back pain in adjusted model results, which showed statistically significant differences across time and highest levels of adverse outcomes at three months post-donation (Table 2). The number of physical symptoms decreased over time from three months to two years post-donation ( $p < 0.001$ ).

The proportions of donors who reported they were unable to do some physical activities as well since donation, were still not feeling physically back to normal, and recovered more slowly than expected, all decreased from three months to two years post-donation (Table 1). In adjusted models, these outcomes had statistically significant differences across time points and were worst at three months post-donation (Table 3). Donors reported an average of 0.68 to 0.98 health-related worries (range from 0 to 4), and the average number of health-related worries also showed a decreasing trend. In contrast, the proportion of donors reporting current donation-related medical problems (20% or higher across time points) and that the donation was physically stressful (43% or higher across time points) remained relatively constant over time ( $p > 0.05$  in adjusted models). Finally, only a small minority of donors (1% to 4%) reported overall negative feelings about donation.

We also investigated whether donors with worse outcomes in one physical domain also reported worse symptoms other domains by reviewing the correlation among outcomes at 3-months and 2-years post-donation (see Supplemental Table 2). At 3-months post-donation, the largest correlation between outcomes was between pain, as measured by the Brief Pain Inventory, and level of abdominal/back pain ( $r = 0.71$ ), with other intercorrelations more



modest. A similar pattern was found at two years post-donation ( $r=0.68$ ). Results from sensitivity analyses among donors who completed all five surveys ( $n=118$ ) showed similar results. Outcomes data for the donors who completed all surveys are included in Supplemental Table 1.

### Predictors of physical outcomes

Donors who were female, who were married or had a long-term partner at pre-donation, who were hospitalized longer during the donation surgery, and whose recipient had died reported more fatigue. Pre-donation fatigue, history of family disapproval (black sheep donor), and anticipation that life would be more worthwhile after donation were also associated with more fatigue (Table 2).

Female gender, recipient death prior to survey administration, post-operative complications in the first month post-donation, and higher level of abdominal/back pain pre-donation were associated with higher levels of post-donation pain. In contrast, better pre-donation MCS and PCS (higher scores), and higher household income were associated with lower post-donation pain (Table 2).

Significant predictor of physical symptoms attributed to donation included recipient death, female gender, and longer hospital stay for donation surgery, while better pre-donation MCS and PCS were associated with fewer symptoms (Table 2). Donors discouraged to donate also had more physical symptoms attributed to donation on average.

Table 3 shows model results for secondary physical outcomes. Longer hospital stay for donation surgery was significantly associated with all secondary outcomes except for current donation-related medical problems. Donors with BMI 25.0 to 29.9 compared to those with BMI  $\leq 24.9$ , and donors who were “black sheep” were more likely to report being unable to do some physical activities as well since donation. Donors whose recipients died were more likely to report being not physically back to normal, while donors with better MCS pre-donation were less likely to report this outcome. Additionally, female gender and higher household income were associated with higher odds of recovering slower than expected.

Predictors of other secondary outcomes including donation-related medical problems, number of health-related worries, and if donation was physically stressful are presented in Table 3.

Model results for both primary and secondary outcomes were unchanged when adjusting for transplant center, and the center effect was only significant in predicting one outcome - number of physical symptoms after donation (overall  $p$ -value=0.04). For this outcome, comparing all other centers to the one with the largest number of donors ( $n=90$ ), the differences in mean number of physical symptoms ranged from  $-0.60$  to  $0.74$ .

## DISCUSSION

We conducted a multi-center, prospective study of LLD clinical and perceived well-being to evaluate their perceptions of their physical outcomes and to determine predictors of key outcomes, such as fatigue, pain, and other unique physical symptoms over time. In our

cohort, donors reported worsening fatigue immediately after surgery that approached pre-donation levels (2% impaired) by two years post-donation, with 4% to 15% of our cohort reporting impaired levels of fatigue after surgery. We observed a similar pattern using a broad measure of donor-reported physical well-being and more pointed questions about ability to perform physical activities, feeling physically back to normal, and recovering more slowly than expected. These findings support and extend findings from previous reviews of donor physical symptoms and well-being.(5,6) While in some respect, these findings may seem intuitive or predictable, ours is one of the largest cohorts of living liver donors to actually substantiate this clinical wisdom with data from a large, multisite cohort, using prospective assessments. Our findings suggest actionable steps that may benefit future LLD outcomes.

We found relatively few donation-related health worries and quite low levels of negative feelings about donation. Abdominal or back pain was also rated relatively low, on average, at all study time points and donors reported low levels of interference, as measured by the BPI. Indeed, we have found that living donors who are further out from their donation – 3–10 years post-donation – experience clinically significant pain at levels similar to the general population.(26) While these data are useful and reassuring for donor education, a sizable minority – up to 21% of donors – reported clinically significant pain at some point. These findings suggest somewhat lower pain in our cohort compared to other single center reports on donor pain.(27) Nonetheless, our prior work in this area (28) suggests that there may still be benefit to adjusting pain control strategies to be more aligned with expert analgesic recommendations for postoperative pain. Identification and optimization of pain control earlier after donation may improve long-term pain outcomes for LLD. Regarding other physical outcomes, it is worrisome that by one year following donation, 20% or more of donors still reported being unable to do some physical activities as well since donation, were recovering slower than expected, or felt they had donation-related medical problems. Interventions to improve these outcomes may be considered, but at the least, better pre-donation education about recovery is needed.

We modeled potential predictors of our primary and secondary outcomes to help identify donors who may be at risk for poor perceptions of their donor experience. Notably, some factors, like incision type, showed lack of variability within center and were not included as covariates in modeling. However, our sensitivity analyses showed that outcomes were similar across centers and a previous report with a shorter follow up found that pain perceptions were not impacted by laparoscopic vs open incision. (28) We identified some risk factors that cut across multiple outcomes, including female donors, those whose recipients died, donors with longer surgery hospital stays, and those whose families discouraged donation. While these risk factors may not be easily modifiable, they do help to identify donors that may warrant more prophylactic care to help ensure optimal symptom management. Donors' health-related quality of life, as measured by the MCS and PCS summaries of the SF-36 also predicted many donor physical outcomes. This may be because both general and donation-specific outcomes were assessed by the same method (i.e. self-report); however, our findings confirm associations found in smaller sample studies and in studies looking at the association of quality of life with donor medical comorbidities.(6)

We recognize that our study has several important limitations. First, we only studied adult-to-adult LLDs from the United States and Canada. It would not be appropriate to generalize our findings to adult-to-child donors or to other geographical areas. Second, given our naturalistic, non-randomized design, we cannot be certain that factors we identify as risks for specific outcomes were in fact causative factors. For example, we found that higher household income is associated with lower post-donation pain, but also with slower recovery. It is possible that donors with higher incomes may have work that requires less physical exertion and at the same time may have higher expectations regarding their recoveries. However, strong inference of these individual findings warrants replication. We were also not able to model all physical symptoms assessed because of low levels of endorsement and data skewness, which may be in part due to only having two-year data for half of our enrolled donors. However, this amount of missing data was likely at random, as most were administratively censored due to donors not reaching this time point by study completion. While we did look at the impact of recipient death on donor pain, fatigue, and other physical outcomes, we did not assess the degree to which other non-fatal recipient outcomes, such as graft rejection or alcohol recidivism, impacted donor symptoms. Finally, while we have previously described the analgesic and other medication use in a short-term follow up report, we did not collect comprehensive medication use for this entire donor sample. (28) While we assessed or recorded many potential covariates, some variability in outcomes may be related to unmeasured factors. That said, our study has several strengths, including the large, multi-center, prospective design and the use of standardized patient-reported outcomes to describe the sample over time.

While our data do provide reassurances for LLD candidates, their families, and their health care providers about post-donation fatigue, pain, and other patient-centered physical outcomes, it also highlights the potential for targeted, long-term follow-up of donors to help optimize these outcomes. While it may not be the case that all LLD and their families require long-term follow-up and education, our data suggest that we can identify donors at-risk for physical symptoms that may benefit from more active surveillance and intervention. Some of this targeted follow-up may be symptom-specific,(28) but there may also be promise in addressing pre-donation factors that may influence patients' post-donation physical symptoms.(29) There may also be value in adapting symptom control interventions used in other populations for use among living liver donors.(30–32)

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

### FUNDING

This study was supported by the National Institute of Diabetes & Digestive & Kidney Diseases through cooperative agreements (grants U01-DK62444, U01-DK62467, U01-DK62483, U01-DK62484, U01-DK62494, U01-DK62496, U01-DK62498, U01-DK62505, U01-DK62531, U01-DK62536, U01-DK85515, U01-DK85563, and U01-DK85587). Additional support was provided by Health Resources and Services Administration (HRSA), and the American Society of Transplant Surgeons (ASTS).

This study was presented in part at the annual meeting of the American Transplant Congress, Boston, MA, June 15, 2016.

This is publication number #41 of the Adult-to-Adult Living Donor Liver Transplantation Cohort Study.

The following individuals were instrumental in the planning and conduct of this study at each of the participating institutions:

Columbia University Medical Center, New York, NY (DK62483): PI: Jean C. Emond, MD; Co-Is: Robert S. Brown, Jr., MD, MPH, James Guarrera, MD, FACS, Martin R. Prince, MD, PhD, Benjamin Samstein, MD, Elizabeth Verna, MD, MS; Study Coordinators: Taruna Chawla, MD, Scott Heese, MPH, Connie Kim, BS, Theresa Lukose, PharmD, Tarek Mansour, MB BCH, Joseph Pisa, BA, Rudina Odeh-Ramadan, PharmD, Jonah Zaretsky, BS.

Lahey Hospital & Medical Center, Burlington, MA (DK85515): PI: Elizabeth A. Pomfret, MD, PhD, FACS; Co-Is: Christiane Ferran, MD, PhD, Fredric Gordon, MD, James J. Pomposelli, MD, PhD, FACS, Mary Ann Simpson, PhD; Study Coordinators: Erick Marangos, Agnes Trabucco, BS, MTASCP.

Northwestern University, Chicago, IL (DK62467): PI: Michael M.I. Abecassis, MD, MBA; Co-Is: Talia B. Baker, MD, Zeeshan Butt, PhD, Laura M. Kulik, MD, Daniela P. Ladner, MD, Donna M. Woods, PhD; Study Coordinator: Patrice Al-Saden, RN, CCRC, Tija Berzins, Amna Daud, MD, MPH, Elizabeth Rauch, BS, Teri Strenski, PhD, Jessica Thurk, BA, MA, Erin Wymore, BA, MS, CHES.

University of California Los Angeles, Los Angeles, CA (DK62496): PI: Johnny C. Hong, MD; Co-I: Ronald W. Busutil, MD, PhD; Study Coordinator: Janet Mooney, RN, BSN.

University of California San Francisco, San Francisco, CA (DK62444): PI: Chris E. Freise, MD, FACS; Co-I: Norah A. Terrault, MD, MPH; Study Coordinators: Alexandra Birch, BS, Dulce MacLeod, RN.

University of Colorado, Aurora, CO (DK62536): PI: James R. Burton, Jr., MD; Co-Is: Gregory T. Everson, MD, FACP, Igal Kam, MD, James Trotter, MD, Michael A. Zimmerman, MD; Study Coordinators: Jessica Fontenot, BS, Carlos Garcia, RN, BS, Anastasia Krajec, RN.

University of Michigan Health System, Ann Arbor, MI (DK62498): PI: Robert M. Merion, MD, FACS; DCC Staff: Yevgeniya Abramovich, BA, Mary Akagi, MS, CCRP, Douglas R. Armstrong, BSN, MS, Charlotte A. Beil, MPH, Carl L. Berg, MD, Abby Brithinee, BA, Tania C. Ghani, MS, MSI, Brenda W. Gillespie, PhD, Beth Golden, BScN, Margaret Hill-Callahan, BS, LSW, Lisa Holloway, BS, CCRC, Terese A. Howell, BS, CCRC, Anna S.F. Lok, MD, Monique Lowe, MSI, Anna Nattie, BA, Akinlolu O. Ojo, MD, PhD, Samia Shaw, AAIT, Abigail Smith, MS, Robert A. Wolfe, PhD, Gary Xia, BA.

University of North Carolina, Chapel Hill, NC (DK62505): PI: Paul H. Hayashi, MD, MPH; Study Coordinator: Tracy Russell, MA.

University of Pennsylvania, Philadelphia, PA (DK62494): PI: Abraham Shaked, MD, PhD, Kim Olthoff MD; Co-Is: David S. Goldberg, MD, Karen L. Krok, MD, K. Rajender Reddy, MD, Mark A. Rosen, MD, PhD, Robert M. Weinrieb, MD; Study Coordinators: Brian Conboy, PA, MBA, Mary Kaminski, PA-C, Debra McCorrison, RN, Mary Shaw, RN, BBA.

University of Pittsburgh Medical Center, Pittsburgh, PA (DK85587): PI: Abhinav Humar, MD; Co-Is: Andrea F. DiMartini, MD, Mary Amanda Dew, PhD, Mark Sturdevant, MD; Study Coordinators: Megan Basch, RN, Sheila Fedorek, RN, CCRC, Leslie Mitrik, BS, Mary L. McNulty, MLS.

University of Toronto, Toronto, ON, CA (DK85563): PI: David Grant, MD, FRCSC; Co-Is: Oyedele Adeyi, MD, FCAP, FRCPC, Susan Abbey, MD, FRCPC, Hance Clarke, MSc, MD, FRCPC, Susan Holtzman, PhD, Joel Katz, CRC, PhD, Gary Levy, BSc, FRCPC, MD, Nazia Selzner, MD, PhD; Study Coordinators: Kimberly Castellano, BSc, Andrea Morillo, BM, BCh, Erin Winter, BSc.

University of Virginia, Charlottesville, VA (DK62484): PI: Carl L. Berg, MD; Co-I: Timothy L. Pruett, MD; Study Coordinator: Jaye Davis, RN.

Virginia Commonwealth University - Medical College of Virginia Campus, Richmond, VA (DK62531): PIs: Adrian H. Cotterell, MD, FACS, Robert A. Fisher, MD, FACS; Co-Is: Martha K. Behnke, PhD, Adrian H. Cotterell, MD, FACS, Ann S. Fulcher, MD, Pamela M. Kimball, PhD, HCLD, Mary E. Olbrisch, PhD, ABPP, Marc P. Posner, MD, FACS, Mark A. Reimers, PhD, Amit Sharma, MD, R. Todd Stravitz, MD, FACP; Study Coordinators: April Ashworth, RN, BSN, Joanne Davis, RN, Sarah Hubbard, Andrea Lassiter, BS, Luke Wolfe, MS.

National Institute of Diabetes and Digestive and Kidney Diseases, Division of Digestive Diseases and Nutrition, Bethesda, MD: Edward Doo, MD, James E. Everhart, MD, MPH, Jay H. Hoofnagle, MD, Stephen James, MD, Patricia R. Robuck, PhD, Leonard B. Seeff, MD, Averell H. Sherker, MD, FRCPC, Rebecca J. Torrance, RN, MS.

## ABBREVIATIONS

<b>A2ALL-2</b>	Adult-to-Adult Living Donor Liver Transplantation Cohort Study
<b>BMI</b>	body mass index
<b>BPI</b>	Brief Pain Inventory
<b>FACIT-F</b>	Functional Assessment of Chronic Illness Therapy – Fatigue subscale
<b>LLD</b>	living liver donor
<b>MCS</b>	mental component summary
<b>PHQ-9</b>	Patient Health Questionnaire-9
<b>PROMIS</b>	Patient-Reported Outcomes Measurement Information System
<b>PCS</b>	physical component summary
<b>SF-36</b>	Short Form-36

## References

- Miyagi S, Kawagishi N, Fujimori K, et al. Risks of donation and quality of donors' life after living donor liver transplantation. *Transpl Int.* 2005; 18:47–51. [PubMed: 15612983]
- Abecassis MM, Fisher RA, Olthoff KM, et al. Complications of living donor hepatic lobectomy--a comprehensive report. *Am J Transplant.* 2012; 12:1208–17. [PubMed: 22335782]
- Quintini C, Hashimoto K, Diago T, Miller C. Is there an advantage of living over deceased donation in liver transplantation? *Transplant Int.* 2013; 26:11–19.
- Butt Z, Parikh ND, Skaro AI, Ladner D, Cella D. Quality of life, risk assessment, and safety research in liver transplantation: new frontiers in health services and outcomes research. *Curr Opin Organ Transplant.* 2012; 17:241–7. [PubMed: 22476225]
- Parikh ND, Ladner D, Abecassis M, Butt Z. Quality of life for donors after living donor liver transplantation: a review of the literature. *Liver Transpl.* 2010; 16:1352–8. [PubMed: 21117194]
- Dew MA, Butt Z, Humar A, DiMartini AF. Long-term medical and psychosocial outcomes in living liver donors. *Am J Transplant.* 2017; 17:88–892.
- Verbesey JE, Simpson MA, Pomposelli JJ, et al. Living donor adult liver transplantation: a longitudinal study of the donor's quality of life. *Am J Transplant.* 2005; 5:2770–7. [PubMed: 16212639]
- Chan SC, Liu CL, Lo CM, Lam BK, Lee EW, Fan ST. Donor quality of life before and after adult-to-adult right liver live donor liver transplantation. *Liver Transpl.* 2006; 12:1529–36. [PubMed: 17004265]
- Hsu HT, Hwang SL, Lee PH, Chen SC. Impact of liver donation on quality of life and physical and psychological distress. *Transplant Proc.* 2006; 38:2102–5. [PubMed: 16980013]
- Walter M, Bronner E, Pascher A, et al. Psychosocial outcome of living donors after living donor liver transplantation: a pilot study. *Clin Transplant.* 2002; 16:339–44. [PubMed: 12225430]
- DiMartini A, Dew MA, Liu Q, et al. Social and financial outcomes of living liver donation: A prospective investigation within the Adult-to-Adult Living Donor Liver Transplantation Cohort Study 2 (A2ALL-2). *Am J Transplant.* 2017; 17:1081–1096. [PubMed: 27647626]
- Butt Z, Dew MA, Liu Q, et al. Psychological outcomes of living liver donors from a multicenter prospective study: Results from the Adult-to-Adult Living Donor Liver Transplantation Cohort Study-2 (A2ALL-2). *Am J Transplant.* 2017; 17:1267–1277. [PubMed: 27865040]

13. Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS). [Last accessed 2/9/16] OPTN Policies, Policy 14: Living donation. Updated 12/1/15. <http://optn.transplant.hrsa.gov/governance/policies/>
14. Yellen SB, Cella DF, Webster K, Blendowski C, Kaplan E. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. *J Pain Symptom Manage.* 1997; 13:63–74. [PubMed: 9095563]
15. Cella D. The Functional Assessment of Cancer Therapy-Anemia (FACT-An) Scale: a new tool for the assessment of outcomes in cancer anemia and fatigue. *Semin Hematol.* 1997; 34(3 Suppl 2): 13–9.
16. Butt Z, Lai JS, Rao D, Heinemann AW, Bill A, Cella D. Measurement of fatigue in cancer, stroke, and HIV using the Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) scale. *J Psychosom Res.* 2013; 74:64–8. [PubMed: 23272990]
17. Cella D, Eton DT, Lai JS, Peterman AH, Merkel DE. Combining anchor and distribution-based methods to derive minimal clinically important differences on the Functional Assessment of Cancer Therapy (FACT) anemia and fatigue scales. *J Pain Symptom Manage.* 2002; 24:547–61. [PubMed: 12551804]
18. Lai JS, Cella D, Yanez B, Stone A. Linking fatigue measures on a common reporting metric. *J Pain Symptom Manage.* 2014; 48:639–48. [PubMed: 24698661]
19. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: The remarkable universality of half a standard deviation. *Med Care.* 2003; 41:582–592. [PubMed: 12719681]
20. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singapore.* 1994; 23:129–38. [PubMed: 8080219]
21. Jay CL, Butt Z, Ladner DP, Skaro AI, Abecassis MM. A review of quality of life instruments used in liver transplantation. *J Hepatol.* 2009; 51:949–59. [PubMed: 19775771]
22. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992; 30:473–83. [PubMed: 1593914]
23. Simmons R, Simmons R, Marine S. Gift of life: The effect of organ transplantation on individual, family, and societal dynamics. New Brunswick, NJ: Transaction Books; 1987.
24. Campbell A, Converse P, Rodgers N. *The Quality of American Life: Perceptions, Evaluations, and Satisfaction.* New York: Russell Sage Foundation; 1976.
25. Harrell FE. *Springer Series in Statistics.* New York, NY: Springer; 2001. Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis.
26. Dew MA, Butt Z, Liu Q, Simpson MA, et al. Prevalence and Predictors of Patient-Reported Long-Term Mental and Physical Health After Donation in the Adult to Adult Living Donor Liver Transplantation Cohort Study (A2ALL). *Transplantation.* 2018; 102:105–118. [PubMed: 28885494]
27. Holtzman S, Clarke HA, McClusky SA, Turcotte K, Grant D, Katz J. Acute and chronic postsurgical pain after living liver donation: incidence and predictors. *Liver Transpl.* 2014; 20:1336–46. [PubMed: 25045167]
28. Mandell MS, Smith AR, Dew MA, et al. Early postoperative pain and its predictors in the Adult to Adult Living Donor Liver Transplantation Cohort Study. *Transplantation.* 2016; 100:2362–2371. [PubMed: 27517726]
29. Dew MA, DiMartini AF, Devito Dabbs AJ, et al. Preventive intervention for living donor psychosocial outcomes: feasibility and efficacy in a randomized controlled trial. *Am J Transplant.* 2013; 13:2672–2684. [PubMed: 23924065]
30. Owen JE, O’Carroll Bantum E, Pagano IS, Stanton A. Randomized Trial of a Social Networking Intervention for Cancer-Related Distress. *Ann Behav Med.* 2017; 51:661–672. [PubMed: 28244002]
31. Rolving N, Nielsen CV, Christensen FB, Holm R, Bünger CE, Oestergaard LG. Does a preoperative cognitive-behavioral intervention affect disability, pain, behavior, pain, and return to work the first year after lumbar spinal fusion surgery? *Spine (Phila Pa 1976).* 2015; 40:593–600. [PubMed: 25705964]

32. Hoffman AJ, Brintnall RA, Given BA, von Eye A, Jones LW, Brown JK. Using Perceived Self-efficacy to Improve Fatigue and Fatigability In Postsurgical Lung Cancer Patients: A Pilot Randomized Controlled Trial. *Cancer Nurs.* 2017; 40:1–12. [PubMed: 27135752]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1

## Physical Outcome Characteristics over Time.

Outcome	Pre-donation (n=253) % (n) or Mean (SD)	3 Months Post- donation (n=250) % (n) or Mean (SD)	6 Months Post- donation (n=241) % (n) or Mean (SD)	1 Year Post-donation (n=201) % (n) or Mean (SD)	2 Years Post- donation (n=139) % (n) or Mean (SD)	Cumulative results (endorsement at any post-donation time point) (n=263) % (n) *
<b>Primary outcomes</b>						
FACIT Fatigue <sup>a</sup>						
Raw scores (0=high, 52=low)	47.95 (4.20)	43.31 (7.57)	45.40 (7.41)	45.82 (7.83)	46.88 (5.96)	-
PROMIS T-scores (30.3=low fatigue to 83.5=high fatigue, normative mean=50, SD=10)	40.25 (6.37)	45.83 (7.90)	43.00 (8.33)	42.49 (8.33)	41.26 (7.49)	-
Clinically significant fatigue (>0.5 SD, >5 points above the PROMIS normative mean)	2.0% (5)	14.8% (37)	8.8% (21)	7.5% (15)	4.3% (6)	20.5% (54)
Level of abdominal or back pain <sup>b</sup>						
Raw scores (0=no pain, 10 = worst pain imaginable)	0.51 (1.27)	1.20 (1.78)	1.00 (1.72)	0.86 (1.78)	0.79 (1.63)	-
Clinically significant pain ( 4)	4.3% (11)	12.8% (32)	8.3% (20)	10.0% (20)	7.9% (11)	21.3% (56)
Brief Pain Inventory Pain Interference <sup>‡</sup>						
Raw scores (0=low, 10 = high)	0.18 (0.67)	0.49 (1.04)	0.32 (0.92)	0.41 (1.23)	0.28 (0.80)	-
Clinically significant interference ( 4)	0.8% (2)	1.6% (4)	1.3% (3)	4.0% (8)	0.7% (1)	5.3% (14)
No. of current physical symptoms attributed to donation (0 to 10) <sup>b</sup>	-	4.59 (2.07)	3.39 (2.12)	2.96 (2.04)	2.30 (2.08)	-
SF-36 Physical Component Summary Score						
Raw scores (US mean = 50, SD = 10, higher is better) <sup>b, ‡</sup>	56.20 (3.88)	48.19 (7.48)	53.65 (6.31)	55.03 (5.37)	54.98 (4.38)	-
Impaired (>0.5 SD, >5 points below mean) <sup>b</sup>	2.8% (7)	28.8% (72)	11.7% (28)	5.0% (10)	5.0% (7)	33.5% (88)
<b>Secondary outcomes</b>						
Number of post-donation health-related worries (0 to 4) <sup>b, §</sup>						
Unable to do some physical activities as well since donation <sup>c</sup>	-	58.2% (145)	33.5% (80)	19.9% (40)	12.9% (18)	60.8% (160)
Still not physically back to normal <sup>b</sup>	-	36.0% (90)	18.8% (45)	9.0% (18)	4.3% (6)	40.7% (107)



Outcome	Pre-donation	3 Months Post-	6 Months Post-	1 Year Post-donation	2 Years Post-	Cumulative results
	(n=253) % (n) or Mean (SD)	donation (n=250) % (n) or Mean (SD)	donation (n=241) % (n) or Mean (SD)	(n=201) % (n) or Mean (SD)	donation (n=139) % (n) or Mean (SD)	(endorsement at any post-donation time point) (n=263) % (n) *
Recovered slower or much slower than expected <sup>d</sup>	-	34.8% (87)	27.5% (66)	29.0% (58)	25.2% (35)	41.4% (109)
Current donation-related medical problems <sup>b</sup>	-	20.0% (50)	22.5% (54)	20.4% (41)	20.1% (28)	36.9% (97)
Donation was physically stressful <sup>e</sup>	-	48.0% (120)	45.2% (109)	50.0% (100)	43.2% (60)	62.4% (164)
Overall negative feelings about donation <sup>f</sup>	-	1.6% (4)	1.3% (3)	1.5% (3)	4.3% (6)	3.0% (8)

Sensitivity analyses among donors who completed all five surveys (n=118) showed results similar to those who completed at least one survey (n=271).

<sup>d</sup>PCS was not modeled because it is not donation specific. Brief Pain Inventory Pain Interference was not modeled due to high skewness even after transformation and few endorsements of clinical significant interference.

<sup>e</sup>Health-related worries include worries about physical effects of donation, current health, future health, and never feeling 100% well again.

\* This may be underestimated given that some respondents did not respond at all time points.

<sup>a</sup>Missing n=2 at 6 months.

<sup>b</sup>Missing n=1 at 6 months.

<sup>c</sup>Missing n=1 at 3 months and n=2 at 6 months.

<sup>d</sup>Missing n=1 at 6 months and n=1 at 1 year.

<sup>e</sup>Missing n=1 at 1 year.

<sup>f</sup>Missing n=4 at 6 months.

**Table 2**  
 Predictors of Primary Physical Outcomes from Repeated Measures Linear Regression Models (n=245).

Predictors <sup>a</sup>	FACTT Fatigue Scale (scale of 30.3=low fatigue to 83.5=high fatigue; PROMIS-T converted) <sup>b</sup>		Level of abdominal/back pain (scale of 0=no pain to 10=pain as bad as you can imagine)		No. of current physical symptoms attributed to donation (0 to 10)	
	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
Post-donation time point		<0.001		0.010		<0.001
3M vs. 2Y	4.00 (2.80, 5.20)	<0.001	0.41 (0.11, 0.71)	0.007	2.25 (1.95, 2.55)	<0.001
6M vs. 2Y	1.30 (0.10, 2.50)	0.03	0.16 (-0.12, 0.45)	0.27	1.03 (0.74, 1.33)	<0.001
1Y vs. 2Y	0.76 (-0.20, 1.73)	0.12	0.01 (-0.30, 0.32)	0.95	0.58 (0.28, 0.89)	<0.001
Recipient death (time dependent)	3.62 (1.23, 6.01)	0.003	0.68 (0.18, 1.19)	0.008	1.04 (0.42, 1.66)	0.001
Female vs. Male	2.23 (0.80, 3.65)	0.002	0.29 (0.01, 0.57)	0.04	0.68 (0.27, 1.08)	0.001
Married or had long-time partner at pre-donation	1.75 (0.28, 3.21)	0.02				
Length of hospital stay (per day)	0.49 (0.12, 0.86)	0.009	0.73 (0.36, 1.11)	<0.001	0.22 (0.12, 0.32)	<0.001
Had post-operative complications during the first month post-donation						
Pre-donation predictors						
Level of abdominal/back pain at pre-donation (scale of 0=no pain to 10=pain as bad as you can imagine)	na	na	0.32 (0.20, 0.44)	<0.001	na	na
FACTT-fatigue scale at pre-donation (per 10 unit increase on scale 30.3 to 83.5; PROMIS T converted)	4.83 (3.69, 5.98)	<0.001	na	na	na	na
MCS pre-donation (per 10 unit increase on scale 1 to 100)			-0.51 (-0.73, -0.28)	<0.001	-0.64 (-0.95, -0.34)	<0.001
PCS pre-donation (per 10 unit increase on scale 1 to 100)			-0.56 (-0.98, -0.14)	0.009	-1.01 (-1.56, -0.45)	<0.001
Black sheep donor	2.39 (0.79, 3.99)	0.003				
Anyone discouraged donor to donate					0.45 (0.05, 0.85)	0.03
If donated, I will feel my life is more worthwhile (scale of 1=very unlikely to 10=very likely)	0.30 (0.05, 0.55)	0.02				
Household income (per \$10,000 increase) <sup>c</sup>			-0.04 (-0.07, -0.01)	0.009		

CI, confidence interval; FACTT, functional assessment of chronic illness therapy; PROMIS, patient-reported outcomes measurement information system; MCS, mental component summary; PCS, physical component summary.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

<sup>g</sup>Variables tested but not significant: donor's age at donation, race/ethnicity, education, body mass index, re-hospitalized within 30days post-donation, donor recipient relationship, Simmons psychosocial background (donation history), Simmons donation decision-making items (other possible donors, ambivalence scale, anyone encouraged donor to donate, and anticipated long-term health effects of donation), Simmons motivation for donating, Campbell global life satisfaction item, and PHQ-9.

<sup>h</sup>FACIT Fatigue scores were converted to Patient-Reported Outcomes Measurement Information System (PROMIS) T-scores for modeling in order to reduce skewness of the distribution. The direction of FACIT Fatigue score (higher score=lower fatigue) is flipped in the PROMIS T-converted score (higher score=higher fatigue).

<sup>c</sup>In the level of abdominal/back pain model where household income was significant, adjusting for household size didn't change results and household size was not statistically significant.

**Table 3**  
 Predictors of Secondary Physical Outcomes from Repeated Measures Logistic/Negative Binomial Regression Models (n=245). Rate ratios or odds ratios greater than 1 are in bold.

Predictors <sup>a</sup>	Number of health-related worries (count of 0 to 4)		Unable to do some physically activities as well since donation		Still not physically back to normal		Recovered slower or much slower than expected (2 or lower on scale of 1-much slower than expected to 3-as expected to 5-much faster)		Current donation-related medical problems		Donation was physically stressful (2 or lower on scale of 1-very stressful to 4-not at all stressful)	
	Rate Ratio (95% CI)	P-value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Post-donation time point		0.003		<0.001		<0.001		0.005		0.45		0.22
3M vs. 2Y	<b>1.31 (1.02, 1.68)</b>	<b>0.04</b>	<b>11.05 (6.37, 19.15)</b>	<b>&lt;0.001</b>	<b>12.20 (5.41, 27.47)</b>	<b>&lt;0.001</b>	<b>1.76 (1.27, 2.45)</b>	<b>&lt;0.001</b>	0.84 (0.52, 1.35)	0.48	<b>1.45 (0.95, 2.20)</b>	<b>0.08</b>
6M vs. 2Y	<b>1.22 (0.96, 1.56)</b>	<b>0.12</b>	<b>3.66 (2.09, 6.40)</b>	<b>&lt;0.001</b>	<b>4.96 (2.13, 11.54)</b>	<b>&lt;0.001</b>	<b>1.19 (0.86, 1.64)</b>	<b>0.30</b>	<b>1.13 (0.73, 1.75)</b>	<b>0.59</b>	<b>1.22 (0.83, 1.78)</b>	<b>0.31</b>
1Y vs. 2Y	0.90 (0.70, 1.17)	0.47	<b>1.63 (0.97, 2.73)</b>	<b>0.051</b>	<b>1.98 (0.85, 4.63)</b>	<b>0.10</b>	<b>1.28 (0.94, 1.75)</b>	<b>0.12</b>	0.94 (0.63, 1.39)	0.75	<b>1.45 (0.97, 2.17)</b>	<b>0.07</b>
Donor recipient relationship (ref=other biological or non-biological relative)												
First degree relative												0.01
Spouse/partner		<b>0.03</b>										<b>0.003</b>
Unrelated		0.004										<b>0.02</b>
Recipient death (time dependent)												<b>0.12</b>
Female vs. Male	<b>1.39 (1.03, 1.87)</b>	<b>0.03</b>										<b>0.04</b>
Age at donation (per 10yrs increase)	0.81 (0.70, 0.94)	0.004										
BMI at donation				0.051								
25.0–29.9 vs. <24.9			<b>1.82 (1.12, 2.98)</b>	<b>0.017</b>								
>= 30 vs. <24.9			<b>1.20 (0.62, 2.32)</b>	<b>0.60</b>								
Length of hospital stay (per day)	<b>1.13 (1.07, 1.20)</b>	<b>0.002</b>	<b>1.32 (1.15, 1.52)</b>	<b>&lt;0.001</b>	<b>1.63 (1.39, 1.92)</b>	<b>&lt;0.001</b>	<b>1.31 (1.10, 1.55)</b>	<b>0.005</b>			<b>1.16 (1.01, 1.32)</b>	<b>0.02</b>
Hospitalized during the first month post-donation												
Had post-operative complications during the first month post-donation										<b>2.33 (1.32, 4.14)</b>	<b>0.01</b>	
Pre-donation predictors												
MCS pre-donation (per 10 increase on scale 1 to 100)	0.79 (0.67, 0.93)	0.01			0.72 (0.54, 0.95)	0.049						0.41 (0.27, 0.60) <0.001
Ambivalence to donate (scale of 0-no ambivalence to 7-ambivalence)	<b>1.17 (1.06, 1.28)</b>	<b>0.003</b>										<b>1.23 (1.05, 1.45)</b> <b>0.01</b>
Anticipated long-term health effects from donation	<b>2.00 (1.48, 2.70)</b>	<b>&lt;0.001</b>										<b>2.03 (1.26, 3.25)</b> <b>0.004</b>
Black sheep donor			<b>1.73 (1.06, 2.80)</b>	<b>0.03</b>								
Anyone discouraged donor to donate										<b>1.89 (1.17, 3.05)</b>	<b>0.01</b>	

Predictors <sup>a</sup>	Rate Ratio (95% CI)	P-value	Number of health-related worries (count of 0 to 4)	Unable to do some physically activities as well since donation	Still not physically back to normal	Recovered slower or much slower than expected (2 or lower on scale of 1-much slower than expected to 3-as expected to 5-much faster)	Current donation-related medical problems	Donation was physically stressful (2 or lower on scale of 1-very stressful to 4-not at all stressful)	OR (95% CI)	P value	OR (95% CI)	P value
Household income (per \$10,000 increase) <sup>b</sup>									1.06 (1.00, 1.12)	0.04		

OR, odds ratio; CI, confidence interval; BMI, body mass index; MCS, mental component summary.

<sup>a</sup>Variables tested but not significant: donor demographics (race/ethnicity, education, marital status), clinical characteristics (hospitalized within 1st month post-donation, donation complications within 1st month), Simmons psychosocial background (donation history), Simmons donation decision-making items (other possible donors, anyone encouraged donor to donate, anticipated feeling life would be more worthwhile after donation), Simmons strength of motivation to donate, Patient Health Questionnaire-9 (PHQ-9)– depression score and Short Form-36 Physical Component Summary

<sup>b</sup>In the level of abdominal/back pain model where household income was significant, adjusting for household size didn't change results and household size was not statistically significant.