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Authors

Ufere, Nneka N
Serper, Marina
Kaplan, Alyson
[et al.](#)

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Financial burden following adult liver transplantation is common and associated with adverse recipient outcomes

Nneka N. Ufere¹, Marina Serper², Alyson Kaplan³, Nora Horick⁴, Teresa Indriolo¹, Lucinda Li¹, Nishant Satapathy⁵, John Donlan⁶, Janeth C. Castano Jimenez⁷, Carlos Lago-Hernandez⁸, Sarah Lieber⁹, Carolina Gonzalez¹⁰, Eileen Keegan¹⁰, Kimberly Schoener¹⁰, Emily Bethea¹, Leigh-Anne Dageforde¹¹, Heidi Yeh¹¹, Areej El-Jawahri¹², Elyse R. Park¹³, Irine Vodkin¹⁴, Emily Schonfeld¹⁵, Ryan Nipp¹⁶, Archita Desai⁷, Jennifer C. Lai¹⁷

¹Department of Medicine, Gastrointestinal Division, Liver Center, Massachusetts General Hospital, Boston, Massachusetts, USA

²Department of Medicine, Division of Gastroenterology & Hepatology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA

³Department of Medicine, Tufts Abdominal Transplant Institute, Tufts University Medical Center, Boston, Massachusetts, USA

⁴Department of Statistics, Massachusetts General Hospital, Boston, Massachusetts, USA

⁵University of Arizona College of Medicine-Phoenix, Phoenix, Arizona, USA

⁶Harvard Medical School, Boston, Massachusetts, USA

⁷Department of Medicine, Division of Gastroenterology & Hepatology, Indiana University School of Medicine, Indianapolis, Indiana, USA

⁸Department of Medicine, Division of Hospital Medicine, University of California San Diego, La Jolla, California, USA

⁹Department of Medicine, Division of Digestive and Liver Diseases, University of Texas Southwestern (UTSW) Medical Center, Dallas, Texas, USA

¹⁰Department of Social Service, Massachusetts General Hospital, Boston, Massachusetts, USA

¹¹Department of Surgery, Division of Transplantation, Massachusetts General Hospital, Boston, Massachusetts, USA

Correspondence: Nneka N. Ufere, Gastrointestinal Unit, Department of Medicine, Liver Center, Massachusetts General Hospital 55 Fruit Street, Boston, MA 02114, USA. nneka.ufere@mgh.harvard.edu.

Marina Serper and Alyson Kaplan contributed equally to this work.

AUTHOR CONTRIBUTIONS

Study concept and idea: Nneka N. Ufere and Jennifer C. Lai. Study design: Nneka N. Ufere, Marina Serper, Alyson Kaplan, Irine Vodkin, Archita Desai, and Jennifer C. Lai. Analysis and interpretation of data: Nneka N. Ufere, Nora Horick, and Jennifer C. Lai. Drafting of the manuscript: Nneka N. Ufere and Alyson Kaplan. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: Nneka N. Ufere and Nora Horick.

CONFLICTS OF INTEREST

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¹²Department of Medicine, Division of Hematology and Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA

¹³Department of Psychiatry, Mongan Institute, Harvard Medical School, Boston, Massachusetts, USA

¹⁴Department of Medicine, Division of Gastroenterology and Hepatology, University of California, San Diego, California, USA

¹⁵Department of Medicine, Division of Gastroenterology and Hepatology, Weill Cornell Medicine, New York, New York, USA

¹⁶Department of Medicine, University of Oklahoma Health Sciences Center, Stephenson Cancer Center, Oklahoma City, Oklahoma, USA

¹⁷Department of Medicine, Division of Gastroenterology and Hepatology, University of California San Francisco, San Francisco, California, USA

Abstract

The financial impact of liver transplantation has been underexplored. We aimed to identify associations between high financial burden (>10% annual income spent on out-of-pocket medical costs) and work productivity, financial distress (coping behaviors in response to the financial burden), and financial toxicity (health-related quality of life, HRQOL) among adult recipients of liver transplant. Between June 2021 and May 2022, we surveyed 207 adult recipients of liver transplant across 5 US transplant centers. Financial burden and distress were measured by 25 items adapted from national surveys of cancer survivors. Participants also completed the Work Productivity and Activity Impairment and EQ-5D-5L HRQOL questionnaires. In total, 23% of recipients reported high financial burden which was significantly associated with higher daily activity impairment (32.9% vs. 23.3%, $p = 0.048$). In adjusted analyses, the high financial burden was significantly and independently associated with delayed or foregone medical care (adjusted odds ratio, 3.95; 95% CI, 1.85–8.42) and being unable to afford basic necessities (adjusted odds ratio, 5.12; 95% CI: 1.61–16.37). Recipients experiencing high financial burden had significantly lower self-reported HRQOL as measured by the EQ-5D-5L compared to recipients with low financial burden (67.8 vs. 76.1, $p = 0.008$) and an age-matched and sex-matched US general population (67.8 vs. 79.1, $p < 0.001$). In this multicenter cohort study, nearly 1 in 4 adult recipients of liver transplant experienced a high financial burden, which was significantly associated with delayed or foregone medical care and lower self-reported HRQOL. These findings underscore the need to evaluate and address the financial burden in this population before and after transplantation.

INTRODUCTION

Over the past decade, advances in liver transplantation have significantly improved, with 5-year graft and overall survival rates for adult recipients of liver transplant now exceeding 75%.^[1] Consequently, there is a crucial need to identify outcomes beyond graft and patient survival to define success after transplantation in terms of patients' overall well-being. Transplant survivorship—a holistic approach to the care of recipients of transplant—focuses

on improving patients' health-related quality of life (HRQOL) by addressing their physical, psychological, social, spiritual, and financial well-being.^[2–4] However, few studies have examined survivorship issues among adult recipients of liver transplant.^[5]

Qualitative studies among adult recipients of liver transplant have identified financial burden as a key aspect of survivorship.^[3,4] Recipients may experience financial burdens due to high out-of-pocket (OOP) transplant-related medical costs and ongoing disability after transplant that may delay their return to work. Prior research has demonstrated that the *financial burden* of high OOP costs experienced by adults with advanced liver disease may result in *financial distress*, or maladaptive coping behaviors, such as delaying or forgoing medical care, which can negatively impact HRQOL (*financial toxicity*).^[6–9] However, there is a dearth of research focusing on the associations of financial burden with work productivity loss, financial distress, and HRQOL of adult recipients of liver transplant.

In this cross-sectional study, we sought to evaluate financial burden as measured by the percentage of income spent on OOP medical costs among adult recipients of liver transplant.^[10] Specifically, we aimed to describe rates of financial burden in a multicenter cohort of US adult recipients of liver transplant and explore associations of financial burden with adverse outcomes such as work productivity loss, financial distress, and poor HRQOL. By describing rates and correlates of financial burden in the liver transplant population, findings from this work will help to inform future efforts to better support the survivorship needs of these individuals.

METHODS

Study population

We analyzed data from the LIFe After Liver Transplant (LIFT) study, a multicenter observational cohort study of adult recipients of liver transplant. Patient eligibility criteria included: (1) adult (age ≥ 18 y) recipient of liver transplant and (2) able to communicate and respond to questionnaires in English or Spanish (given the availability of study materials translated into these languages). We excluded patients who had a prior history of solid organ transplantation other than liver transplantation, had a history of advanced malignancies other than HCC, had an uncontrolled psychiatric illness, or impaired cognition precluding the ability to provide informed consent. All enrolled patients had a history of cirrhosis and/or HCC and were at least 1 month after transplant. All research was conducted in accordance with both the Declarations of Helsinki and Istanbul. Study participants provided written informed consent and the Institutional Review Board at each participating site approved this study, which adhered to the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines.^[11]

Adult recipients of liver transplant were enrolled across all sites between June 2021 and May 2022. The patient cohort included participants from 5 US transplant centers: Massachusetts General Hospital (Boston, Massachusetts; n = 66), University of Pennsylvania (Philadelphia, Pennsylvania; n = 59), Indiana University (Indianapolis, Indiana; n = 43), University of California, San Francisco (n = 27), and New York Presbyterian Weill Cornell (New York, New York; n = 12). Either transplant clinicians or trained research coordinators at each site

enrolled patients and administered questionnaires. Enrolled participants had up to 30 days after providing consent to complete questionnaires either in person, by telephone, paper, or online.

We obtained information about patients' transplant history (date of transplant, etiology of liver disease, history of HCC, and Model for End-Stage Liver Disease-Sodium score at transplant), health insurance plan at transplant, clinical comorbidities (hypertension, diabetes mellitus, cerebrovascular disease, coronary artery disease, chronic obstructive pulmonary disease, and chronic kidney disease) from the electronic health records. We categorized time since transplant by survivorship periods as follows: early (1 y or below), mid (1–5 y), late (5–10 y), and advanced (10 y or above).^[12] Patients provided self-reported age, sex, race, ethnicity, marital status, educational attainment, annual household income, living situation, employment status at the time of liver transplantation, and current employment status.

Patient-reported surveys

Financial burden and distress—To understand issues related to financial burden and distress among adult recipients of liver transplant, we created a 25-item financial burden and distress survey using items from a health insurance substudy conducted within the Childhood Cancer Survivors Study (n = 21) and a medication tradeoffs survey (n = 4) (Supplemental Table S1, <http://links.lww.com/LVT/A560>).^[10,13–15] The Childhood Cancer Survivors Study uses survey items created by the US government-led National Health Interview Survey and Medical Expenditure Panel Survey that have been previously cognitively tested in the general US population to assess financial hardship in cancer survivors.^[16,17] Survey measures and items were selected based on an established conceptual framework for financial burden, distress, and toxicity in chronic liver disease (Figure 1).^[6]

Financial burden related to OOP medical costs was assessed using the following single-item question: “In the past year, have you spent more than 10% of your income on medical expenses?” (yes vs. no/don't know) with “yes” indicating high financial burden.^[10] OOP spending above a threshold of 10% of household income has been found to be a marker of under-insurance associated with financial distress in multiple studies of US adults.^[10,18–22] This was the primary explanatory variable for the study. We additionally assessed subjective financial burden using the following single-item question: “To what degree has the cost of your illness care been a financial burden to you/your family?” (with high burden characterized as “catastrophic” or “significant” and low as “moderate,” “mild,” or “none”).^[18]

We characterized financial distress in 3 domains—material, behavioral, and psychological—consistent with prior studies.^[23–25] Material financial distress (ie, material consequences of medical expenses) was measured by 5 questions asking whether recipients of transplant ever had to do any of the following actions due to medical expenses over the past year: (i) take money out of savings; (ii) sell property or possessions; (iii) take out a mortgage against their own home or take out a loan; (iv) take on credit card debt; and (v) file for bankruptcy. Behavioral financial distress (ie, financial coping strategies to manage financial burden) was assessed using 18 questions related to whether the recipient had engaged in

(i) increased support-seeking (eg, increased borrowing, family needing to work more); (ii) making tradeoffs for their health care (eg, delaying or foregoing their medical care); or (iii) making tradeoffs for (or being unable to afford) basic necessities (eg, food, heat, or rent) due to their medical expenses. Psychological financial distress (ie, psychological worry due to financial burden) was measured by 1 item asking whether recipients worried about needing to file for bankruptcy due to medical expenses.

Work productivity and activity impairment—The Work Productivity and Activity Impairment Questionnaire (WPAI) consists of 6 questions assessing employment status, work hours missed due to health problems, hours missed due to other reasons, and hours worked in total. Four main outcomes can be generated from the WPAI: absenteeism (work time missed), presenteeism (impairment at work), overall work productivity loss (combined absenteeism and presenteeism), and daily activity impairment (impairment in daily activities other than work).^[26] The absenteeism, presenteeism, and work productivity loss domains are assessed only in those who report being employed at the time of completing the questionnaire. The daily activity impairment domain is assessed in all participants regardless of their current employment status. The recall period for the WPAI is 7 days. The measure allows for health problem specificity by replacing “health problems” in the general health version with “liver transplantation.” The WPAI domains are scaled from a minimum value of 0% (indicating no impairment) to a maximum value of 100% (indicating complete impairment).

HRQOL—We assessed recipients’ HRQOL using the EQ-5D-5L questionnaire.^[27] The EQ-5D-5L questionnaire allows the calculation of 2 separate scores: (1) EQ-5D Index and (2) EQ-5D-5L visual analog scale (EQ-VAS).

The EQ-5D Index consists of 5 dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) with each dimension having 5 response levels (scored from 1 to 5): 1, no problems; 2, slight problems; 3, moderate problems; 4, severe problems; and 5, extreme/unable to problems. These dimensions of health can be dichotomized into “no problems” (level 1) and “any problem” (levels 2–5), thereby changing the profile into frequencies of reported problems.^[28] These 5 dimensions are used to generate a health state that can be converted into a single utility index value (EQ-5D Index) using the EQ-5D-5L value set for the United States, which reflects population-based preferences for HRQOL.^[29,30] A respondent’s EQ-5D Index score can thus be compared to the range of HRQOL scores reported for the US adult general population: The US EQ-5D Index score ranges from –0.573 (worst possible health state) to 1 (best possible health state).

The EQ-VAS allows respondents to separately self-rate their own HRQOL on a graduated visual analog scale ranging from 0 (the worst health you can imagine) to 100 (the best health you could imagine).

The EQ-5D-5L has been shown to have strong construct and criterion validity among candidates and recipients of liver transplant.^[31] The accepted minimal clinically important differences (MCIDs) on the US EQ-5D Index and EQ-VAS are 0.074 points and 7 points, respectively.^[32,33]

Statistical analysis

All sociodemographic, clinical characteristics, and survey scores were summarized as n (%), mean (\pm SD), or median (IQR). These parameters were compared to the primary explanatory variable of interest—patient-reported financial burden level (high: OOP costs > 10% of household income, low: 10%)—using Fisher exact tests, chi-square tests, independent t tests, or Wilcoxon rank sum tests, as appropriate. We used multivariable logistic regression analysis to evaluate sociodemographic and clinical characteristics associated with the high financial burdens.

Study outcomes included work productivity loss, financial distress, and HRQOL. To examine associations between high financial burden and material, behavioral, and psychological financial distress metrics, we used multivariable logistic regression models adjusting for only covariates with $p < 0.10$ on univariable analyses. We used multivariable linear regression to evaluate the association between high financial burden and HRQOL (EQ-5D Index and EQ-VAS), adjusting for only covariates with $p < 0.10$ on univariable analyses. EQ-5D Index and EQ-VAS scores were compared among recipients reporting high versus low financial burden and those for the general population after matching for age and sex.^[34]

We conducted additional sensitivity analyses adjusting for the survivorship stage in the models, using high subjective financial burden as the explanatory variable, and reclassifying all patients who answered “I don’t know” to the primary explanatory variable as “yes.”

There was a 100% response rate for the primary explanatory variable of financial burden and < 2% missingness within each of the survey measures, and thus only observed survey data were used; no imputation was performed. All individual variables in the multivariable analyses had variance inflation factor values < 1.5, showing no evidence of multicollinearity. Statistical analyses were performed using STATA version 15.1 and SAS version 9.4. Hypothesis tests were 2-sided and considered significant at a p value < 0.05. Outcomes with 95% CI were reported.

RESULTS

Baseline characteristics

A total of 207/377 (55%) of recipients of liver transplant were enrolled in the study. Participants completed the surveys in person by paper ($n = 77$, 37%), by telephone ($n = 71$, 34%), or online ($n = 59$, 29%). Baseline characteristics are shown in Table 1. Recipients had a median age of 63 years (range, 22–78), 66% were male, 86% were White, 7% were Hispanic, and 69% were married. Over 43% of recipients were employed before transplant, and 100% were insured (41% Medicare or Medicaid, 59% private). The median Model for End-Stage Liver Disease-Sodium score at transplant was 22.5 (IQR, 15–30) and the median time since transplant was 34 months (IQR, 9–87). In total, 37% of recipients had an annual household income under \$50,000, and 28% were currently employed.

Characteristics associated with high financial burden

Overall, 23% (48 of 207) reported “yes” to spending more than 10% of their household income on OOP medical costs (high financial burden) while 146 (71%) reported “no” and 13 (6%) reported “I don’t know.” Recipients experiencing high financial burden were younger on average at transplant (55.2 y vs. 58.2 y, $p = 0.04$). Otherwise, there were no other significant differences in any other sociodemographic or clinical characteristics between recipients reporting high versus low financial burdens. In adjusted models, the level of educational attainment was the only independent predictor of high financial burden. Recipients who had a high school education or less had higher odds (adjusted odds ratio [aOR], 2.2; 95% CI, 1.02–4.71) of having a high financial burden compared to those with higher educational attainment (Supplemental Table S2, <http://links.lww.com/LVT/A560>).

Association of financial burden with work productivity loss

Figure 2 shows WPAI scores among recipients experiencing high versus a low financial burden. Among the entire cohort ($n = 207$), recipients experiencing high financial burden experienced significantly higher daily activity impairment (32.9% vs. 23.3%, $p = 0.048$). Among those who were currently employed ($n = 62$), there were no significant differences in absenteeism, presenteeism, and overall work impairment between recipients with high versus low financial burden.

Association of financial burden with material, behavioral, and psychological financial distress

Figures 3A, B show the prevalence of material, behavioral, and psychological financial distress among adult recipients of liver transplant based on their financial burden status. Recipients with high financial burden were significantly more likely to report loss of savings or assets (85% vs. 28%, $p < 0.001$), having experienced medical debt or bankruptcy (42% vs. 15%, $p < 0.001$), support-seeking (52% vs. 22%, $p < 0.001$), having delayed or foregone medical care (58% vs. 28%, $p < 0.001$), and being unable to pay for basic necessities (23% vs. 8%, $p = 0.005$). Recipients with high financial burden were significantly more likely to experience material (88% vs. 33%, $p < 0.001$) and behavioral (77% vs. 38%, $p < 0.001$) financial distress. There were no significant differences in rates of psychological financial distress between those with high versus low financial burden (13% vs. 6%, $p = 0.12$).

In adjusted models (Table 2), the high financial burden was significantly and independently associated with recipients reporting medical debt or bankruptcy (aOR, 3.58; 95% CI, 1.62–7.91), delayed or foregone medical care (aOR, 3.95; 95% CI, 1.85–8.42), and being unable to pay for basic necessities (aOR, 5.12; 95% CI, 1.61–16.37). We also found significant associations between high financial burden and loss of savings or assets, support-seeking, and reporting any material or behavioral financial distress. These findings did not significantly change with including the survivorship stage in the model (Supplemental Table S3, <http://links.lww.com/LVT/A560>).

Association of financial burden with financial toxicity (HRQOL)

Table 3 presents the unadjusted and adjusted analyses examining the association of financial burden with HRQOL as measured using the EQ-5D Index and EQ-VAS scores. High

financial burden was not associated with EQ-5D Index scores among recipients in either unadjusted (coefficient, -0.045 ; 95% CI, -0.096 to 0.006) or adjusted (coefficient, -0.032 ; 95% CI -0.080 to 0.015) analyses after controlling for age, marital status, household income, current employment status, and insurance type, as well as survivorship stage in a sensitivity analysis (Supplemental Table S4, <http://links.lww.com/LVT/A560>). In unadjusted analysis, high financial burden was associated with lower EQ-VAS scores among recipients (coefficient, -8.34 ; 95% CI, -14.61 to -2.07). This association remained significant (coefficient, -6.57 ; 95% CI, -12.63 to -0.51) after adjusting for marital status, household income, current employment status, and insurance type, as well as survivorship stage in a sensitivity analysis (Supplemental Table S4, <http://links.lww.com/LVT/A560>). Household income and current employment status were also significantly associated with EQ-VAS scores.

Recipients experiencing high financial burden had significantly lower EQ-VAS (67.8 vs. 76.1, $p = 0.008$) but similar EQ-5D Index (0.76 vs. 0.81, $p = 0.055$) scores compared to recipients experiencing low burden. Recipients experiencing high financial burden were significantly more likely to report having any problems in the EQ-5D Index dimensions of usual care (67% vs. 48%, $p = 0.027$) and depression/anxiety (65% vs. 48%, $p = 0.041$) (Figure 4, Supplemental Table S5, <http://links.lww.com/LVT/A560>).

Figures 5A, B compare differences in mean EQ-5D Index and EQ-VAS scores among the high and low financial burden, and age-matched and sex-matched general US populations.^[34] Recipients experiencing high financial burden had significantly lower EQ-5D Index scores (0.76 vs. 0.82, $p < 0.001$) as compared to the US general population, while recipients experiencing low financial burden had similar EQ-5D Index scores (0.805 vs. 0.824, $p = 0.07$). The mean differences in EQ-5D Index scores in the high financial burden (M_{diff} , -0.06 ; 95% CI, -0.09 to -0.04) and low financial burden (M_{diff} , -0.02 ; 95% CI, -0.04 to 0.002) groups did not exceed accepted MCIDs when compared to the US general population (Figure 5A).^[32,33]

On EQ-VAS, both recipients experiencing high financial burden (67.8 vs. 79.1, $p < 0.001$) and low financial burden (76.1 vs. 79.1, $p = 0.019$) had significantly lower scores as compared to the US general population.^[34] The mean differences in EQ-VAS scores between the high financial burden group and the US general population exceeded accepted MCIDs (M_{diff} , -11.36 ; 95% CI, -14.37 to -8.35). The mean differences in EQ-VAS scores between the low financial burden group and the US general population did not exceed accepted MCIDs (M_{diff} , -3.02 ; 95% CI, -5.55 to -0.50) (Figure 5B). When comparing recipients experiencing high versus low financial burden, only mean differences in EQ-VAS (M_{diff} , -8.3 ; 95% CI, -14.61 to -2.07) but not EQ-5D Index (M_{diff} , -0.05 ; 95% CI, -0.10 to 0.01) scores exceeded accepted MCIDs.

Sensitivity analyses

We conducted 2 additional sensitivity analyses. First, we examined the association of a surrogate metric—high subjective financial burden—with financial distress metrics (Supplemental Table S6, <http://links.lww.com/LVT/A560>). Second, we examined the association of high financial burden with financial distress metrics when including both

patients who answered “yes” and patients who answered “I don’t know” to spending greater than 10% of their income on OOP medical expenses (Supplemental Table S7, <http://links.lww.com/LVT/A560>). These sensitivity analyses showed similar results as our primary analyses.

DISCUSSION

In this multisite cohort study of 207 ambulatory adult recipients of liver transplant, nearly 1 in 4 reported high financial burden defined as spending 10% or higher of their OOP costs on health care, and fewer than 1 in 3 were employed after transplant. Recipients experiencing high financial burden had increased daily activity impairment and significantly higher odds of experiencing material financial distress (such as loss of savings or incurring medical debt) and behavioral financial distress (such as delayed or foregone medical care or being unable to afford basic necessities). The high financial burden was independently associated with financial toxicity through lower self-reported HRQOL including problems performing usual activities and feeling anxious or depressed. Furthermore, recipients experiencing high financial burdens had clinically meaningful deficits in their self-reported HRQOL as compared to the US general population. Collectively, these findings demonstrate that adult recipients of liver transplant experiencing high financial burdens are at risk for multiple adverse outcomes including financial distress and financial toxicity. These results underscore the need to proactively address high OOP medical costs in this population.

The present study provides critical insight into how financial burden impacts the survivorship of adult recipients of liver transplant. The mean EQ-5D Index and VAS scores among those experiencing high financial burden (0.76 and 68, respectively) closely approximated those reported among a national cohort of patients with advanced cancer (0.78 and 68, respectively), highlighting the devastating impact that high financial burden has on recipients’ HRQOL despite receiving curative therapy.^[32] While we did not observe clinically meaningful differences in EQ-5D Index scores between recipients experiencing high versus low financial burden, it is important to note that EQ-5D Index scores represent US population–based preferences for HRQOL as compared to the EQ-VAS which represents self-reported HRQOL.^[32] Furthermore, those experiencing high financial burdens reported more problems in the EQ-5D dimensions of performing their usual activities and feeling anxious or depressed, revealing deficits in physical, social, and psychological well-being that need further study.^[2]

In this study, recipients experiencing high financial burden had 4 times higher odds of experiencing financial distress due to delaying or foregoing medical care and 5 times higher odds of being unable to afford basic necessities. A prior study of adult recipients of liver transplant demonstrated that those who faced tradeoffs between paying for their medications versus basic necessities were significantly more likely to have medication nonadherence and experience posttransplant hospitalizations.^[15] In turn, episodes of transplant rejection and other posttransplant complications may represent consequences of high financial burden, such as foregone medical care among recipients of transplant. Because posttransplant complications are often the financial responsibility of the patient, hospitalizations associated with these complications could further compound patients’ ability to pay and contribute to

debt.^[35] Importantly, recent data suggest that financial distress may correlate with increased all-cause mortality among adults with chronic liver disease.^[9] Thus, efforts to screen and address the financial burden among adult recipients of liver transplant have the potential to not only improve the lives of transplant survivors but also improve traditional transplant center quality metrics of graft and patient survival.

We found that a single-item question about financial burden (spending 10% or higher of OOP costs on health care) was a sensitive screen for financial distress and financial toxicity among adult recipients of liver transplant in our cohort. Notably, neither household income, survivorship stage, insurance status, nor current employment status were found to be significant predictors of financial burden. All study participants answered this single-item question about OOP costs, which may be a less intrusive way to assess financial burden compared to questions assessing household income or current employment status. This suggests the potential feasibility and usefulness of this metric in the routine posttransplant setting to identify recipients who may need additional psychosocial support and survivorship care.^[2-4]

In addition to screening for financial burden, there are additional strategies and interventions that liver transplant programs can employ to promote enhanced survivorship care among recipients by targeting OOP medical costs. First, including information in the pretransplant informed consent process on expected OOP costs of medications, hospitalizations, and treatments and education regarding possible changes in insurance after transplant may help patients and families better prepare for and anticipate their future financial responsibilities and merits further study. In a 2007 study at a single US liver transplant center, recipients of liver transplant reported spending an average of ~\$7500 (inflation-adjusted) annually in OOP medical costs for their transplant care.^[36] This is one of few studies quantifying OOP medical cost for recipients of transplant and future studies need to confirm these findings and disseminate results to transplant candidates. Second, the use of dedicated transplant financial planners and/or social workers to assist patients in navigating OOP medical costs, insurance, employment, disability, and financial counseling in both the pretransplant and posttransplant periods should be tested in future intervention work. Third, pharmaceutical companies often offer reduced-price or free medication programs for patients in need. Transplant pharmacists can be especially helpful in leveraging these pharmaceutical initiatives. Fourth, transplant programs can also help to accommodate patients who may have high travel-related costs by offering video visits, parking vouchers, transportation assistance, or overnight accommodations.

Several limitations of this study merit discussion. First, this was a cross-sectional study of patients who were surveyed in the immediate years after the start of the COVID-19 pandemic. This study design precludes causal inference or assessment of the directionality of the association of financial burden with examined outcomes. Furthermore, given the study period, sample size, response rate, and lack of data on the sociodemographic characteristics of nonresponders, the reported prevalence of financial burden and rates of employment in this population should be contextualized in the setting of the negative economic effects of the COVID-19 pandemic and the risk for selection bias. Second, the financial burden and distress survey has not been specifically validated or pretested within the adult liver

transplant population. However, the survey items were developed and cognitively tested in the US general population and a national cohort of childhood cancer survivors, lending validity to their use in survivorship studies.^[16,17,37] Furthermore, from a clinical care perspective, the current data highlight a valuable 1-question metric assessing financial burden that can be used to identify a group of recipients of liver transplant at risk for experiencing financial distress and toxicity. Third, our assessment was limited to the financial burden in the past year and there was a broad range in the time since transplant in the cohort. To address this, we adjusted for survivorship stage in sensitivity analyses. However, longitudinal data examining changes in financial burden and distress over time, including pretransplant, are needed to provide a comprehensive picture of survivorship after transplant and to identify at-risk individuals who could benefit from early interventions. Fourth, White patients were overrepresented in our study cohort relative to the US adult liver transplant population, which may limit the generalizability of our results to other racial and ethnic groups.^[1] Fifth, we lacked granular data to assess metrics of socioeconomic disadvantage of our study participants beyond income. Lastly, we did not collect data on clinical outcomes such as rates of rejection, hospitalizations, graft loss, or patient mortality. Future work would benefit from prospective, longitudinal data from a larger sample size of patients to provide more precise estimates of the association of financial burden with adverse clinical outcomes among recipients of liver transplant.

In conclusion, in this multicenter cohort study, nearly 1 in 4 adult recipients of liver transplant experienced a high financial burden, which was significantly associated with delayed or foregone medical care and lower self-reported health-related quality of life. These findings underscore the need to evaluate and address the financial burden in this population before and after transplantation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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DATA AVAILABILITY STATEMENT

Individual participant data will not be shared.

Abbreviations:

aOR	adjusted odds ratio
EQ-VAS	EQ-5D-5L visual analog scale
EQ-5D-5L	EuroQol-5 Dimension Scale

HRQOL	health-related quality of life
LIFT	LIFe After Liver Transplant
MASH	metabolic dysfunction–associated steatohepatitis
MCID	minimal clinically important difference
OOP	out-of-pocket
WPAI	Work Productivity and Activity Impairment questionnaire

REFERENCES

1. Kwong AJ, Ebel NH, Kim WR, Lake JR, Smith JM, Schladt DP, et al. OPTN/SRTR 2021 Annual Data Report: Liver. *Am J Transplant* 2023;23:S178–S263. [PubMed: 37132348]
2. Lai JC, Ufere NN, Bucuvalas JC. Liver transplant survivorship. *Liver Transpl* 2020;26:1030–1033. [PubMed: 32372563]
3. Lieber SR, Kim HP, Baldelli L, Nash R, Teal R, Magee G, et al. What survivorship means to liver transplant recipients: Qualitative groundwork for a survivorship conceptual model. *Liver Transpl* 2021;27:1454–1467. [PubMed: 33942480]
4. Lieber SR, Kim HP, Baldelli L, Nash R, Teal R, Magee G, et al. Early survivorship after liver transplantation: A qualitative study identifying challenges in recovery from the patient and caregiver perspective. *Liver Transpl* 2022;28:422–436. [PubMed: 34529886]
5. Kaplan A, Korenjak M, Brown RS. Post-liver transplantation patient experience. *J Hepatol* 2023;78:1234–1244. [PubMed: 37208108]
6. Ufere NN, Satapathy N, Philpotts L, Lai JC, Serper M. Financial burden in adults with chronic liver disease: A scoping review. *Liver Transpl* 2022;28:1920–1935. [PubMed: 35644920]
7. Lago-Hernandez C, Nguyen NH, Khera R, Loomba R, Asrani SK, Singh S, et al. Cost-Related Nonadherence to Medications Among US Adults With Chronic Liver Diseases. *Mayo Clin Proc* 2021;96:2639–2650. [PubMed: 34120754]
8. Lago-Hernandez C, Nguyen NH, Khera R, Loomba R, Asrani SK, Singh S, et al. Financial hardship from medical bills among adults with chronic liver diseases: National estimates from the United States. *Hepatology* 2021;74:1509–1522. [PubMed: 33772833]
9. Ayyala-Somayajula D, Dodge JL, Farias A, Terrault N, Lee BP, et al. Healthcare affordability and effects on mortality among adults with liver disease from 2004–2018 in the United States. *J Hepatol* 2023;79:329–339. [PubMed: 36996942]
10. Nipp RD, Kirchhoff AC, Fair D, Rabin J, Hyland KA, Kuhlthau K, et al. Financial burden in survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. *J Clin Oncol* 2017; 35:3474–3481. [PubMed: 28817372]
11. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Ann Intern Med* 2007; 147:573–577. [PubMed: 17938396]
12. Lieber SR, Baldelli L, Kim HP, Nash RP, Noriega Ramirez A, Magee G, et al. Active coping, resilience, post-traumatic growth, and psychiatric symptoms among early and late liver transplant survivors. *Liver Transpl* 2023;29:290–306. [PubMed: 36811878]
13. Nipp RD, Shui AM, Perez GK, Kirchhoff AC, Peppercorn JM, Moy B, et al. Patterns in health care access and affordability among cancer survivors during implementation of the Affordable Care Act. *JAMA Oncol* 2018;4:791–797. [PubMed: 29596618]
14. Park ER, Kirchhoff AC, Nipp RD, Donelan K, Leisenring WM, Armstrong GT, et al. Assessing health insurance coverage characteristics and impact on health care cost, worry, and access: A report from the Childhood Cancer Survivor Study. *JAMA Intern Med* 2017;177:1855–1858. [PubMed: 28973059]

15. Serper M, Reese PP, Patzer RR, Levitsky J, Wolf MS. The prevalence, risk factors, and outcomes of medication trade-offs in kidney and liver transplant recipients: A pilot study. *Transpl Int* 2018;31:870–879. [PubMed: 29178601]
16. Cohen JW, Monheit AC, Beauregard KM, Cohen SB, Lefkowitz DC, Potter DE, et al. The Medical Expenditure Panel Survey: A national health information resource. *Inquiry* 1996;33:373–389. [PubMed: 9031653]
17. Parsons VL, Moriarity C, Jonas K, Moore TF, Davis KE, Tompkins L. Design and estimation for the national health interview survey, 2006–2015. *Vital Health Stat 2* 2014;165:1–53.
18. Zafar SY, Peppercorn JM, Schrag D, Taylor DH, Goetzinger AM, Zhong X, et al. The financial toxicity of cancer treatment: A pilot study assessing out-of-pocket expenses and the insured cancer patient's experience. *Oncologist* 2013;18:381–390. [PubMed: 23442307]
19. Schoen C, Doty MM, Robertson RH, Collins SR. Affordable Care Act reforms could reduce the number of underinsured US adults by 70 percent. *Health Aff (Millwood)* 2011;30:1762–1771. [PubMed: 21900668]
20. Banthin JS, Cunningham P, Bernard DM. Financial burden of health care, 2001–2004. *Health Aff (Millwood)* 2008;27:188–195. [PubMed: 18180494]
21. Banthin JS, Bernard DM. Changes in financial burdens for health care: National estimates for the population younger than 65 years, 1996 to 2003. *JAMA* 2006;296:2712–2719. [PubMed: 17164457]
22. Gabel JR, McDevitt R, Lore R, Pickreign J, Whitmore H, Ding T. Trends in underinsurance and the affordability of employer coverage, 2004–2007. *Health Aff (Millwood)* 2009;28:w595–w606. [PubMed: 19491136]
23. Altice CK, Banegas MP, Tucker-Seeley RD, Yabroff KR, et al. Financial hardships experienced by cancer survivors: A systematic review. *J Natl Cancer Inst* 2017;109:109.
24. Fair D, Park ER, Nipp RD, Rabin J, Hyland K, Kuhlthau K, et al. Material, behavioral, and psychological financial hardship among survivors of childhood cancer in the Childhood Cancer Survivor Study. *Cancer* 2021;127:3214–3222. [PubMed: 34061973]
25. Tucker-Seeley RD, Thorpe RJ. Material-psychosocial-behavioral aspects of financial hardship: A conceptual model for cancer prevention. *Gerontologist* 2019;59:S88–S93. [PubMed: 31100144]
26. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics* 1993;4:353–365. [PubMed: 10146874]
27. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011;20:1727–1736. [PubMed: 21479777]
28. EuroQol Research Foundation. EQ-5D-5L User Guide 2019. Accessed June 1, 2021. <https://euroqol.org/publications/user-guides>.
29. Pickard AS, Law EH, Jiang R, Pullenayegum E, Shaw JW, Xie F, et al. United States valuation of EQ-5D-5L health states using an international protocol. *Value Health* 2019;22:931–941. [PubMed: 31426935]
30. Devlin N, Roudijk B, Ludwig K. Value Sets for EQ-5D-5L: A Compendium, Comparative Review & User Guide Springer Nature; 2022.
31. Russell RT, Feurer ID, Wisawatapnimit P, Pinson CW. The validity of EQ-5D US preference weights in liver transplant candidates and recipients. *Liver Transpl* 2009;15:88–95. [PubMed: 19109831]
32. Pickard AS, Neary MP, Cella D. Estimation of minimally important differences in EQ-5D utility and VAS scores in cancer. *Health Qual Life Outcomes* 2007;5:70. [PubMed: 18154669]
33. Walters SJ, Brazier JE. Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D. *Qual Life Res* 2005;14:1523–1532. [PubMed: 16110932]
34. Jiang R, Janssen MFB, Pickard AS. US population norms for the EQ-5D-5L and comparison of norms from face-to-face and online samples. *Qual Life Res* 2021;30:803–816. [PubMed: 33025373]
35. Ammori JB, Pelletier SJ, Lynch R, Cohn J, Ads Y, Campbell DA, et al. Incremental costs of post-liver transplantation complications. *J Am Coll Surg* 2008;206:89–95. [PubMed: 18155573]

36. Rodrigue JR, Reed AI, Nelson DR, Jamieson I, Kaplan B, Howard RJ. The financial burden of transplantation: A single-center survey of liver and kidney transplant recipients. *Transplantation* 2007;84:295–300. [PubMed: 17700152]
37. Nathan PC, Huang IC, Chen Y, Henderson TO, Park ER, Kirchhoff AC, et al. Financial hardship in adult survivors of childhood cancer in the era after implementation of the Affordable Care Act: A report from the Childhood Cancer Survivor Study. *J Clin Oncol* 2023;41:1000–1010. [PubMed: 36179267]

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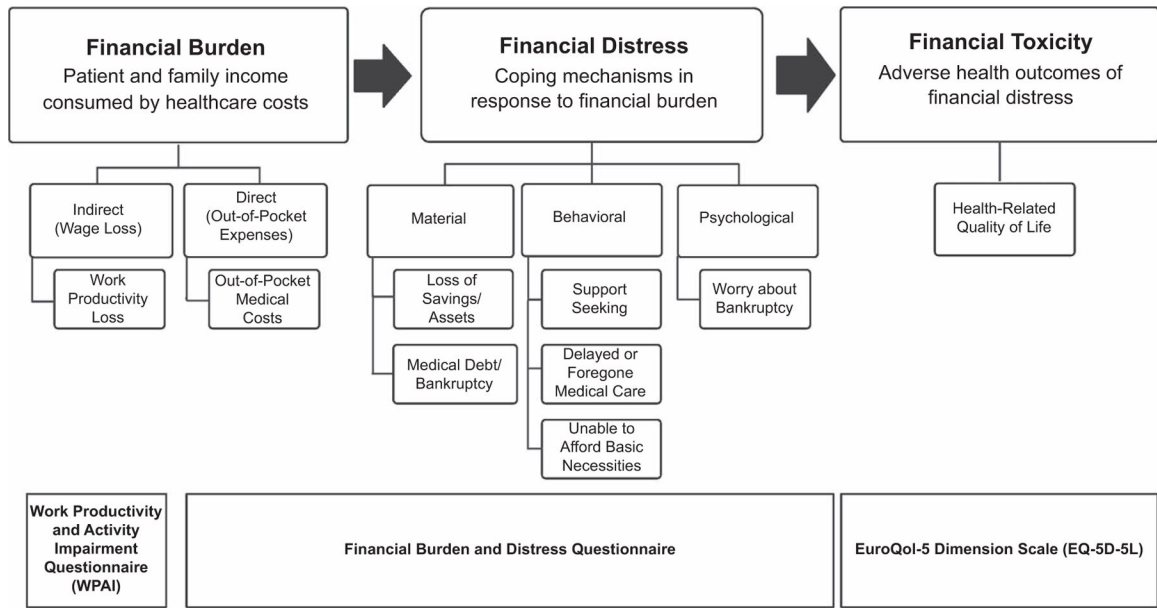


FIGURE 1.
Survey conceptual framework.

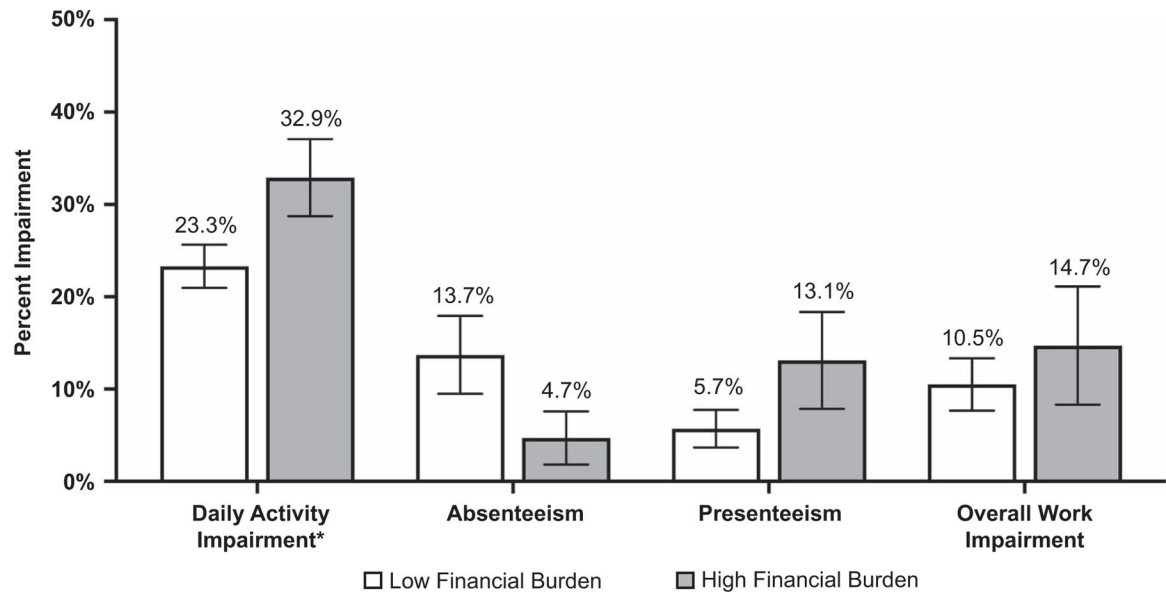


FIGURE 2.

Work Productivity and Activity Impairment (WPAI) according to financial burden status among adult recipients of liver transplant. Daily activity impairment was reported by the entire cohort (207). Absenteeism, presenteeism, and overall work impairment were reported only by currently employed recipients ($n = 62$). $*p < 0.05$.

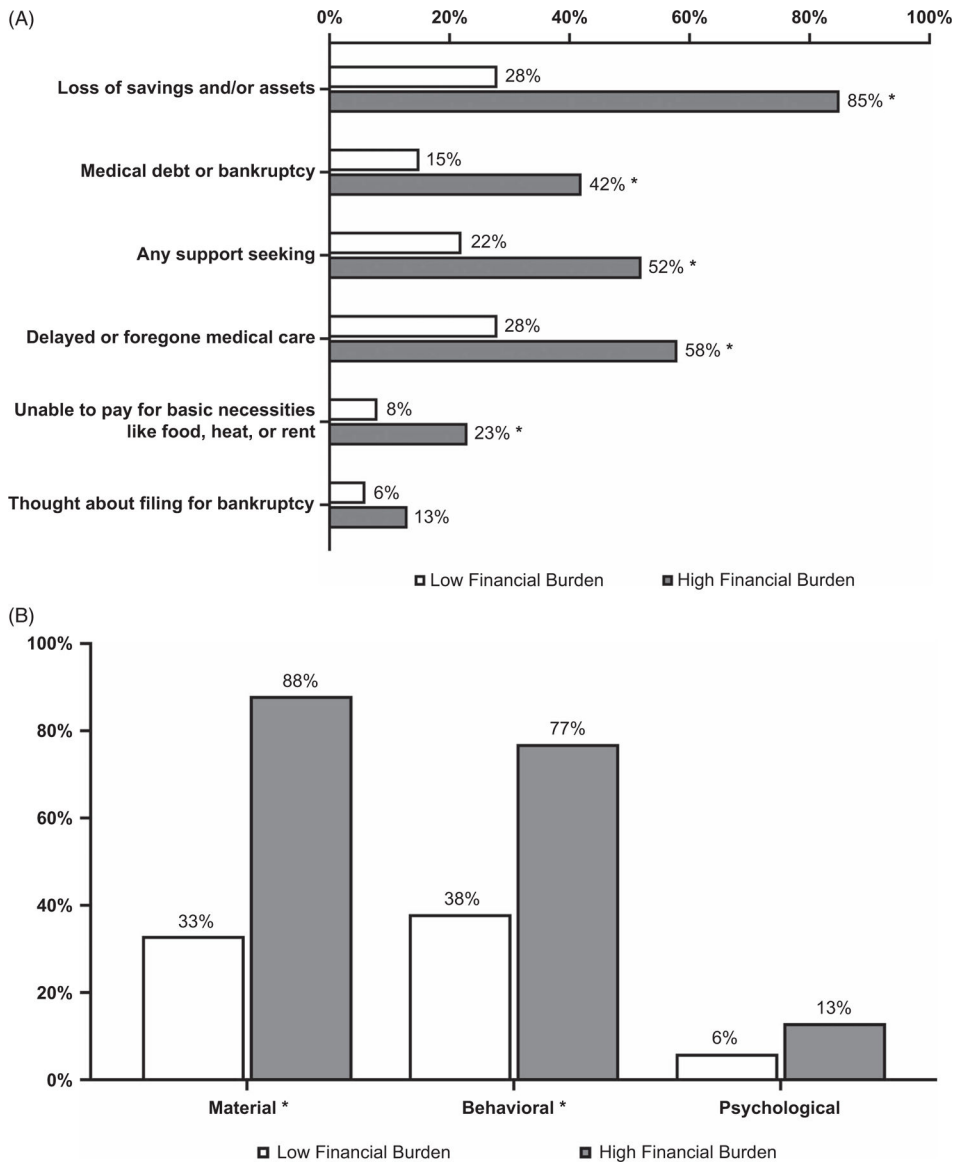


FIGURE 3. (A) Financial distress among adult recipients of liver transplant. (B) Proportions of adult recipients of liver transplant reporting material, behavioral, and psychological financial distress during the past year by financial burden status. * $p < 0.05$.

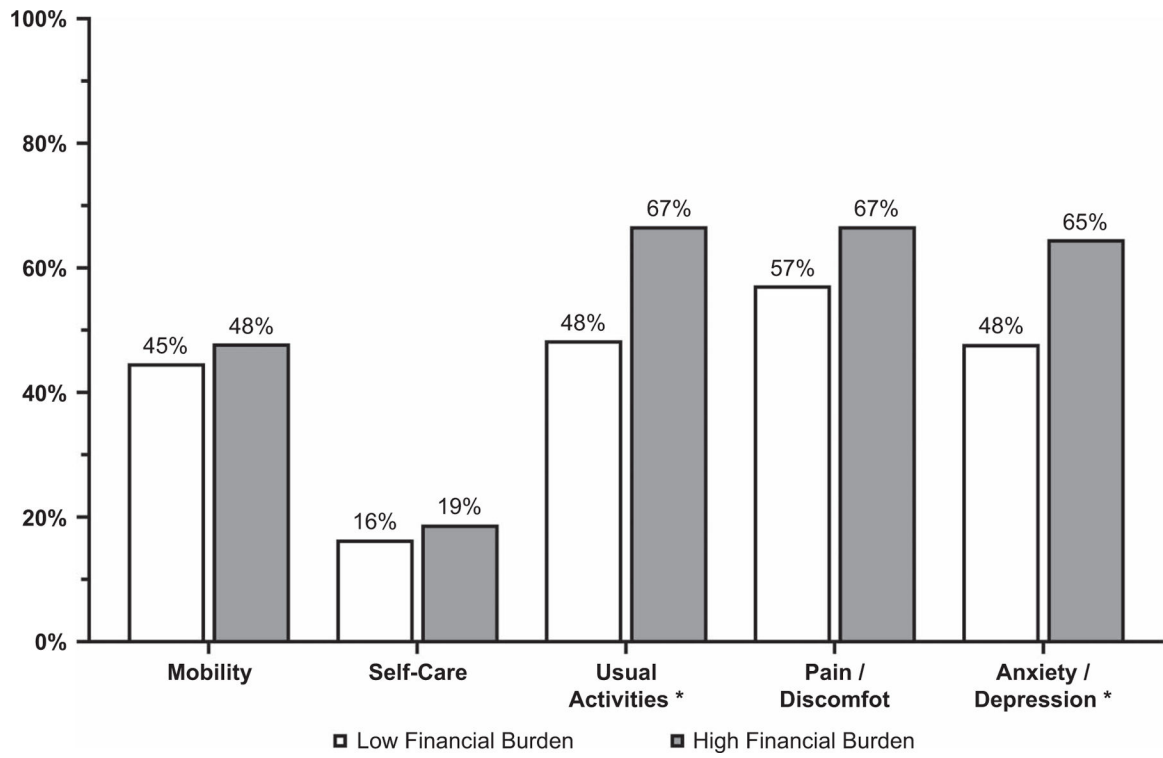


FIGURE 4.

Proportions of adult recipients of liver transplant reporting any problems in the EQ-5D-5L domains by financial burden status. Abbreviation: EQ-5D-5L, EuroQol-5 Dimension Scale.

* $p < 0.05$.

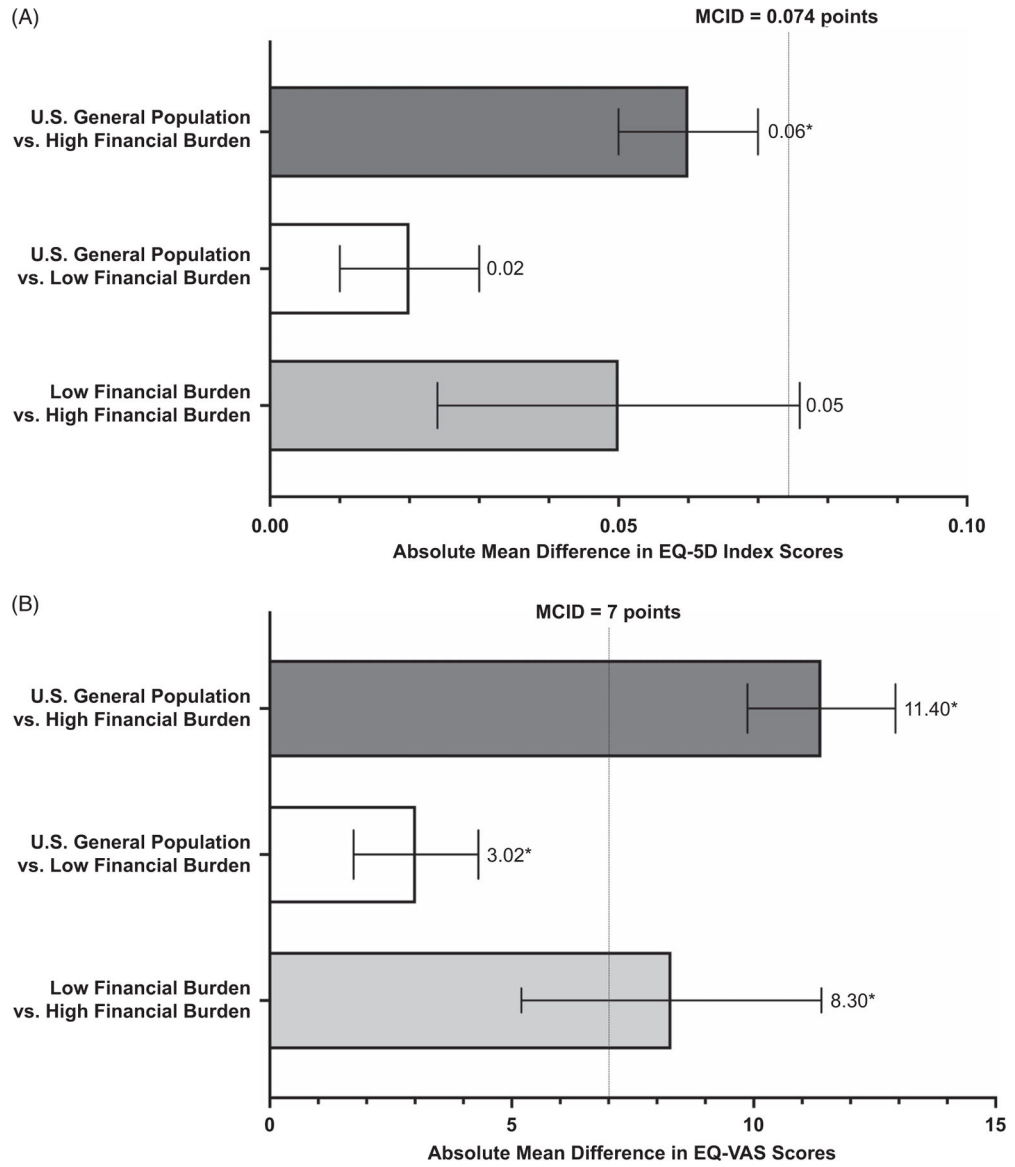


FIGURE 5. (A) Absolute mean differences in EQ-5D Index scores among adult recipients of liver transplant by financial burden status and compared to age-matched and sex-matched US general population. (B) Absolute mean differences in EQ-VAS scores among adult recipients of liver transplant by financial burden status and compared to age-matched and sex-matched US general population. Abbreviations: EQ-5D, EuroQol-5 Dimension; EQ-VAS, EQ-5D-5L visual analog scale; MCID, minimal clinically important difference. * $p < 0.05$.

Sociodemographic and clinical characteristics of adult liver transplant recipients by financial burden status

TABLE 1

	All adult liver transplant recipients (n = 207)		Low financial burden (n = 159)	High financial burden (n = 48)	P
Age at survey, y	62.6 [53.9–68.7]	63.2 [55.1–69.0]	59.1 [53.2–66.4]	0.09	
Age at transplant, y	57.2 [49.5–63.5]	58.2 [51.2–64.5]	55.2 [45.6–60.6]	0.04	
MELD-Na at transplant	22.5 [15–30]	22 [16–30]	23 [15–31]	0.82	
Months since transplant	34 [9–89]	37 [7–88]	30.5 [13.5–96]	0.26	
Survivorship stage (y), n (%)					
1	64 (30.9)	53 (33.3)	11 (22.9)	0.30	
1–5	57 (27.5)	41 (25.8)	16 (33.3)		
5–10	62 (30.0)	49 (30.8)	13 (27.1)		
> 10	24 (11.6)	16 (10.1)	8 (16.7)		
Sex, n (%)					
Male	136 (65.7)	107 (67.3)	29 (60.4)	0.39	
Female	71 (34.3)	52 (32.7)	19 (39.6)		
Marital status, n (%)					
Married	143 (69.1)	111 (69.8)	32 (66.7)	0.72	
Not married	64 (30.9)	48 (30.2)	16 (33.3)		
Race, n (%)					
Non-Hispanic White	178 (86.0)	136 (85.5)	42 (87.5)	0.55	
Non-Hispanic Black	13 (6.3)	10 (6.3)	3 (6.3)		
Non-Hispanic Asian	11 (5.3)	10 (6.3)	1 (2.1)		
Other	5 (2.4)	3 (1.9)	2 (4.2)		
Hispanic, n (%)	14 (6.8)	10 (6.3)	4 (8.3)	0.74	
Educational attainment ^a , n (%)					
High school or lower	78 (37.9)	55 (34.6)	23 (48.9)	0.09	
Some college or higher	128 (62.1)	104 (65.4)	24 (51.1)		
Annual household income, US\$ ^b , n (%)					
< 25,000	46 (22.7)	36 (23.1)	10 (21.3)	0.19	
25,000–49,999	30 (14.8)	21 (13.5)	9 (19.3)		
50,000–99,999	62 (30.5)	43 (27.6)	19 (40.4)		

	All adult liver transplant recipients (n = 207)	Low financial burden (n = 159)	High financial burden (n = 48)	P
100,000–149,999	37 (18.2)	31 (19.9)	6 (12.8)	
> 150,000	28 (13.8)	25 (16.0)	3 (6.4)	
Insurance status ^c , n (%)				0.83
Medicare or Medicaid	82 (41.2)	62 (40.8)	20 (42.6)	
Any private	117 (58.8)	90 (59.2)	27 (57.4)	
Current employment status, n (%)				0.46
Employed	58 (28.0)	47 (29.6)	11 (22.9)	
Unemployed	149 (72.0)	112 (70.4)	37 (77.1)	
Employment status at time of transplant ^d , n (%)				0.43
Working for income	90 (43.3)	67 (42.3)	23 (46.8)	
Not working for income	115 (55.7)	91 (57.1)	24 (51.1)	
Primary indication for transplant, n (%)				0.35
Alcohol	49 (23.7)	35 (22.0)	14 (29.2)	
MASH	42 (20.3)	34 (21.4)	8 (16.7)	
HBV or HCV	46 (22.2)	36 (22.6)	10 (20.8)	
Autoimmune or cholestatic liver disease	34 (16.4)	24 (15.1)	10 (20.8)	
HCC	22 (10.6)	20 (12.6)	2 (4.2)	
Other	14 (6.8)	10 (6.3)	4 (8.3)	
HCC, n (%)	74 (35.7)	60 (37.7)	14 (29.2)	0.28
Number of comorbidities, n (%)				0.23
0	30 (14.5)	26 (16.4)	4 (8.3)	
1	56 (27.1)	45 (28.3)	11 (22.9)	
2	121 (58.5)	88 (55.3)	33 (68.8)	

^aOne subject with missing data.

^bFour subjects with missing data.

^cEight subjects with missing data.

^dTwo subjects with missing data.

Abbreviations: MASH, metabolic dysfunction–associated steatohepatitis; MELD-Na, Model for End-Stage Liver Disease-Sodium.

Associations between high financial burden and financial distress outcomes among adult recipients of liver transplant

TABLE 2

Outcomes	Unadjusted OR (95% CI)	Adjusted^a OR (95% CI)
Loss of savings/assets (n = 85)	15.30 (6.39–36.66)	20.95 (7.90–55.58)
Medical debt/bankruptcy (n = 44)	3.99 (1.94–8.19)	3.58 (1.62–7.91)
Support-seeking (n = 60)	3.85 (1.95–7.60)	5.65 (2.49–12.83)
Delayed or foregone medical care (n = 72)	3.66 (1.87–7.16)	3.95 (1.85–8.42)
Unable to pay for basic necessities (n = 30)	3.64 (1.49–8.91)	5.14 (1.61–16.37)
Any material financial distress (n = 95)	14.00 (5.60–35.02)	19.29 (6.96–53.45)
Any behavioral financial distress (n = 98)	5.40 (2.57–11.38)	8.68 (3.58–21.04)
Any psychological financial distress (n = 15)	2.38 (0.80–7.07)	1.62 (0.37–7.06)

Statistical significance values are bolded.

^aModels adjusted for marital status, household income, current employment, insurance type, and center (p value <0.10).

TABLE 3
Association between high financial burden and HRQOL among adult recipients of liver transplant

Characteristic	EQ-5D Index				EQ-5D VAS			
	Unadjusted		Adjusted ^a		Unadjusted		Adjusted ^a	
	Beta	95% CI	Beta	95% CI	Beta	95% CI	Beta	95% CI
OOP medical costs > 10% of household income	-0.045	-0.096 to 0.006	-0.032	-0.080 to 0.015	-8.34	-14.61 to -2.07	-6.57	-12.63 to -0.51
Current age	0.002	0.000 to 0.003	0.001	-0.001 to 0.003	0.01	-0.20 to 0.23		
Female	-0.007	-0.053 to 0.038			-0.52	-6.13 to 5.09		
Non-White	-0.002	-0.064 to 0.061			1.57	-6.05 to 9.19		
Hispanic	-0.036	-0.123 to 0.050			-4.48	-14.99 to 6.04		
High school education or less	0.003	-0.042 to 0.048			-2.49	-8.00 to 3.02		
Unmarried	-0.070	-0.116 to -0.024	-0.055	-0.102 to -0.007	-3.92	-9.64 to 1.79	-1.05	-6.84 to 4.75
Household income <\$50,000	-0.095	-0.138 to -0.053	-0.058	-0.104 to -0.012	-11.50	-16.69 to -6.31	-8.98	-14.77 to -3.18
Unemployed	-0.094	-0.140 to -0.047	-0.081	-0.130 to -0.032	-10.70	-16.44 to -4.95	-6.69	-12.82 to -0.55
Non-private insurance	-0.040	-0.085 to 0.004	0.002	-0.042 to 0.046	-6.85	-12.34 to -1.37	-2.27	-7.78 to 3.24
Alcohol-associated liver disease	-0.008	-0.060 to 0.044			-1.30	-7.66 to 5.07		
HCC	0.010	-0.064 to 0.080			2.54	-6.22 to 11.30		
1 comorbidity	0.016	-0.045 to 0.078			0.99	-6.53 to 8.50		

Statistical significance values are bolded.

^aModels adjusted for covariates with *p* values <0.10 on univariable analysis.

Abbreviations: EQ-5D, EuroQol-5 Dimension; EQ-VAS, EQ-5D-5L visual analog scale; HRQOL, health-related quality of life; OOP, out-of-pocket.