BMJ Open

The influence of socioeconomic deprivation on quality of life, anxiety and depression in liver transplant recipients: a prospective cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-070422
Article Type:	Original research
Date Submitted by the Author:	23-Nov-2022
Keywords:	Transplant surgery < SURGERY, SOCIAL MEDICINE, Anxiety disorders < PSYCHIATRY, Depression & mood disorders < PSYCHIATRY

Complete List of Authors:
Sgro, Alessandro; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit
Cambridge, WA; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit
Mclean, Kenneth ; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit
Drake, Thomas ; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit
Camilleri-Brennan, J; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit
Knight, Stephen; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit
Pius, Riinu; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics
Diana, Wu; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit
Wigmore, Stephen; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit
Harrison, Ewen ; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

The influence of socioeconomic deprivation on quality of life, anxiety and depression in liver transplant recipients: a prospective cohort study

Sgrò A[1,2], Cambridge WA[1,2], McLean KA[1,2], Drake TM[1,2], Camilleri-Brennan J[2], Knight SR[1,2], Pius R[1], Wu DA[2], Wigmore SJ[2], Harrison EM[1,2].

1. Centre for Medical Informatics, Usher Institute, University of Edinburgh, Edinburgh, UK.

2. Scottish Liver Transplant Unit, University of Edinburgh, Royal Infirmary of Edinburgh, Edinburgh, UK.

Corresponding author:

Prof Ewen Harrison

Centre for Medical Informatics, Usher Institute

University of Edinburgh

Edinburgh EH16 4UX

E-mail: ewen.harrison@ed.ac.uk

Phone Number: 0131 242 3614

Running title: Socioeconomic deprivation in liver recipients

Key words: socioeconomic factors, liver clinical outcome, quality of life

Abstract

Introduction

Socioeconomic deprivation is frequently associated with poor healthcare outcomes. However, the effect of deprivation in liver transplantation (LT) remains poorly understood. This study aimed to identify whether socioeconomic deprivation affects health-related quality of life (HR-QoL), anxiety, depression following LT.

Methods

Post-transplantation patients completed the condition-specific 'Short form of liver disease QOL' questionnaire, the Generalised Anxiety Disorder Questionnaire (GAD-7) and the Patient Health Questionnaire (PHQ-9). The aggregate HR-QoL score (range: 0-100) was derived and multivariable linear regression performed based on sociodemographic and clinical variables to estimate its independent association with Scottish Index of Multiple Deprivation (SIMD) quintiles. The GAD-7 and PHQ-9 questionnaires were used to screen respondents for anxiety and depression, and multivariable logistic regression performed to estimate their independent association with SIMD quintiles.

Results

Of 331 eligible post-transplantation patients, 97.3% (n=322) had a valid SIMD quintile. Quintiles were equally distributed in the cohort, with no significant differences observed in underlying patient characteristics. Following multivariable adjustment, greater socioeconomic deprivation was associated with lower post-transplantation HR-QoL scores, with a difference of 9.7 points (95%CI: 4.6-14.9, p<0.001) between the most and least deprived quintiles. Recipients living in areas of least deprivation were less likely to suffer from anxiety (OR 0.05, 95%CI: 0.00-0.28, p=0.003), depression (OR 0.13, 95%CI: 0.02-0.56, p=0.009).

Conclusion

Despite the highly selected nature of liver transplant recipients, those living in the most deprived areas have a significantly lower HR-QoL and are more likely to suffer from anxiety, depression. More work is required to ensure there is equitable benefit from LT.

Strength and limitations of this study

- Large sample size with a high response rate
- The validated and disease-specific SF-LDQOL questionnaire was used
- Association between SIMD and outcomes not adjusted for comorbidities
- Lack of pre-transplantation HR-QoL scores

Introduction

Liver transplantation (LT) is the only curative treatment for end-stage liver disease. Over the course of the last 50 years, advances in operative technique, immunosuppressive therapy and postoperative management have transformed LT from an experimental procedure to a standard treatment, with 1-year and 5-year survival rates in the UK currently exceeding 90% and 80%, respectively (1,2). More recently, efforts have focused on exploring the impact of LT on health-related quality of life (HR-QoL) (3,4).

Studies have demonstrated that most LT recipients experience a significant improvement in HR-QoL after transplantation compared to pre-transplantation scores, and this is observed across most quality of life domains (5–7). Despite the improvement remaining consistent over time, LT recipients have lower HR-QoL scores than the healthy general population (8,9). Pre-transplantation and post-transplantation variables, such as primary liver disease, re-transplantation or postoperative complications, fail to fully explain this discrepancy between LT recipients and the general population, and it is plausible that socioeconomic disparities may have a causative role (10,11).

Socioeconomic deprivation is known to be a determinant of poor health, shorter life expectancy and increased prevalence of chronic diseases, and, in the field of LT, it has been demonstrated to be associated with poor post-transplantation outcomes (12–16). In the United States of America, inferior insurance cover is linked with greater mortality in adult recipients (17,18). Similarly, greater socioeconomic deprivation is associated with diminished graft and patient survival after paediatric LT (19,20). Lower literacy and education level have also been shown to be associated with increased complication rates post LT (21,22).

Limited evidence is available in the literature on whether deprivation adversely influences HR-QoL and causes psychological distress in LT recipients. This study aimed to estimate the association between socioeconomic deprivation and HR-QoL, anxiety and depression following LT.

Methods

Population

Consecutive adult (≥ 18 years of age) liver transplantation recipients attending the Scottish Liver Transplantation Unit for an outpatient clinic in two different periods (16th July – 3rd September 2015; 15th August – 14th September 2017) were enrolled on a voluntary basis. Formal institutional ethical approval was waived as this study was considered a service evaluation, otherwise involving routinely collected data. This analysis was performed according to STROBE reporting guidelines for observational studies (23).

Data collection

Eligible patients, after verbal consent was obtained, were invited to fill out the validated 'Short form of liver disease quality of life' (SF-LDQOL) questionnaire (24). This tool was used to assess the condition-specific HR-QoL and it includes 36 items distributed over nine domains (symptoms of liver disease, effects of liver disease, concentration/memory, health-related distress, sexual function, quality of sleep, loneliness, hopelessness and stigma of liver disease). The SF-LDQOL questionnaire provides a score for each domain and an overall HR-QoL score (range zero to 100, with higher scores denoting better QoL).

Patients recruited in the second period were also invited to complete the Generalised Anxiety Disorder-7 (GAD-7) and Patient Health Questionnaire-9 (PHQ-9) questionnaires (25,26). The total GAD-7 score ranges from zero to 21, with higher scores indicating greater self-reported anxiety and a total score of ≥10 suggesting a possible diagnosis of anxiety (sensitivity 89%, specificity 82%) (27). The PHQ-9 is used to quantify depression symptoms. It provides a zero to 27 total score and scores ≥10 are 88% sensitive and 88% specific for detecting depression (28).

Socioeconomic deprivation scores were obtained by referencing the patients' postcodes with the Scottish Index of Multiple Deprivation (SIMD) tool (29). The SIMD is the Scottish Government's tool used to identify areas subject to deprivation, based upon factors including income, employment, education, health, housing, crime, and access to essential services. It enables a deprivation score to be assigned to any postcode and the lower the

score, the more deprived the area. The SIMD is a very granular epidemiological tool, with each data zone consisting of between 500 and 1000 household residents. We used the tool to assign every patient to a SIMD quintile from 1 to 5, with quintile 1 representing the most deprived postcodes in Scotland and quintile 5 the least.

Statistical analyses

Patient characteristics were summarized to compare differences between SIMD quintiles. Continuous data were summarised as a median and analysed using the Kruskal-Wallis test. Categorical data are presented as frequencies and percentages, and differences in proportions were tested using chi-squared (X^2) or Fisher's exact tests. All SF-LDQOL questionnaire responses were assigned to a value based upon the original Likert scale and summated into a mean score for each domain (scaled to value out of 100). All domains were equally weighted before being summated into a mean overall score. The total GAD-7 and PHQ-9 scores were used to determine whether respondents had a possible diagnosis of anxiety and depression, respectively, by using the validated ≥10 cut-off.

Differences in overall HR-QoL were adjusted using a multiple linear regression model. Variables used included: SIMD quintile; age (years); sex (male, female); body mass index (BMI); time since transplantation (years); primary liver disease (alcoholic, cholestatic, non-alcoholic fatty liver disease (NAFLD), viral (hepatitis B or C), or other aetiology); hepatocellular carcinoma (HCC) status (present, absent); pre-transplantation Model of End-Stage Liver Disease (MELD) category (<15, 15–20, ≥21); transplantation status (first transplant, re-transplanted); and type of organ (donation after brainstem death organ (DBD-organ), donation after circulatory death organ (DCD-organ)). These variables are routinely available at UK Liver Transplant Units and could plausibly affect HR-QoL. First-order interactions were checked and included in the model if found to be influential. Final model selection was guided by minimisation of the Akaike Information Criterion (AIC).

Multivariable logistic regression was used to estimate the independent association of SIMD with anxiety (GAD-7 score ≥10) and depression (PHQ-9 score ≥10). In addition to the variables used in the multiple linear

regression model, clinical history of anxiety (yes, no) and depression (yes, no) were included in the logistic regression models. These were defined as either a documented diagnosis of anxiety/depression made by a mental health specialist or the patient having a long-term (>4 weeks) prescription for anxiolytics/antidepressants. First order interactions were checked before final model selection, which was guided by minimisation of the AIC.

The threshold of statistical significance was set at P <0.05 *a priori*. Statistical analyses were conducted in R v3.3.4 (R Foundation for Statistical Computing, Vienna, Austria) with the tidyverse and finalfit packages.

Patient and Public Involvement

No patients were engaged in setting the research question or the outcome measures, nor were any patients involved in the study's design or implementation. There are no plans to disseminate the results of the research directly to study participants.

Results

Over both study periods, 468 patients were found to be eligible for inclusion (**Fig. 1**). Of these, 74 (15.8%) did not participate, 47 (10.0%) were not encountered at the outpatient clinic and 16 (3.4%) handed in incomplete questionnaires. Out of the 331 respondents (70.7%) with complete questionnaires, nine had an invalid postcode and could not be allocated to a SIMD quintile. Therefore, 322 patients (68.8%) were included in the final analyses, with all 322 having a complete SF-LDQOL questionnaire and 150 also having filled out both GAD-7 and PHQ-9 tools.

Patients' characteristics for the overall cohort and the GAD-7 and PHQ-9 subgroup are summarised in **Table 1** and **Table 2**, respectively. The SIMD quintiles were equally distributed in both groups with no major differences observed in the underlying patient characteristics. The median post-transplantation HR-QoL score was 77.0 (IQR: 66.0-84.0) and the overall prevalence of symptoms of anxiety and depression was 21.3% (32/150) and 28% (42/150), respectively. A description of primary liver diseases included within the "other" category is provided in **Table S1**.

Multiple linear regression

In the overall cohort, patients living in most deprived areas had a significantly lower overall HR-QoL score (**Table 1**). Following multivariable adjustment, greater socioeconomic deprivation remained associated with lower post-transplantation HR-QoL, with a difference of 9.7 points (95% CI: 4.5-14.9, p<0.001) between the most and least deprived quintiles (**Fig. 2, Table S2**). There was no significant difference in HR-QoL associated with primary liver disease, transplantation status or receipt of a DCD-organ, and the overall HR-QoL remained stable over time (**Table S2**).

Multivariable logistic regression

In the GAD-7 and PHQ-9 subgroup, recipients living in areas of least deprivation were less likely to suffer from anxiety and depression (**Table 2**). This persisted after adjustment for baseline characteristics, with the least deprived quintile significantly associated with fewer possible diagnoses

Table 1: Patients' demographics for the overall cohort.

		Scottish Index of Multiple Deprivation (SIMD)						
		SIMD 1 (most deprived) (n=57)	SIMD 2 (n=66)	SIMD 3 (n=77)	SIMD 4 (n=60)	SIMD 5 (least deprived) (n=62)	Total (n=322)	p
Quality of Life (SF-LDQOL)	Median (IQR)	71.0 (62.0-82.0)	74.0 (60.8-82.8)	75.0 (66.0-86.0)	79.0 (73.5-86.0)	80.0 (69.8-87.8)	77.0 (66.0-84.0)	0.002
Age (years)	Median (IQR)	55.0 (45.0-62.0)	57.5 (49.0-65.0)	57.0 (47.0-66.0)	61.5 (55.5-72.2)	61.0 (55.0-64.0)	59.0 (49.0-65.0)	0.070
Sex	Male	34 (59.6)	26 (39.4)	47 (61.0)	31 (51.7)	38 (61.3)	176 (54.7)	0.053
	Female	23 (40.4)	40 (60.6)	30 (39.0)	29 (48.3)	24 (38.7)	146 (45.3)	
BMI (kg/m^2)	Median (IQR)	26.6 (23.3-31.2)	27.2 (22.9-30.9)	27.5 (24.0-30.1)	26.7 (24.1-30.3)	26.7 (23.5-30.2)	26.8 (6.9)	0.922
Time since transplantation (years)	Median (IQR)	2.2 (1.1-5.8)	2.4 (0.9-6.4)	3.7 (0.9-8.0)	1.0 (0.5-3.9)	2.7 (1.0-6.5)	2.4 (0.8-6.1)	0.021
Primary liver disease	ALD	15 (26.3)	12 (18.2)	17 (22.1)	15 (25.0)	13 (21.0)	73 (22.7)	0.938
	Cholestatic	11 (19.3)	19 (28.8)	19 (24.7)	13 (21.7)	16 (25.8)	78 (24.2)	
	Viral	9 (15.8)	8 (12.1)	9 (11.7)	8 (13.3)	10 (16.1)	44 (13.7)	
	NAFLD	5 (8.8)	4 (6.1)	7 (9.1)	9 (15.0)	7 (11.3)	32 (9.9)	
	Other	17 (29.8)	23 (34.8)	25 (32.5)	15 (25.0)	16 (25.8)	95 (29.5)	
HCC status	No	44 (77.2)	51 (77.3)	64 (83.1)	48 (80.0)	49 (79.0)	256 (79.5)	0.906
	Yes	13 (22.8)	15 (22.7)	13 (16.9)	12 (20.0)	13 (21.0)	66 (20.5)	
MELD score	<15	20 (35.1)	13 (19.7)	21 (27.3)	21 (35.0)	14 (22.6)	89 (27.6)	0.158
	15-20	13 (22.8)	19 (28.8)	16 (20.8)	11 (18.3)	23 (37.1)	82 (25.5)	
	>20	22 (38.6)	33 (50.0)	37 (48.1)	28 (46.7)	23 (37.1)	141 (43.8)	
	Missing	2 (3.5)	1 (1.5)	3 (3.9)	2 (3.3)	2 (3.2)	10 (3.1)	
Transplantation status	First transplant	49 (86.0)	59 (89.4)	69 (89.6)	56 (93.3)	50 (80.6)	283 (87.9)	0.260
	Re-transplanted	8 (14.0)	7 (10.6)	8 (10.4)	4 (6.7)	12 (19.4)	39 (12.1)	
Type of organ	DBD-organ	49 (86.0)	56 (84.8)	65 (84.4)	51 (85.0)	49 (79.0)	269 (83.5)	0.596
	DCD-organ	6 (10.5)	9 (13.6)	10 (13.0)	7 (11.7)	13 (21.0)	46 (14.3)	
	Missing	2 (3.5)	1 (1.5)	2 (2.6)	2 (3.3)	0 (0.0)	7 (2.2)	

Data are percentages unless otherwise stated.

Abbreviations: SIMD: Scottish Index of Multiple Deprivation; SF-LDQOL: Short Form of Liver Disease Quality of Life; IQR: Interquartile Range; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

Table 2: Patients' demographics for the subgroup that completed the GAD-7 and PHQ-9 questionnaires.

		Scottish Index of Multiple Deprivation (SIMD)						
		SIMD 1 (most deprived) (n=30)	SIMD 2 (n=29)	SIMD 3 (n=37)	SIMD 4 (n=29)	SIMD 5 (least deprived) (n=25)	Total (n=150)	p
Anxiety (GAD-7 score ≥10)	No	16 (53.3)	22 (75.9)	31 (83.8)	26 (89.7)	23 (92.0)	118 (78.7)	0.002
	Yes	14 (46.7)	7 (24.1)	6 (16.2)	3 (10.3)	2 (8.0)	32 (21.3)	
Depression (PHQ-9 score ≥10)	No	14 (46.7)	20 (69.0)	28 (75.7)	26 (89.7)	20 (80.0)	108 (72.0)	0.004
	Yes	16 (53.3)	9 (31.0)	9 (24.3)	3 (10.3)	5 (20.0)	42 (28.0)	
Age (years)	<40	7 (23.3)	7 (24.1)	6 (16.2)	2 (6.9)	4 (16.0)	26 (17.3)	0.295
	40-59	15 (50.0)	12 (41.4)	16 (43.2)	9 (31.0)	11 (44.0)	63 (42.0)	
	≥60	8 (26.7)	10 (34.5)	15 (40.5)	18 (62.1)	10 (40.0)	61 (40.7)	
Sex	Male	21 (70.0)	14 (48.3)	24 (64.9)	14 (48.3)	13 (52.0)	86 (57.3)	0.281
	Female	9 (30.0)	15 (51.7)	13 (35.1)	15 (51.7)	12 (48.0)	64 (42.7)	
BMI	Underweight-Normal	13 (43.3)	9 (31.0)	15 (40.5)	6 (20.7)	8 (32.0)	51 (34.0)	0.289
	Overweight	9 (30.0)	10 (34.5)	15 (40.5)	8 (27.6)	9 (36.0)	51 (34.0)	
	Obese	8 (26.7)	10 (34.5)	7 (18.9)	15 (51.7)	8 (32.0)	48 (32.0)	
Time since transplantation (years)	<1	6 (20.0)	11 (37.9)	16 (43.2)	16 (55.2)	4 (16.0)	53 (35.3)	0.013
	1-5	18 (60.0)	12 (41.4)	10 (27.0)	5 (17.2)	13 (52.0)	58 (38.7)	
	>5	6 (20.0)	6 (20.7)	11 (29.7)	8 (27.6)	8 (32.0)	39 (26.0)	
Primary liver disease	ALD	7 (23.3)	5 (17.2)	12 (32.4)	6 (20.7)	6 (24.0)	36 (24.0)	0.707
	Cholestatic	8 (26.7)	9 (31.0)	8 (21.6)	6 (20.7)	8 (32.0)	39 (26.0)	
	Viral	4 (13.3)	6 (20.7)	3 (8.1)	3 (10.3)	3 (12.0)	19 (12.7)	
	NAFLD	4 (13.3)	1 (3.4)	4 (10.8)	7 (24.1)	1 (4.0)	17 (11.3)	
	Other	7 (23.3)	8 (27.6)	10 (27.0)	7 (24.1)	7 (28.0)	39 (26.0)	
HCC status	No	25 (83.3)	19 (65.5)	30 (81.1)	23 (79.3)	20 (80.0)	117 (78.0)	0.490
	Yes	5 (16.7)	10 (34.5)	7 (18.9)	6 (20.7)	5 (20.0)	33 (22.0)	
MELD score	<15	12 (40.0)	9 (31.0)	15 (40.5)	11 (37.9)	9 (36.0)	56 (37.3)	0.173
	15-20	7 (23.3)	13 (44.8)	10 (27.0)	3 (10.3)	9 (36.0)	42 (28.0)	
	>20	10 (33.3)	6 (20.7)	10 (27.0)	13 (44.8)	5 (20.0)	44 (29.3)	
	Missing	1 (3.3)	1 (3.4)	2 (5.4)	2 (6.9)	2 (8.0)	8 (5.3)	
Transplantation status	First transplant	24 (80.0)	27 (93.1)	33 (89.2)	27 (93.1)	15 (60.0)	126 (84.0)	0.004
	Re-transplanted	6 (20.0)	2 (6.9)	4 (10.8)	2 (6.9)	10 (40.0)	24 (16.0)	
Type of organ	DBD-organ	26 (86.7)	23 (79.3)	29 (78.4)	22 (75.9)	20 (80.0)	120 (80.0)	0.707
	DCD-organ	2 (6.7)	5 (17.2)	6 (16.2)	5 (17.2)	5 (20.0)	23 (15.3)	
	Missing	2 (6.7)	1 (3.4)	2 (5.4)	2 (6.9)	0 (0.0)	7 (4.7)	
Clinical history of depression	No	24 (80.0)	25 (86.2)	32 (86.5)	27 (93.1)	23 (92.0)	131 (87.3)	0.578
	Yes	6 (20.0)	4 (13.8)	5 (13.5)	2 (6.9)	2 (8.0)	19 (12.7)	
Clinical history of anxiety	No	29 (96.7)	28 (96.6)	37 (100.0)	28 (96.6)	25 (100.0)	147 (98.0)	0.707
	Yes	1 (3.3)	1 (3.4)	0 (0.0)	1 (3.4)	0 (0.0)	3 (2.0)	

Data are percentages unless otherwise stated.

Abbreviations: SIMD: Scottish Index of Multiple Deprivation; GAD-7: Generalised Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9; IQR: Interquartile Range; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

of anxiety (OR 0.05, 95% CI: 0.00-0.28, p=0.003) and depression (OR 0.13, 95% CI: 0.02-0.56, p=0.009) (**Fig. 3, Fig. 4, Table S3, Table S4**). Pre-transplantation MELD scores >20 were found to be protective towards post-transplantation anxiety (OR 0.21, 95% CI: 0.04-0.82, p=0.033), whereas receipt of a DCD-organ was associated with greater anxiety (OR 4.65, 95% CI: 1.11-20.07, p=0.034) (**Table S3**). Although a post-transplantation survival time greater than five years was associated with worse depression (OR 4.52, 95% CI: 1.15-19.40, p=0.035), recipients older than 60 years of age were found to be less likely to suffer from depressive disorders (**Table S4**).

Discussion

Most LT recipients experience a significant improvement in HR-QoL after transplantation, but it is not completely understood why they do not achieve HR-QoL scores comparable with the healthy general population (6,8). There is a paucity of data on the factors that may influence HR-QoL outcomes after LT. This study aimed to explore the relationship between socioeconomic deprivation and HR-QoL, anxiety and depression among LT recipients.

In our study, greater socioeconomic deprivation was associated with lower post-transplantation HR-QoL scores and recipients living in the most deprived areas were more likely to suffer from anxiety and depression. There is evidence to suggest that psychological problems after LT are associated with increased morbidity and mortality, and that outcomes could be improved with adequate treatment (30–32). This makes it important to identify at an early stage patients who are at risk of psychological problems. Our findings can help clinicians identify LT recipients at risk for anxiety, depression and lower HR-QoL scores, and who may require earlier interventions aimed at improving long-term HR-QoL and minimising morbidity and mortality.

Scarce evidence is available in the literature on the impact of deprivation on HR-QoL, anxiety and depression in LT recipients. A cross-sectional study from Brazil suggested that higher income and education level were predictors of higher HR-QoL scores in some quality of life domains (33). Similarly, employment was associated with higher HR-QoL scores and fewer depressive symptoms in German LT recipients (34). Income, education level and employment were also found to positively influence post-transplantation HR-QoL in a study conducted at the University of California Los Angeles (35). Although these are significant findings, the above studies failed to include important social determinants of health, such as access to essential services, housing and crime (16). To overcome this limitation, we used a more inclusive socioeconomic deprivation score, calculated as the level of deprivation of an area across seven domains: income, employment, education, health, access to services, crime and housing.

In our study, long-term HR-QoL remained stable over time and was not affected by re-transplantation or primary liver disease. This is consistent with the current balance of evidence (9,36–39).

The prevalence rates of symptoms of anxiety in our cohort (21.3%) was in line with prevalence rates described by other studies (range 20% to 25%) (40,41). Patients who received a DCD-organ were estimated to have significantly worse anxiety symptoms and this may reflect the increased risk of morbidity in DCD-organ recipients (42,43). It is not clear why pre-transplantation MELD scores >20 were found to be protective towards post-transplantation anxiety. We can hypothesise that recipients with MELD scores >20 had the greatest benefit from LT and the much improved health is now contributing to lower anxiety prevalence rates.

Depressive symptoms were more prevalent in our sample (28.0%) than in other studies (range 15% to 20%) (40,44,45). A possible explanation is that most studies have focused on the first five years after LT, whilst in our study over one fourth of patients that completed the PHQ-9 questionnaire were over five years post-transplantation. There is evidence to suggest that depressive symptoms might be highly prevalent in long-term (>10 years) LT recipients and this is reflected by a post-transplantation survival time greater than five years being associated with greater odds of depression in our study (46).

In contrast with the prevalence rates of symptoms of anxiety and depression found in our sample, a significantly smaller proportion of LT recipients had a clinical history of anxiety (2%, 19/150) and depression (12.7%, 3/150). This highlights how psychological problems might be underdiagnosed following LT and reinforces the concept that monitoring psychological problems and psychological counselling should be part of the routine care of transplant recipients.

There are some limitations to this study. The cross-sectional design of the study may have influenced the HR-QoL, anxiety and depression results observed. Frequent clinic attendees, due to shorter postoperative period or complications, were more likely to have been encountered, and patients who died, or were too unwell to attend the clinic, were not included in the study. We tried to minimise the resulting bias with a large sample size, high response rate and two different data collection periods. Secondly, although it should be mentioned

that England, Wales and Northern Ireland have indexes of multiple deprivation based on the same domains of the SIMD, this was a single-centre study that used a Scotland-specific index of deprivation and therefore the results may not be generalisable to other centres. Thirdly, differently from individual-based scores, SIMD gives an area-based deprivation score. This introduces potential bias since not every person in a highly deprived area will themselves be experiencing high levels of deprivation. However, area-based scores have been shown to be valid proxies in the absence of individual-based scores (47,48). Moreover, we did not adjust for any comorbidities. This could be an important confounding factor since socioeconomic deprivation has been shown to be associated with higher rates of comorbidity and the presence of comorbidities may lead to poorer quality of life (14,15,49). Future studies should adjust for comorbidities to enable a more accurate estimation of the association between socioeconomic deprivation and HR-QoL. In addition, to the best of our knowledge, no data is currently available in the literature about the relationship between SIMD quintiles and QoL, anxiety and depression scores in healthy subjects. Therefore, we could not determine whether the observed association between high deprivation and worse QoL, anxiety, depression scores is also present in the general population, irrespective of LT. Finally, we did not collect pre-transplantation HR-QoL scores. It is plausible that the lower HR-QoL scores in more deprived recipients could be explained by lower pre-transplantation scores than less deprived transplant candidates. However, this assumes that there is an equal increase in HR-QoL after LT across socioeconomic deprivation quintiles. Future studies should explore the association between socioeconomic deprivation and change in HR-QoL before and after LT to assess whether there is equitable benefit from LT.

In conclusion, despite the highly selected nature of liver transplant recipients, those living in the most deprived areas had a significantly lower HR-QoL and were more likely to suffer from anxiety and depression. Our results also suggest psychological problems might be underdiagnosed in transplant recipients. These findings may help clinicians identify patients at risk for anxiety, depression and lower HR-QoL scores, and who may require earlier interventions aimed at improving long-term HR-QoL and minimising morbidity and mortality. More work is required to ensure there is equitable benefit from LT.

Contributorship statement

KAM, AS, EMH and RP designed the study. KAM, AS, WAC and JC collected data. KAM, AS, TMD and EMH analysed data, and all the authors contributed to writing and critical revision of this paper.

Competing interests

TMD receives research funding from Aligos therapeutics for unrelated work.

Funding

None

Data sharing statement

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval statement

Formal institutional ethical approval was waived as this study was considered a service evaluation, otherwise involving routinely collected data.

References

1. Zarrinpar A, Busuttil RW. Liver transplantation: past, present and future. Nat Rev Gastroenterol Hepatol 2013 107. 2013 Jun 11;10(7):434–40.
2. National Health Service Blood and Transplant. Annual report on liver transplantation: Report for 2019/2020 (1 April 2010–31 March 2020). NHS. 2020.
3. Onghena L, Develtere W, Poppe C, Geerts A, Troisi R, Vanlander A, et al. Quality of life after liver transplantation: State of the art. World J Hepatol. 2016 Jun 28;8(18):749.
4. Cristin DJ, Forman LM, Jackson WE. Beyond Survival: Targeting Health-Related Quality of Life Outcomes After Liver Transplantation. Clin Liver Dis. 2021 May 1;17(5):359–64.
5. McLean KA, Drake TM, Sgrò A, Camilleri-Brennan J, Knight SR, Ots R, et al. The effect of liver transplantation on patient-centred outcomes: a propensity-score matched analysis. Transpl Int. 2019 Aug 1;32(8):808–19.
6. Telles-Correia D, Barbosa A, Mega I, Mateus E, Monteiro E. When Does Quality of Life Improve After Liver Transplantation? A Longitudinal Prospective Study. Transplant Proc. 2009 Apr 1;41(3):904–5.
7. Ratcliffe J, Longworth L, Young T, Bryan S, Burroughs A, Buxton M. Assessing health-related quality of life pre– and post–liver transplantation: A prospective multicenter study. Liver Transplant. 2002 Mar 1;8(3):263–70.
8. Tome S, Wells JT, Said A, Lucey MR. Quality of life after liver transplantation. A systematic review. J Hepatol. 2008 Apr 1;48(4):567–77.
9. Duffy JP, Kao K, Ko CY, Farmer DG, McDiarmid S V., Hong JC, et al. Long-term patient outcome and quality of life after liver transplantation: Analysis of 20-year survivors. Ann Surg. 2010 Oct;252(4):652–9.
10. Bona M De, Ponton P, Ermani M, Iemmolo RM, Feltrin A, Boccagni P, et al. The impact of liver disease and medical complications on quality of life and psychological distress before and after liver transplantation. J Hepatol. 2000 Oct 1;33(4):609–15.
11. Kousoulas L, Neipp M, Barg-Hock H, Jackobs S, Strassburg CP, Klempnauer J, et al. Health-related quality of life in adult transplant recipients more than 15 years after orthotopic liver transplantation.

Transpl Int. 2008 Nov 1;21(11):1052–8.

12. Shaw M, Gordon D, Dorling D, Mitchell R, Davey Smith G. Increasing mortality differentials by residential area level of poverty: Britain 1981–1997. Soc Sci Med. 2000 Jul 1;51(1):151–3.
13. Waitzman NJ, Smith KR. Phantom of the area: poverty-area residence and mortality in the United States. Am J Public Health. 1998;88(6):973.
14. Roux AVD, Merkin SS, Arnett D, Chambless L, Massing M, Nieto FJ, et al. Neighborhood of residence and incidence of coronary heart disease. N Engl J Med. 2001 Jul 12;345(2):99–106.
15. Drey N, Roderick P, Mullee M, Rogerson M. A population-based study of the incidence and outcomes of diagnosed chronic kidney disease. Am J Kidney Dis. 2003 Oct 1;42(4):677–84.
16. Adler JT, Yeh H. Social determinants in liver transplantation. Clin Liver Dis. 2016 Jan 1;7(1):15.
17. Stepanova M, Qahtani S Al, Mishra A, Younossi I, Venkatesan C, Younossi ZM. Outcomes of liver transplantation by insurance types in the United States. Am J Manag Care. 2020 Apr 1;26(4):E121–6.
18. Young Yoo H, Thuluvath PJ. Outcome of liver transplantation in adult recipients: Influence of neighborhood income, education, and insurance. Liver Transplant. 2004 Feb 1;10(2):235–43.
19. Wadhwani SI, Beck AF, Bucuvalas J, Gottlieb L, Kotagal U, Lai JC. Neighborhood socioeconomic deprivation is associated with worse patient and graft survival following pediatric liver transplantation. Am J Transplant. 2020 Jun 1;20(6):1597–605.
20. Dick AAS, Winstanley E, Ohara M, Blondet NM, Healey PJ, Perkins JD, et al. Do funding sources influence long-term patient survival in pediatric liver transplantation? Pediatr Transplant. 2021 Mar 1;25(2):e13887.
21. Serper M, Patzer RE, Reese PP, Przytula K, Koval R, Ladner DP, et al. Medication misuse, nonadherence, and clinical outcomes among liver transplant recipients. Liver Transplant. 2015 Jan 1;21(1):22–8.
22. Lieber SR, Volk ML. Non-adherence and graft failure in adult liver transplant recipients. Dig Dis Sci. 2013 Mar 2;58(3):824–34.
23. 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. J Clin Epidemiol. 2008;61(4):344–9.

24. Kanwal F, Spiegel BMR, Hays RD, Durazo F, Han SB, Saab S, et al. Prospective validation of the short form liver disease quality of life instrument. Aliment Pharmacol Ther. 2008 Nov 1;28(9):1088–101.

25. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A Brief Measure for Assessing Generalized Anxiety Disorder: The GAD-7. Arch Intern Med. 2006 May 22;166(10):1092–7.

26. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001 Sep 1;16(9):606–13.

27. Löwe B, Decker O, Müller S, Brähler E, Schellberg D, Herzog W, et al. Validation and standardization of the generalized anxiety disorder screener (GAD-7) in the general population. Med Care. 2008 Feb;46(3):266–74.

28. Levis B, Benedetti A, Thombs BD. Accuracy of Patient Health Questionnaire-9 (PHQ-9) for screening to detect major depression: individual participant data meta-analysis. BMJ. 2019 Apr 9;365.

29. Scottish Executive National Statistics. Scottish Index of Multiple Deprivation (SIMD): Technical Notes. 2016.

30. Rogal SS, Dew MA, Fontes P, Dimartini AF. Early Treatment of Depressive Symptoms and Long-Term Survival After Liver Transplantation. Am J Transplant. 2013 Apr 1;13(4):928–35.

31. Amanda Dew M, Rosenberger EM, Myaskovsky L, DiMartini AF, DeVito Dabbs AJ, Posluszny DM, et al. Depression and anxiety as risk factors for morbidity and mortality after organ transplantation: A systematic review and meta-analysis. Transplantation. 2016;100(5):988–1003.

32. Rogal SS, Landsittel D, Surman O, Chung RT, Rutherford A. Pretransplant depression, antidepressant use, and outcomes of orthotopic liver transplantation. Liver Transplant. 2011 Mar 1;17(3):251–60.

33. de Aguiar MIF, Braga VAB, Garcia JHP, de Lima CA, de Almeida PC, e Souza AMA, et al. Quality of life in liver transplant recipients and the influence of sociodemographic factors. Rev da Esc Enferm da USP. 2016;50(3):0411–8.

34. Zahn A, Seubert L, Jünger J, Schellberg D, Heinz Weiss K, Schemmer P, et al. Factors influencing long-term quality of life and depression in German liver transplant recipients: A single-centre cross-sectional study. Ann Transplant. 2013;18(1):327–35.

35. Saab S, Bownik H, Ayoub N, Younossi Z, Durazo F, Han S, et al. Differences in health-related quality of life scores after orthotopic liver transplantation with respect to selected socioeconomic factors. Liver

Transplant. 2011 May;17(5):580–90.

36. Estraviz B, Quintana JM, Valdivieso A, Bilbao A, Padierna A, de Urbina JO, et al. Factors influencing change in health-related quality of life after liver transplantation. Clin Transplant. 2007 Jul 1;21(4):481–99.

37. Åberg F, Höckerstedt K, Roine RP, Sintonen H, Isoniemi H. Influence of liver-disease etiology on long-term quality of life and employment after liver transplantation. Clin Transplant. 2012 Sep 1;26(5):729–35.

38. Desai R, Jamieson N V., Gimson AE, Watson CJ, Gibbs P, Bradley JA, et al. Quality of life up to 30 years following liver transplantation. Liver Transplant. 2008 Oct 1;14(10):1473–9.

39. Yang LS, Shan LL, Saxena A, Morris DL. Liver transplantation: a systematic review of long-term quality of life. Liver Int. 2014 Oct 1;34(9):1298–313.

40. Russell RT, Feurer ID, Wisawatapnimit P, Salomon RM, Pinson CW. The effects of physical quality of life, time, and gender on change in symptoms of anxiety and depression after liver transplantation. J Gastrointest Surg. 2008 Jan 23;12(1):138–44.

41. Van Ginneken BTJ, van den Berg-Emons RJG, van der Windt A, Tilanus HW, Metselaar HJ, Stam HJ, et al. Persistent fatigue in liver transplant recipients: a two-year follow-up study. Clin Transplant. 2010 Jan 1;24(1):E10–6.

42. Callaghan CJ, Charman SC, Muiesan P, Powell JJ, Gimson AE, Van Der Meulen JHP. Outcomes of transplantation of livers from donation after circulatory death donors in the UK: a cohort study. BMJ Open. 2013;3(9).

43. De Vera ME, Lopez-Solis R, Dvorchik I, Campos S, Morris W, Demetris AJ, et al. Liver Transplantation Using Donation After Cardiac Death Donors: Long-Term Follow-Up from a Single Center. Am J Transplant. 2009 Apr 1;9(4):773–81.

44. Aadahl M, Hansen BA, Kirkegaard P, Groenvold M. Fatigue and physical function after orthotopic liver transplantation. Liver Transplant. 2002 Mar 1;8(3):251–9.

45. Collis I, Burroughs A, Rolles K, Lloyd G. Psychiatric and Social Outcome of Liver Transplantation. Br J Psychiatry. 1995;166(4):521–4.

46. Annema C, Roodbol PF, Stewart RE, Porte RJ, Ranchor A V. Prevalence of psychological problems

and associated transplant-related variables at different time periods after liver transplantation. Liver Transplant. 2015 Apr 1;21(4):524–38.

47. Krieger N. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. Am J Public Health. 1992;82(5):703–10.

48. Krieger N, Chen JT, Waterman PD, Soobader MJ, Subramanian S V., Carson R. Geocoding and Monitoring of US Socioeconomic Inequalities in Mortality and Cancer Incidence: Does the Choice of Area-based Measure and Geographic Level Matter?The Public Health Disparities Geocoding Project. Am J Epidemiol. 2002 Sep 1;156(5):471–82.

49. Xuan J, Kirchdoerfer LJ, Boyer JG, Norwood GJ. Effects of comorbidity on health-related quality-of-life scores: an analysis of clinical trial data. Clin Ther. 1999 Feb 1;21(2):383–403.

Figure legends

Figure 1. Flow diagram of patient inclusion.

Abbreviations: SIMD: Scottish Index of Multiple Deprivation; SF-LDQOL: Short Form of Liver Disease Quality of Life; GAD-7: Generalised Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9

Figure 2. Forest plots of the effect size for socioeconomic deprivation on post-transplantation HR-QoL: A) reduced model; B) final model.

Abbreviations: SF-LDQOL: Short Form of Liver Disease Quality of Life; SIMD: Scottish Index of Multiple Deprivation; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

Figure 3. Forest plots of the effect size for socioeconomic deprivation on post-transplantation anxiety: A) reduced model; B) final model.

Abbreviations: SF-LDQOL: Short Form of Liver Disease Quality of Life; SIMD: Scottish Index of Multiple Deprivation; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death; GAD-7: Generalised Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9.

Figure 4. Forest plots of the effect size for socioeconomic deprivation on post-transplantation depression: A) reduced model; B) final model.

Abbreviations: SF-LDQOL: Short Form of Liver Disease Quality of Life; SIMD: Scottish Index of Multiple Deprivation; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death; GAD-7: Generalised Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Primary liver disease of patients in the cohort.

Table S2. Multiple linear regression: effect of socioeconomic deprivation on post-transplantation HR-QoL.

Table S3. Multivariable logistic regression: effect of socioeconomic deprivation on post-transplantation anxiety.

Table S4. Multivariable logistic regression: effect of socioeconomic deprivation on post-transplantation depression.

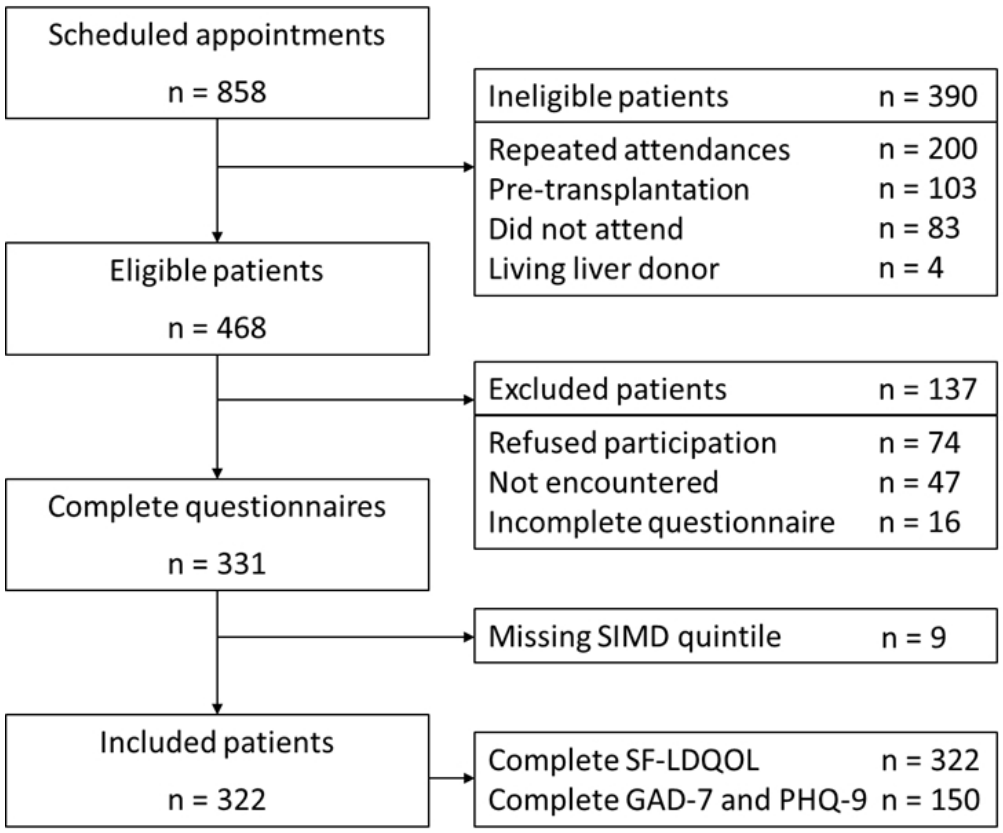


Figure 1

192x160mm (96 x 96 DPI)

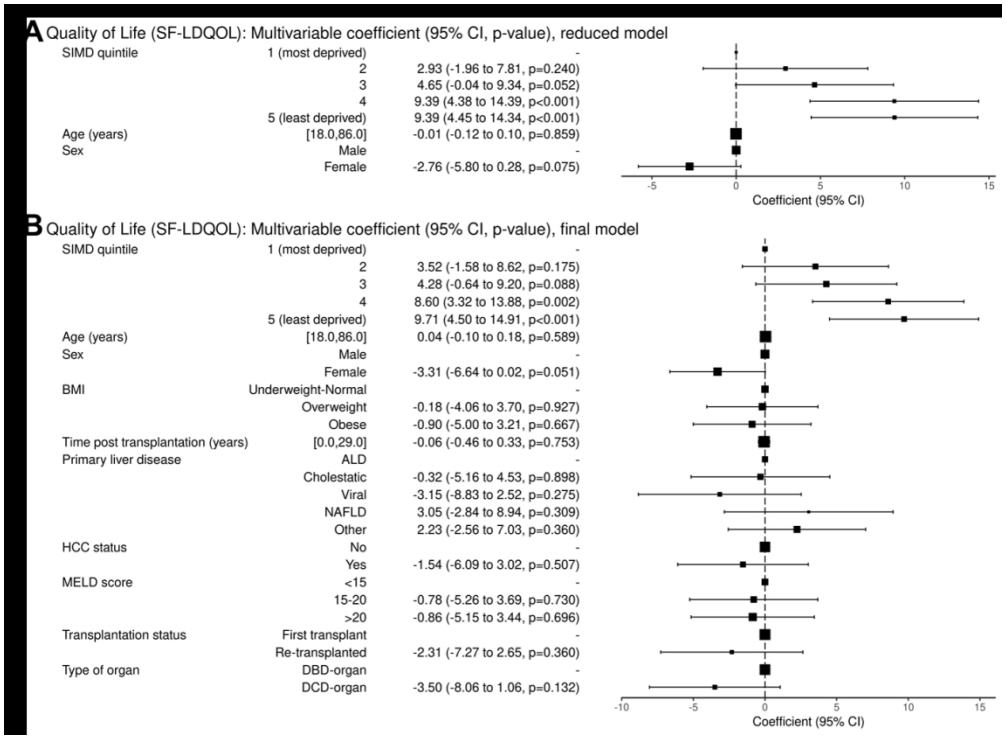


Figure 2

237x173mm (150 x 150 DPI)

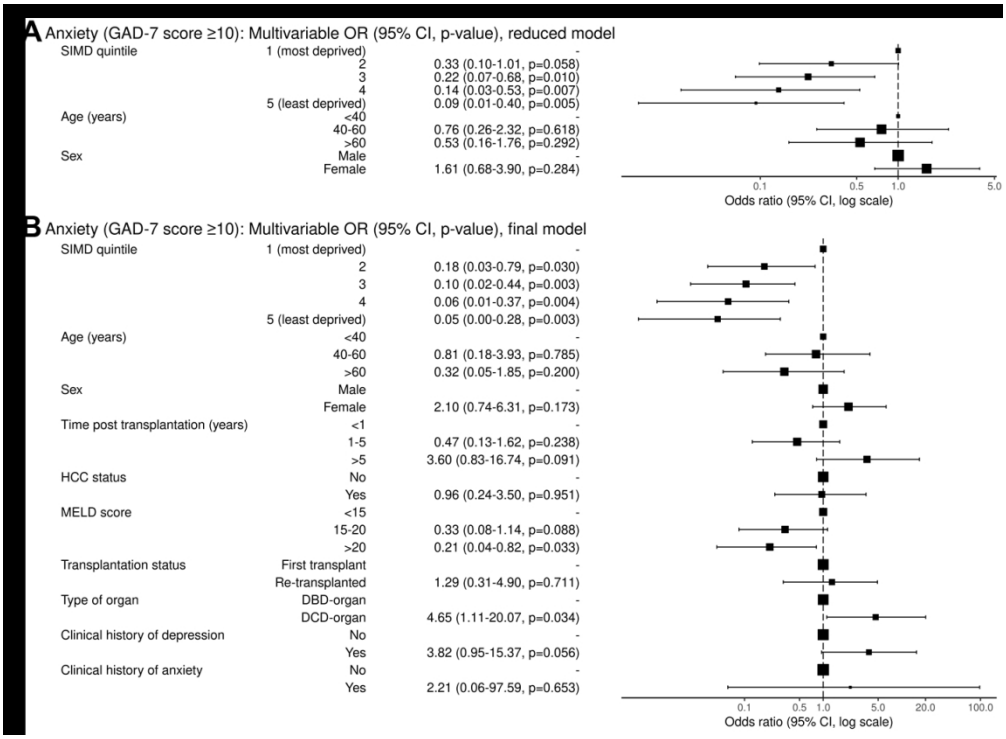


Figure 3

241x176mm (150 x 150 DPI)

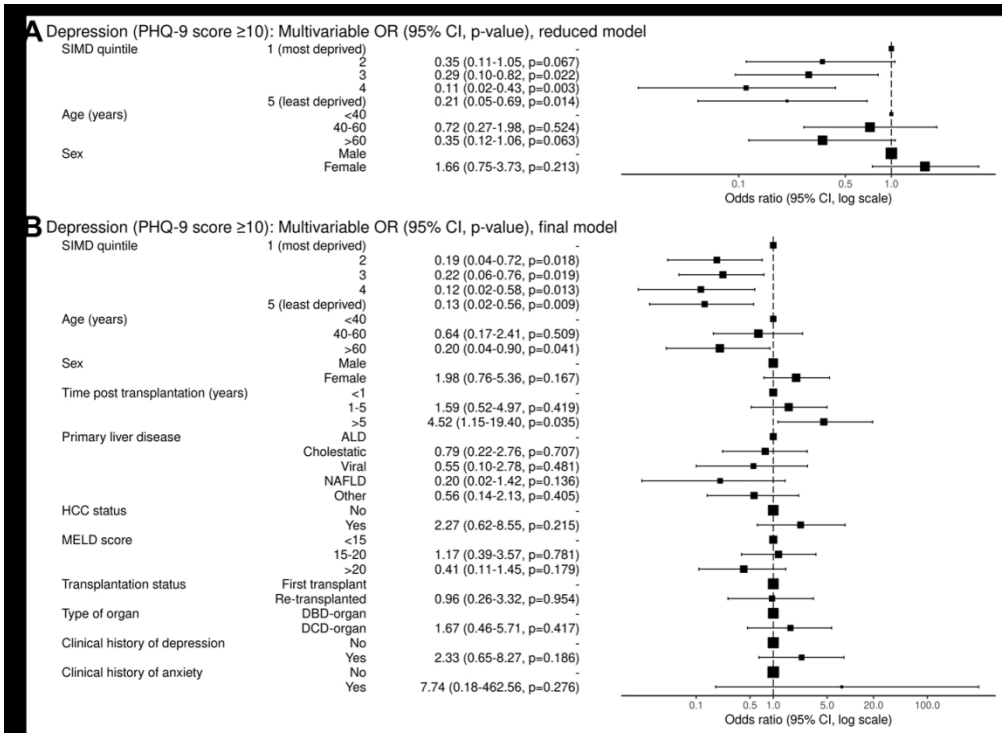


Figure 4

241x175mm (150 x 150 DPI)

The influence of socioeconomic deprivation on quality of life, anxiety and depression in liver transplant recipients: a prospective cohort study

Sgrò A[1,2], Cambridge WA[1,2], McLean KA[1,2], Drake TM[1,2], Camilleri-Brennan J[2], Knight SR[1,2], Pius R[1], Wu DA[2], Wigmore SJ[2], Harrison EM[1,2].

1. Centre for Medical Informatics, Usher Institute, University of Edinburgh, Edinburgh, UK.

2. Scottish Liver Transplant Unit, University of Edinburgh, Royal Infirmary of Edinburgh, Edinburgh, UK.

Supplementary files

Table S1: Primary liver disease of patients in the cohort.

	(n=322)
Alcoholic liver disease	73
Non-alcoholic fatty liver disease (NAFLD)	32
Viral Hepatitis	
Acute hepatic failure - HBV	3
Hepatitis B cirrhosis	1
Hepatitis C cirrhosis	43
Cholestatic	
Biliary atresia	5
Primary biliary cirrhosis	38
Primary sclerosing cholangitis	30
Secondary biliary cirrhosis	1
Congenital biliary disease	1
Paediatric cholestatic liver disease	3
Other primary liver disease	
Acute hepatic failure - other drug toxicity	1
Acute hepatic failure - other	7
Acute hepatic failure - paracetamol hepatotoxicity	6
Acute hepatic failure - serologically indeterminate	4
Alpha-1-antitrypsin deficiency	2
Autoimmune chronic active liver disease	17
Budd-Chiari syndrome	1
Chronic rejection	6
Cryptogenic cirrhosis	16
Hepatic artery thrombosis	4
Hepatocellular carcinoma - cirrhotic	5
Hepatocellular carcinoma - non-cirrhotic	2
Hereditary haemachromatosis	7
Polycystic liver disease	3
Primary non-function	1
Recurrent disease	2
Wilsons disease	3
Other	5

Table S2: Multiple linear regression: effect of socioeconomic deprivation on post-transplantation HR-QoL.

			Quality of Life (SF-LDQOL)		
		Mean (SD)	Univariable coefficient (95% CI)	Multivariable coefficient (95% CI)[1]	Multivariable coefficient (95% CI)[2]
SIMD quintile	1 (most deprived)	69.6 (15.6)	-	-	-
	2	71.9 (15.4)	2.34 (-2.51 to 7.19, p=0.343)	2.93 (-1.96 to 7.81, p=0.240)	3.52 (-1.58 to 8.62, p=0.175)
	3	74.3 (13.3)	4.66 (-0.02 to 9.35, p=0.051)	4.65 (-0.04 to 9.34, p=0.052)	4.28 (-0.64 to 9.20, p=0.088)
	4	78.7 (10.9)	9.10 (4.14 to 14.06, p<0.001)	9.39 (4.38 to 14.39, p<0.001)	8.60 (3.32 to 13.88, p=0.002)
	5 (least deprived)	79.0 (12.4)	9.39 (4.47 to 14.31, p<0.001)	9.39 (4.45 to 14.34, p<0.001)	9.71 (4.50 to 14.91, p<0.001)
Age (years)	[18.0,86.0]	74.7 (14.0)	0.03 (-0.08 to 0.14, p=0.606)	-0.01 (-0.12 to 0.10, p=0.859)	0.04 (-0.10 to 0.18, p=0.589)
Sex	Male	76.0 (13.1)	-	-	-
	Female	73.1 (14.9)	-2.95 (-6.03 to 0.12, p=0.060)	-2.76 (-5.80 to 0.28, p=0.075)	-3.31 (-6.64 to 0.02, p=0.051)
BMI	Underweight-Normal	74.2 (15.0)	-	-	-
	Overweight	75.2 (13.1)	1.03 (-2.70 to 4.77, p=0.586)	-	-0.18 (-4.06 to 3.70, p=0.927)
	Obese	74.1 (14.1)	-0.05 (-3.92 to 3.83, p=0.982)	-	-0.90 (-5.00 to 3.21, p=0.667)
Time post transplantation (years)	[0.0,29.0]	0.2 (0.04)	-0.00 (-0.00 to 0.00, p=0.789)	-	-0.00 (-0.00 to 0.00, p=0.753)
Primary liver disease	ALD	75.2 (11.9)	-	-	-
	Cholestatic	73.7 (15.3)	-1.54 (-6.01 to 2.93, p=0.498)	-	-0.32 (-5.16 to 4.53, p=0.898)
	Viral	70.8 (15.1)	-4.44 (-9.68 to 0.80, p=0.097)	-	-3.15 (-8.83 to 2.52, p=0.275)
	NAFLD	78.1 (12.8)	2.86 (-2.96 to 8.68, p=0.334)	-	3.05 (-2.84 to 8.94, p=0.309)
	Other	75.8 (14.1)	0.54 (-3.74 to 4.81, p=0.805)	-	2.23 (-2.56 to 7.03, p=0.360)
HCC status	No	75.1 (14.1)	-	-	-
	Yes	73.1 (13.8)	-2.02 (-5.82 to 1.79, p=0.297)	-	-1.54 (-6.09 to 3.02, p=0.507)
MELD score	<15	75.1 (11.4)	-	-	-
	15-20	74.7 (14.9)	-0.40 (-4.62 to 3.82, p=0.853)	-	-0.78 (-5.26 to 3.69, p=0.730)
	>20	74.3 (14.9)	-0.74 (-4.48 to 2.99, p=0.695)	-	-0.86 (-5.15 to 3.44, p=0.696)
Transplantation status	First transplant	74.9 (14.2)	-	-	-
	Re-transplanted	73.5 (12.3)	-1.40 (-6.12 to 3.31, p=0.558)	-	-2.31 (-7.27 to 2.65, p=0.360)
Type of organ	DBD-organ	75.1 (13.5)	-	-	-
	DCD-organ	72.1 (16.2)	-3.04 (-7.42 to 1.34, p=0.173)	-	-3.50 (-8.06 to 1.06, p=0.132)

[1]Number in dataframe = 322, Number in model = 322, Missing = 0, Log-likelihood = -1293.93, AIC = 2603.9, R-squared = 0.075, Adjusted R-squared = 0.057
[2]Number in dataframe = 322, Number in model = 306, Missing = 16, Log-likelihood = -1225.31, AIC = 2490.6, R-squared = 0.1, Adjusted R-squared = 0.047
Data are percentages unless otherwise stated.
Abbreviations: SF-LDQOL: Short Form of Liver Disease Quality of Life; SIMD: Scottish Index of Multiple Deprivation; IQR: Interquartile Range; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

Table S3: Multivariable logistic regression: effect of socioeconomic deprivation on post-transplantation anxiety.

				Anxiety (GAD-7 score ≥10)		
		No (n=132)	Yes (n=18)	Univariable OR (95% CI)	Multivariable OR (95% CI)[1]	Multivariable OR (95% CI)[2]
SIMD quintile	1 (most deprived)	16 (53.3)	14 (46.7)	-	-	-
	2	22 (75.9)	7 (24.1)	0.36 (0.11-1.08, p=0.075)	0.33 (0.[illegible]01, p=0.058)	0.18 (0.03-0.79, p=0.030)
	3	31 (83.8)	6 (16.2)	0.22 (0.07-0.66, p=0.009)	0.22 (0.[illegible]68, p=0.010)	0.10 (0.02-0.44, p=0.003)
	4	26 (89.7)	3 (10.3)	0.13 (0.03-0.48, p=0.004)	0.14 (0.[illegible]53, p=0.007)	0.06 (0.01-0.37, p=0.004)
	5 (least deprived)	23 (92.0)	2 (8.0)	0.10 (0.01-0.42, p=0.005)	0.09 (0.[illegible]40, p=0.005)	0.05 (0.00-0.28, p=0.003)
Age (years)	<40	18 (69.2)	8 (30.8)	-	-	-
	40-60	48 (76.2)	15 (23.8)	0.70 (0.26-2.00, p=0.496)	0.76 (0.[illegible]2.32, p=0.618)	0.81 (0.18-3.93, p=0.785)
	>60	52 (85.2)	9 (14.8)	0.39 (0.13-1.18, p=0.091)	0.53 (0.[illegible]1.76, p=0.292)	0.32 (0.05-1.85, p=0.200)
Sex	Male	69 (80.2)	17 (19.8)	-	-	-
	Female	49 (76.6)	15 (23.4)	1.24 (0.56-2.73, p=0.588)	1.61 (0.[illegible]3.90, p=0.284)	2.10 (0.74-6.31, p=0.173)
BMI	Underweight-Normal	38 (74.5)	13 (25.5)	-	-	-
	Overweight	44 (86.3)	7 (13.7)	0.47 (0.16-1.26, p=0.140)	-	-
	Obese	36 (75.0)	12 (25.0)	0.97 (0.39-2.42, p=0.955)	-	-
Time post transplantation (years)	<1	43 (81.1)	10 (18.9)	-	-	-
	1-5	48 (82.8)	10 (17.2)	0.90 (0.34-2.38, p=0.824)	-	0.47 (0.13-1.62, p=0.238)
	>5	27 (69.2)	12 (30.8)	1.91 (0.73-5.12, p=0.189)	-	3.60 (0.83-16.74, p=0.091)
Primary liver disease	ALD	28 (77.8)	8 (22.2)	-	-	-
	Cholestatic	29 (74.4)	10 (25.6)	1.21 (0.42-3.59, p=0.729)	-	-
	Viral	15 (78.9)	4 (21.1)	0.93 (0.22-3.50, p=0.920)	-	-
	NAFLD	15 (88.2)	2 (11.8)	0.47 (0.06-2.16, p=0.372)	-	-
	Other	31 (79.5)	8 (20.5)	0.90 (0.29-2.77, p=0.857)	-	-
HCC status	No	91 (77.8)	26 (22.2)	-	-	-
	Yes	27 (81.8)	6 (18.2)	0.78 (0.27-1.98, p=0.617)	-	0.96 (0.24-3.50, p=0.951)
MELD score	<15	42 (75.0)	14 (25.0)	-	-	-
	15-20	34 (81.0)	8 (19.0)	0.71 (0.26-1.85, p=0.486)	-	0.33 (0.08-1.14, p=0.088)
	>20	36 (81.8)	8 (18.2)	0.67 (0.24-1.74, p=0.416)	-	0.21 (0.04-0.82, p=0.033)
Transplantation status	First transplant	100 (79.4)	26 (20.6)	-	-	-
	Re-transplanted	18 (75.0)	6 (25.0)	1.28 (0.43-3.41, p=0.633)	-	1.29 (0.31-4.90, p=0.711)
Type of organ	DBD-organ	96 (80.0)	24 (20.0)	-	-	-
	DCD-organ	16 (69.6)	7 (30.4)	1.75 (0.61-4.61, p=0.270)	-	4.65 (1.11-20.07, p=0.034)
Clinical history of depression	No	110 (84.0)	21 (16.0)	-	-	-
	Yes	8 (42.1)	11 (57.9)	7.20 (2.62-20.74, p<0.001)	-	3.82 (0.95-15.37, p=0.056)
Clinical history of anxiety	No	117 (79.6)	30 (20.4)	-	-	-
	Yes	1 (33.3)	2 (66.7)	7.80 (0.72-171.18, p=0.098)	-	2.21 (0.06-97.59, p=0.653)

[1]Number in dataframe = 150, Number in model = 150, Missing = 0, AIC = 153.1, C-statistic = 0.745, H&L = Chi-sq(8) 3.37 (p=0.909)
[2]Number in dataframe = 150, Number in model = 140, Missing = 10, AIC = 142.3, C-statistic = 0.828, H&L = Chi-sq(8) 6.73 (p=0.566)
Data are percentages unless otherwise stated.
Abbreviations: GAD-7: Generalised Anxiety Disorder-7; SIMD: Scottish Index of Multiple Deprivation; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

Table S4: Multivariable logistic regression: effect of socioeconomic deprivation on post-transplantation depression.

				Depression (PHQ-9 score ≥10)		
		No (n=108)	Yes (n=42)	Univariable OR (95% CI)	Multivariable OR (95% CI)[1]	Multivariable OR (95% CI)[2]
SIMD quintile	1 (most deprived)	14 (46.7)	16 (53.3)	-	-	-
	2	20 (69.0)	9 (31.0)	0.39 (0.13-1.12, p=0.086)	0.35 (0.11-1.15, p=0.067)	0.19 (0.04-0.72, p=0.018)
	3	28 (75.7)	9 (24.3)	0.28 (0.10-0.78, p=0.017)	0.29 (0.09-0.92, p=0.022)	0.22 (0.06-0.76, p=0.019)
	4	26 (89.7)	3 (10.3)	0.10 (0.02-0.36, p=0.001)	0.11 (0.02-0.43, p=0.003)	0.12 (0.02-0.58, p=0.013)
	5 (least deprived)	20 (80.0)	5 (20.0)	0.22 (0.06-0.70, p=0.014)	0.21 (0.06-0.79, p=0.014)	0.13 (0.02-0.56, p=0.009)
Age (years)	<40	15 (57.7)	11 (42.3)	-	-	-
	40-60	42 (66.7)	21 (33.3)	0.68 (0.27-1.76, p=0.424)	0.72 (0.26-1.98, p=0.524)	0.64 (0.17-2.41, p=0.509)
	>60	51 (83.6)	10 (16.4)	0.27 (0.09-0.75, p=0.012)	0.35 (0.12-1.06, p=0.063)	0.20 (0.04-0.90, p=0.041)
Sex	Male	64 (74.4)	22 (25.6)	-	-	-
	Female	44 (68.8)	20 (31.2)	1.32 (0.64-2.71, p=0.445)	1.66 (0.77-3.63, p=0.213)	1.98 (0.76-5.36, p=0.167)
BMI	Underweight-Normal	34 (66.7)	17 (33.3)	-	-	-
	Overweight	40 (78.4)	11 (21.6)	0.55 (0.22-1.32, p=0.186)	-	-
	Obese	34 (70.8)	14 (29.2)	0.82 (0.35-1.93, p=0.655)	-	-
Time post transplantation (years)	<1	42 (79.2)	11 (20.8)	-	-	-
	1-5	41 (70.7)	17 (29.3)	1.58 (0.67-3.87, p=0.302)	-	1.59 (0.52-4.97, p=0.419)
	>5	25 (64.1)	14 (35.9)	2.14 (0.85-5.53, p=0.110)	-	4.52 (1.15-19.40, p=0.035)
Primary liver disease	ALD	26 (72.2)	10 (27.8)	-	-	-
	Cholestatic	25 (64.1)	14 (35.9)	1.46 (0.55-3.96, p=0.452)	-	0.79 (0.22-2.76, p=0.707)
	Viral	14 (73.7)	5 (26.3)	0.93 (0.25-3.18, p=0.908)	-	0.55 (0.10-2.78, p=0.481)
	NAFLD	15 (88.2)	2 (11.8)	0.35 (0.05-1.54, p=0.207)	-	0.20 (0.02-1.42, p=0.136)
	Other	28 (71.8)	11 (28.2)	1.02 (0.37-2.84, p=0.967)	-	0.56 (0.14-2.13, p=0.405)
HCC status	No	84 (71.8)	33 (28.2)	-	-	-
	Yes	24 (72.7)	9 (27.3)	0.95 (0.39-2.21, p=0.916)	-	2.27 (0.62-8.55, p=0.215)
MELD score	<15	42 (75.0)	14 (25.0)	-	-	-
	15-20	27 (64.3)	15 (35.7)	1.67 (0.70-4.03, p=0.252)	-	1.17 (0.39-3.57, p=0.781)
	>20	33 (75.0)	11 (25.0)	1.00 (0.40-2.49, p=1.000)	-	0.41 (0.11-1.45, p=0.179)
Transplantation status	First transplant	91 (72.2)	35 (27.8)	-	-	-
	Re-transplanted	17 (70.8)	7 (29.2)	1.07 (0.39-2.72, p=0.890)	-	0.96 (0.26-3.32, p=0.954)
Type of organ	DBD-organ	86 (71.7)	34 (28.3)	-	-	-
	DCD-organ	16 (69.6)	7 (30.4)	1.11 (0.40-2.84, p=0.838)	-	1.67 (0.46-5.71, p=0.417)
Clinical history of depression	No	100 (76.3)	31 (23.7)	-	-	-
	Yes	8 (42.1)	11 (57.9)	4.44 (1.65-12.42, p=0.003)	-	2.33 (0.65-8.27, p=0.186)
Clinical history of anxiety	No	107 (72.8)	40 (27.2)	-	-	-
	Yes	1 (33.3)	2 (66.7)	5.35 (0.50-117.00, p=0.176)	-	7.74 (0.18-462.56, p=0.276)

[1]Number in dataframe = 150, Number in model = 150, Missing = 0, AIC = 172.8, C-statistic = 0.736, H&L = Chi-sq(8) 4.13 (p=0.845)
[2]Number in dataframe = 150, Number in model = 140, Missing = 10, AIC = 176.2, C-statistic = 0.806, H&L = Chi-sq(8) 9.60 (p=0.295)
Data are percentages unless otherwise stated.
Abbreviations: PHQ-9: Patient Health Questionnaire-9; SIMD: Scottish Index of Multiple Deprivation; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	N/A
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	7
Outcome data	15*	Report numbers of outcome events or summary measures	7/8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7/8

		(*b*) Report category boundaries when continuous variables were categorized	7/8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11/12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11/12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Is socioeconomic deprivation associated with worse quality of life, anxiety and depression in liver transplant recipients? A cross-sectional study in a national transplantation programme

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-070422.R1
Article Type:	Original research
Date Submitted by the Author:	25-Apr-2023
Complete List of Authors:	Sgro, Alessandro; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit Cambridge, WA; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit Mclean, Kenneth ; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit Drake, Thomas ; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit Camilleri-Brennan, J; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit Knight, Stephen; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit Pius, Riinu; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics Diana, Wu; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit Wigmore, Stephen; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit Harrison, Ewen ; The University of Edinburgh Usher Institute of Population Health Sciences and Informatics, Centre for Medical Informatics; Royal Infirmary of Edinburgh, Scottish Liver Transplant Unit
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Gastroenterology and hepatology, Mental health
Keywords:	Transplant surgery < SURGERY, SOCIAL MEDICINE, Anxiety disorders < PSYCHIATRY, Depression & mood disorders < PSYCHIATRY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Is socioeconomic deprivation associated with worse quality of life, anxiety and depression in liver transplant recipients? A cross-sectional study in a national transplantation programme

Sgrò A[1,2], Cambridge WA[1,2], McLean KA[1,2], Drake TM[1,2], Camilleri-Brennan J[2], Knight SR[1,2], Pius R[1], Wu DA[2], Wigmore SJ[2], Harrison EM[1,2].

1. Centre for Medical Informatics, Usher Institute, University of Edinburgh, Edinburgh, UK.

2. Scottish Liver Transplant Unit, University of Edinburgh, Royal Infirmary of Edinburgh, Edinburgh, UK.

Correspondence to:

Prof Ewen Harrison

Centre for Medical Informatics, Usher Institute, University of Edinburgh, Edinburgh EH16 4UX, UK

E-mail: ewen.harrison@ed.ac.uk

Phone number: 0131 242 3614

Running title: Socioeconomic deprivation in liver recipients

Keywords: socioeconomic factors, liver clinical outcome, quality of life

Abstract

Objective To identify whether socioeconomic deprivation is associated with worse health-related quality of life (HR-QoL), anxiety, depression following liver transplantation.

Design Cross-sectional study.

Setting and participants Liver transplant recipients within a national transplantation programme.

Methods Participants completed the condition-specific 'Short form of liver disease QOL' questionnaire, the Generalised Anxiety Disorder Questionnaire (GAD-7) and the Patient Health Questionnaire (PHQ-9). The aggregate HR-QoL score (range: 0-100) was derived and multivariable linear regression performed based on sociodemographic and clinical variables to estimate its independent association with Scottish Index of Multiple Deprivation (SIMD) quintiles. The GAD-7 and PHQ-9 questionnaires were used to screen respondents for anxiety and depression, and multivariable logistic regression performed to estimate their independent association with SIMD quintiles.

Results Some 331 patients completed the questionnaires. Quintiles were equally distributed in the cohort, with no significant differences observed in underlying patient characteristics. Following multivariable adjustment, greater socioeconomic deprivation was associated with lower post-transplantation HR-QoL scores, with a difference of 9.7 points (95%CI: 4.6-14.9, p<0.001) between the most and least deprived quintiles. Recipients living in areas of least deprivation were less likely to suffer from anxiety (OR 0.05, 95%CI: 0.00-0.28, p=0.003) or depression (OR 0.13, 95%CI: 0.02-0.56, p=0.009).

Conclusion Despite the highly selected nature of liver transplant recipients, those living in the most deprived areas have a significantly lower HR-QoL and are more likely to suffer from anxiety and depression.

Strengths and limitations of this study

- Large sample size with a high response rate.
- The validated and disease-specific SF-LDQOL questionnaire was used.
- Association between SIMD and outcomes not adjusted for comorbidities.
- Lack of pre-transplantation HR-QoL scores.

Introduction

Liver transplantation (LT) is the only curative treatment for end-stage liver disease. Over the course of the last 50 years, advances in operative technique, immunosuppressive therapy and postoperative management have transformed LT from an experimental procedure to a standard treatment, with 1-year and 5-year survival rates in the UK currently exceeding 90% and 80%, respectively.[1,2] More recently, efforts have focused on exploring the impact of LT on health-related quality of life (HR-QoL).[3,4]

Studies have demonstrated that most LT recipients experience a significant improvement in HR-QoL after transplantation compared to pre-transplantation scores, and this is observed across most quality of life domains.[5–7] Despite the improvement remaining consistent over time, LT recipients have lower HR-QoL scores than the healthy general population.[8,9] Pre-transplantation and post-transplantation variables, such as primary liver disease, re-transplantation or postoperative complications, fail to fully explain this discrepancy between LT recipients and the general population, and it is plausible that socioeconomic disparities may have a causative role.[10,11]

Socioeconomic deprivation is known to be a determinant of poor health, shorter life expectancy and increased prevalence of chronic diseases, and, in the field of LT, it has been demonstrated to be associated with poor post-transplantation outcomes.[12–16] In the United States of America, inferior insurance cover is linked with greater mortality in adult recipients.[17,18] Similarly, greater socioeconomic deprivation is associated with diminished graft and patient survival after paediatric LT.[19,20] Lower literacy and education level have also been shown to be associated with increased complication rates post LT.[21,22]

Limited evidence is available in the literature on whether deprivation adversely influences HR-QoL and causes psychological distress in LT recipients. This study aimed to estimate the association between socioeconomic deprivation and HR-QoL, anxiety and depression following LT.

Methods

Population

Consecutive adult (≥ 18 years of age) liver transplantation recipients attending the Scottish Liver Transplant Unit for an outpatient clinic in two different periods (16th July – 3rd September 2015; 15th August – 14th September 2017) were enrolled on a voluntary basis. Formal institutional ethical approval was waived by the South East Scotland Research Ethics Service as this study was considered a service evaluation, otherwise involving routinely collected data. This analysis was performed according to STROBE reporting guidelines for cross-sectional studies.[23]

Data collection

Eligible patients, after verbal consent was obtained, were invited to fill out the validated 'Short form of liver disease quality of life' (SF-LDQOL) questionnaire.[24] This tool was used to assess the condition-specific HR-QoL and it includes 36 items distributed over nine domains (symptoms of liver disease, effects of liver disease, concentration/memory, health-related distress, sexual function, quality of sleep, loneliness, hopelessness and stigma of liver disease). The SF-LDQOL questionnaire provides a score for each domain and an overall HR-QoL score (range zero to 100, with higher scores denoting better QoL).

Patients recruited in the second period were also invited to complete the Generalised Anxiety Disorder-7 (GAD-7) and Patient Health Questionnaire-9 (PHQ-9) questionnaires.[25,26] The total GAD-7 score ranges from zero to 21, with higher scores indicating greater self-reported anxiety and a total score of ≥10 suggesting a possible diagnosis of anxiety (sensitivity 89%, specificity 82%).[27] The PHQ-9 is used to quantify depression symptoms. It provides a zero to 27 total score and scores ≥10 are 88% sensitive and 88% specific for detecting depression.[28]

Socioeconomic deprivation scores were obtained by referencing the patients' postcodes with the Scottish Index of Multiple Deprivation (SIMD) tool.[29] The SIMD is the Scottish Government's tool used to identify areas subject to deprivation, based upon factors including income, employment, education, health, housing, crime, and access to essential services. It enables a deprivation score to be assigned to any postcode and the lower the

score, the more deprived the area. The SIMD is a very granular epidemiological tool, with each data zone consisting of between 500 and 1000 household residents. We used the tool to assign every patient to a SIMD quintile from 1 to 5, with quintile 1 representing the most deprived postcodes in Scotland and quintile 5 the least.

Statistical analyses

Patient characteristics were summarized to compare differences between SIMD quintiles. Continuous data were summarised as a median and analysed using the Kruskal-Wallis test. Categorical data are presented as frequencies and percentages, and differences in proportions were tested using chi-squared (X^2) or Fisher's exact tests. All SF-LDQOL questionnaire responses were assigned to a value based upon the original Likert scale and summated into a mean score for each domain (scaled to value out of 100). All domains were equally weighted before being summated into a mean overall score. The total GAD-7 and PHQ-9 scores were used to determine whether respondents had a possible diagnosis of anxiety and depression, respectively, by using the validated ≥10 cut-off.

Differences in overall HR-QoL were adjusted using a multiple linear regression model. Variables used included: SIMD quintile; age (years); sex (male, female); body mass index (BMI); time since transplantation (years); primary liver disease (alcoholic, cholestatic, non-alcoholic fatty liver disease (NAFLD), viral (hepatitis B or C), or other aetiology); hepatocellular carcinoma (HCC) status (present, absent); pre-transplantation Model of End-Stage Liver Disease (MELD) category (<15, 15–20, ≥21); transplantation status (first transplant, re-transplanted); and type of organ (donation after brainstem death organ (DBD-organ), donation after circulatory death organ (DCD-organ)). These variables are routinely available at UK Liver Transplant Units and could plausibly affect HR-QoL. First-order interactions were checked and included in the model if found to be influential. Final model selection was guided by minimisation of the Akaike Information Criterion (AIC).

Multivariable logistic regression was used to estimate the independent association of SIMD with anxiety (GAD-7 score ≥10) and depression (PHQ-9 score ≥10). In addition to the variables used in the multiple linear

regression model, clinical history of anxiety (yes, no) and depression (yes, no) were included in the logistic regression models. These were defined as either a documented diagnosis of anxiety/depression made by a mental health specialist or the patient having a long-term (>4 weeks) prescription for anxiolytics/antidepressants. First order interactions were checked before final model selection, which was guided by minimisation of the AIC.

Directed acyclic graphs of the exposure-outcome relationship are provided in the supplementary file (Fig. S1 and S2). The threshold of statistical significance was set at P <0.05 *a priori*. Statistical analyses were conducted in R v3.3.4 (R Foundation for Statistical Computing, Vienna, Austria) with the tidyverse and finalfit packages.

Patient and public involvement

None.

Results

Over both study periods, 468 patients were found to be eligible for inclusion (**Fig. 1**). Of these, 74 (15.8%) did not participate, 47 (10.0%) were not encountered at the outpatient clinic and 16 (3.4%) handed in incomplete questionnaires. Out of the 331 respondents (70.7%) with complete questionnaires, nine had an invalid postcode and could not be allocated to a SIMD quintile. Therefore, 322 patients (68.8%) were included in the final analyses, with all 322 having a complete SF-LDQOL questionnaire and 150 also having filled out both GAD-7 and PHQ-9 tools.

Patients' characteristics for the overall cohort and the GAD-7 and PHQ-9 subgroup are summarised in **Table 1** and **Table 2**, respectively. The SIMD quintiles were equally distributed in both groups with no major differences observed in the underlying patient characteristics, bar a shorter time since transplantation for SIMD quintile 4 respondents in both subgroups and greater prevalence of re-transplantation in recipients living in areas of least deprivation in the GAD-7 and PHQ-9 subgroup. The median post-transplantation HR-QoL score was 77.0 (IQR: 66.0-84.0) and the overall prevalence of symptoms of anxiety and depression was 21.3% (32/150) and 28% (42/150), respectively. A description of primary liver diseases included within the "other" category is provided in **Table S1**. The scores of the nine SF-LDQOL domains are presented in Table S2.

Multiple linear regression

In the overall cohort, patients living in most deprived areas had a significantly lower overall HR-QoL score (**Table 1**). Following multivariable adjustment, greater socioeconomic deprivation remained associated with lower post-transplantation HR-QoL, with a difference of 9.7 points (95% CI: 4.5-14.9, $p<0.001$) between the most and least deprived quintiles (**Fig. 2, Table S3**). There was no significant difference in HR-QoL associated with primary liver disease, transplantation status or receipt of a DCD-organ, and the overall HR-QoL remained stable over time (**Table S3**).

Multivariable logistic regression

In the GAD-7 and PHQ-9 subgroup, recipients living in areas of least deprivation were less likely to suffer from anxiety and depression (**Table 2**). This persisted after adjustment for baseline characteristics, with the least deprived quintile significantly associated with fewer possible diagnoses of anxiety (OR 0.05, 95% CI: 0.00-0.28, p=0.003) and depression (OR 0.13, 95% CI: 0.02-0.56, p=0.009) (**Fig. 3, Fig. 4, Table S4, Table S5**). Pre-transplantation MELD scores >20 were found to be protective towards post-transplantation anxiety (OR 0.21, 95% CI: 0.04-0.82, p=0.033), whereas receipt of a DCD-organ was associated with greater anxiety (OR 4.65, 95% CI: 1.11-20.07, p=0.034) (**Table S4**). Although a post-transplantation survival time greater than five years was associated with worse depression (OR 4.52, 95% CI: 1.15-19.40, p=0.035), recipients older than 60 years of age were found to be less likely to suffer from depressive disorders (**Table S5**).

Table 1. Patients' demographics for the overall cohort

		Scottish Index of Multiple Deprivation (SIMD)						
		SIMD 1 (most deprived) (n=57)	SIMD 2 (n=66)	SIMD 3 (n=77)	SIMD 4 (n=60)	SIMD 5 (least deprived) (n=62)	Total (n=322)	p
Quality of Life (SF-LDQOL)	Median (IQR)	71.0 (62.0-82.0)	74.0 (60.8-82.8)	75.0 (66.0-86.0)	79.0 (73.5-86.0)	80.0 (69.8-87.8)	77.0 (66.0-84.0)	0.002
Age (years)	Median (IQR)	55.0 (45.0-62.0)	57.5 (49.0-65.0)	57.0 (47.0-66.0)	61.5 (55.5-69.2)	61.0 (55.0-64.0)	59.0 (49.0-65.0)	0.070
Sex	Male	34 (59.6)	26 (39.4)	47 (61.0)	31 (51.7)	38 (61.3)	176 (54.7)	0.053
	Female	23 (40.4)	40 (60.6)	30 (39.0)	29 (48.3)	24 (38.7)	146 (45.3)	
BMI (kg/m^2)	Median (IQR)	26.6 (23.3-31.2)	27.2 (22.9-30.9)	27.5 (24.0-30.1)	26.7 (24.1-30.3)	26.7 (23.5-30.2)	26.8 (6.9)	0.922
Time since transplantation (years)	Median (IQR)	2.2 (1.1-5.8)	2.4 (0.9-6.4)	3.7 (0.9-8.0)	1.0 (0.5-3.9)	2.7 (1.0-6.5)	2.4 (0.8-6.1)	0.021
Primary liver disease	ALD	15 (26.3)	12 (18.2)	17 (22.1)	15 (25.0)	13 (21.0)	73 (22.7)	0.938
	Cholestatic	11 (19.3)	19 (28.8)	19 (24.7)	13 (21.7)	16 (25.8)	78 (24.2)	
	Viral	9 (15.8)	8 (12.1)	9 (11.7)	8 (13.3)	10 (16.1)	44 (13.7)	
	NAFLD	5 (8.8)	4 (6.1)	7 (9.1)	4 (6.7)	7 (11.3)	32 (9.9)	
	Other	17 (29.8)	23 (34.8)	25 (32.5)	10 (16.7)	16 (25.8)	95 (29.5)	
HCC status	No	44 (77.2)	51 (77.3)	64 (83.1)	48 (80.0)	49 (79.0)	256 (79.5)	0.906
	Yes	13 (22.8)	15 (22.7)	13 (16.9)	12 (20.0)	13 (21.0)	66 (20.5)	
MELD score	<15	20 (35.1)	13 (19.7)	21 (27.3)	21 (35.0)	14 (22.6)	89 (27.6)	0.158
	15-20	13 (22.8)	19 (28.8)	16 (20.8)	11 (18.3)	23 (37.1)	82 (25.5)	
	>20	22 (38.6)	33 (50.0)	37 (48.1)	28 (46.7)	23 (37.1)	141 (43.8)	
	Missing	2 (3.5)	1 (1.5)	3 (3.9)	2 (3.3)	2 (3.2)	10 (3.1)	
Transplantation status	First transplant	49 (86.0)	59 (89.4)	69 (89.6)	56 (93.3)	50 (80.6)	283 (87.9)	0.260
	Re-transplanted	8 (14.0)	7 (10.6)	8 (10.4)	4 (6.7)	12 (19.4)	39 (12.1)	
Type of organ	DBD-organ	49 (86.0)	56 (84.8)	65 (84.4)	51 (85.0)	49 (79.0)	269 (83.5)	0.596
	DCD-organ	6 (10.5)	9 (13.6)	10 (13.0)	7 (11.7)	13 (21.0)	46 (14.3)	
	Missing	2 (3.5)	1 (1.5)	2 (2.6)	2 (3.3)	0 (0.0)	7 (2.2)	

Data are percentages unless otherwise stated.

Abbreviations: SIMD: Scottish Index of Multiple Deprivation; SF-LDQOL: Short Form of Liver Disease Quality of Life; IQR: Interquartile Range; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

Table 2. Patients' demographics for the subgroup that completed the GAD-7 and PHQ-9 questionnaires

		Scottish Index of Multiple Deprivation (SIMD)						
		SIMD 1 (most deprived) (n=30)	SIMD 2 (n=29)	SIMD 3 (n=37)	SIMD 4 (n=29)	SIMD 5 (least deprived) (n=25)	Total (n=150)	p
Anxiety (GAD-7 score ≥10)	No	16 (53.3)	22 (75.9)	31 (83.8)	26 (89.7)	23 (92.0)	118 (78.7)	0.002
	Yes	14 (46.7)	7 (24.1)	6 (16.2)	3 (10.3)	2 (8.0)	32 (21.3)	
Depression (PHQ-9 score ≥10)	No	14 (46.7)	20 (69.0)	28 (75.7)	26 (89.7)	20 (80.0)	108 (72.0)	0.004
	Yes	16 (53.3)	9 (31.0)	9 (24.3)	3 (10.3)	5 (20.0)	42 (28.0)	
Age (years)	<40	7 (23.3)	7 (24.1)	6 (16.2)	2 (6.9)	4 (16.0)	26 (17.3)	0.295
	40-59	15 (50.0)	12 (41.4)	16 (43.2)	9 (31.0)	11 (44.0)	63 (42.0)	
	≥60	8 (26.7)	10 (34.5)	15 (40.5)	18 (62.1)	10 (40.0)	61 (40.7)	
Sex	Male	21 (70.0)	14 (48.3)	24 (64.9)	14 (48.3)	13 (52.0)	86 (57.3)	0.281
	Female	9 (30.0)	15 (51.7)	13 (35.1)	15 (51.7)	12 (48.0)	64 (42.7)	
BMI	Underweight-Normal	13 (43.3)	9 (31.0)	15 (40.5)	6 (20.7)	8 (32.0)	51 (34.0)	0.289
	Overweight	9 (30.0)	10 (34.5)	15 (40.5)	8 (27.6)	9 (36.0)	51 (34.0)	
	Obese	8 (26.7)	10 (34.5)	7 (18.9)	15 (51.7)	8 (32.0)	48 (32.0)	
Time since transplantation (years)	<1	6 (20.0)	11 (37.9)	16 (43.2)	16 (55.2)	4 (16.0)	53 (35.3)	0.013
	1-5	18 (60.0)	12 (41.4)	10 (27.0)	5 (17.2)	13 (52.0)	58 (38.7)	
	>5	6 (20.0)	6 (20.7)	11 (29.7)	8 (27.6)	8 (32.0)	39 (26.0)	
Primary liver disease	ALD	7 (23.3)	5 (17.2)	12 (32.4)	6 (20.7)	6 (24.0)	36 (24.0)	0.707
	Cholestatic	8 (26.7)	9 (31.0)	8 (21.6)	6 (20.7)	8 (32.0)	39 (26.0)	
	Viral	4 (13.3)	6 (20.7)	3 (8.1)	3 (10.3)	3 (12.0)	19 (12.7)	
	NAFLD	4 (13.3)	1 (3.4)	4 (10.8)	7 (24.1)	1 (4.0)	17 (11.3)	
	Other	7 (23.3)	8 (27.6)	10 (27.0)	7 (24.1)	7 (28.0)	39 (26.0)	
HCC status	No	25 (83.3)	19 (65.5)	30 (81.1)	23 (79.3)	20 (80.0)	117 (78.0)	0.490
	Yes	5 (16.7)	10 (34.5)	7 (18.9)	6 (20.7)	5 (20.0)	33 (22.0)	
MELD score	<15	12 (40.0)	9 (31.0)	15 (40.5)	11 (37.9)	9 (36.0)	56 (37.3)	0.173
	15-20	7 (23.3)	13 (44.8)	10 (27.0)	3 (10.3)	9 (36.0)	42 (28.0)	
	>20	10 (33.3)	6 (20.7)	10 (27.0)	13 (44.8)	5 (20.0)	44 (29.3)	
	Missing	1 (3.3)	1 (3.4)	2 (5.4)	2 (6.9)	2 (8.0)	8 (5.3)	
Transplantation status	First transplant	24 (80.0)	27 (93.1)	33 (89.2)	27 (93.1)	15 (60.0)	126 (84.0)	0.004
	Re-transplanted	6 (20.0)	2 (6.9)	4 (10.8)	2 (6.9)	10 (40.0)	24 (16.0)	
Type of organ	DBD-organ	26 (86.7)	23 (79.3)	29 (78.4)	22 (75.9)	20 (80.0)	120 (80.0)	0.707
	DCD-organ	2 (6.7)	5 (17.2)	6 (16.2)	5 (17.2)	5 (20.0)	23 (15.3)	
	Missing	2 (6.7)	1 (3.4)	2 (5.4)	2 (6.9)	0 (0.0)	7 (4.7)	
Clinical history of depression	No	24 (80.0)	25 (86.2)	32 (86.5)	27 (93.1)	23 (92.0)	131 (87.3)	0.578
	Yes	6 (20.0)	4 (13.8)	5 (13.5)	2 (6.9)	2 (8.0)	19 (12.7)	
Clinical history of anxiety	No	29 (96.7)	28 (96.6)	37 (100.0)	28 (96.6)	25 (100.0)	147 (98.0)	0.707
	Yes	1 (3.3)	1 (3.4)	0 (0.0)	1 (3.4)	0 (0.0)	3 (2.0)	

Data are percentages unless otherwise stated.

Abbreviations: SIMD: Scottish Index of Multiple Deprivation; GAD-7: Generalised Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9; IQR: Interquartile Range; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

Discussion

Most LT recipients experience a significant improvement in HR-QoL after transplantation, but it is not completely understood why they do not achieve HR-QoL scores comparable with the healthy general population.[6,8] There is a paucity of data on the factors that may influence HR-QoL outcomes after LT. This study aimed to explore the relationship between socioeconomic deprivation and HR-QoL, anxiety and depression among LT recipients.

In our study, greater socioeconomic deprivation was associated with lower post-transplantation HR-QoL scores and recipients living in the most deprived areas were more likely to suffer from anxiety and depression. There is evidence to suggest that psychological problems after LT are associated with increased morbidity and mortality, and that outcomes could be improved with adequate treatment.[30–32] This makes it important to identify at an early stage patients who are at risk of psychological problems. Our findings can help clinicians use deprivation scores to identify LT recipients at risk for anxiety, depression and lower HR-QoL scores, and who may require earlier interventions aimed at improving long-term HR-QoL and minimising morbidity and mortality.

Scarce evidence is available in the literature on the impact of deprivation on HR-QoL, anxiety and depression in LT recipients. A cross-sectional study from Brazil suggested that higher income and education level were predictors of higher HR-QoL scores in some quality of life domains.[33] Similarly, employment was associated with higher HR-QoL scores and fewer depressive symptoms in German LT recipients.[34] Income, education level and employment were also found to positively influence post-transplantation HR-QoL in a study conducted at the University of California Los Angeles.[35] Although these are significant findings, the above studies failed to include important social determinants of health, such as access to essential services, housing and crime.[16] To overcome this limitation, we used a more inclusive socioeconomic deprivation score, calculated as the level of deprivation of an area across seven domains: income, employment, education, health, access to services, crime and housing.

In our study, long-term HR-QoL remained stable over time and was not associated with re-transplantation or primary liver disease. This is consistent with the current balance of evidence.[9,36–39] In the final multivariable model, the association between gender and HR-QoL almost reached statistical significance, suggesting that female recipients might be at risk of worse HR-QoL. However, previous studies confirmed that gender is not associated with overall HR-QoL post LT .[34,35]

The prevalence rates of symptoms of anxiety in our cohort (21.3%) was in line with prevalence rates described by other studies (range 20% to 25%).[40,41] Patients who received a DCD-organ were estimated to have significantly worse anxiety symptoms and this may reflect the increased risk of morbidity in DCD-organ recipients.[42,43] It is not clear why pre-transplantation MELD scores >20 were found to be protective towards post-transplantation anxiety. We can hypothesise that recipients with MELD scores >20 had the greatest benefit from LT and the much improved health is now contributing to lower anxiety prevalence rates. Patients with a clinical history of depression had worse anxiety symptoms, although this association did not reach statistical significance. Anxiety occurring as a symptom of clinical depression is well documented in the literature.[44]

Depressive symptoms were more prevalent in our sample (28.0%) than in other studies (range 15% to 20%).[40,45,46] A possible explanation is that most studies have focused on the first five years after LT, whilst in our study over one fourth of patients that completed the PHQ-9 questionnaire were over five years post-transplantation. There is evidence to suggest that depressive symptoms might be highly prevalent in long-term (>10 years) LT recipients and this is reflected by a post-transplantation survival time greater than five years being associated with greater odds of depression in our study.[47]

When comparing the Scottish population with our cohort of post-transplantation patients, symptoms of depression and anxiety were more prevalent in LT recipients.[48] Although different assessment tools were used, 6% of Scottish people living in areas of least deprivation had symptoms of anxiety and depression, in contrast with the prevalence rates observed in our cohort (anxiety: 8%, depression: 20%). When comparing areas of most socioeconomic deprivation, the Scottish population had symptoms of anxiety and depression in

15% and 22% of cases, respectively, whereas post-transplantation patients had significantly greater prevalence rates (anxiety: 47%, depression: 53%). In contrast with the prevalence rates of symptoms of anxiety and depression found in our sample, a small proportion of LT recipients had a clinical history of anxiety (2%, 19/150) and depression (12.7%, 3/150). This highlights how psychological problems might be underdiagnosed following LT, particularly in patients living in areas of most deprivation, and reinforces the concept that monitoring psychological problems and psychological counselling should be part of the routine care of transplant recipients.

There are some limitations to this study. The cross-sectional design of the study may have impacted the HR-QoL, anxiety and depression results observed. Frequent clinic attendees, due to shorter postoperative period or complications, were more likely to have been encountered, and patients who died, or were too unwell to attend the clinic, were not included in the study. We tried to minimise the resulting bias with a large sample size, high response rate and two different data collection periods. Secondly, although it should be mentioned that England, Wales and Northern Ireland have indexes of multiple deprivation based on the same domains of the SIMD, this was a single-centre study that used a Scotland-specific index of deprivation and therefore the results may not be generalisable to other centres. Thirdly, differently from individual-based scores, SIMD gives an area-based deprivation score. This introduces potential bias since not every person in a highly deprived area will themselves be experiencing high levels of deprivation. However, area-based scores have been shown to be valid proxies in the absence of individual-based scores.[49,50] Moreover, we did not adjust for any comorbidities. This could be an important confounding factor since socioeconomic deprivation has been shown to be associated with higher rates of comorbidity and the presence of comorbidities may lead to poorer quality of life.[14,15,51] Future studies should adjust for comorbidities to enable a more accurate estimation of the association between socioeconomic deprivation and HR-QoL. Finally, we did not collect pre-transplantation HR-QoL scores. It is plausible that the lower HR-QoL scores in more deprived recipients could be explained by lower pre-transplantation scores than less deprived transplant candidates. However, this assumes that there is an equal increase in HR-QoL after LT across socioeconomic deprivation quintiles. Future studies should explore the association between socioeconomic deprivation and change in HR-QoL before and after LT to assess whether there is equitable benefit from LT.

In conclusion, despite the highly selected nature of liver transplant recipients, those living in the most deprived areas had a significantly lower HR-QoL and were more likely to suffer from anxiety and depression. Our results also suggest psychological problems might be underdiagnosed in transplant recipients. These findings may help clinicians identify patients at risk for anxiety, depression and lower HR-QoL scores, and who may require earlier interventions aimed at improving long-term HR-QoL and minimising morbidity and mortality.

Contributors

Conception and design: KAM, AS, EMH and RP. Data collection: KAM, AS, WAC and JCB. Analysis and interpretation of the data: KAM, AS, TMD and EMH. Drafting of the article: AS. Critical revision of the article for important intellectual content: AS, WAC, KAM, TMD, JCB, SRK, RP, DAW, SJW and EMH. Final approval of the article: AS, WAC, KAM, TMD, JCB, SRK, RP, DAW, SJW and EMH. EMH is responsible for the overall content of the research as the guarantor.

Competing interests

TMD receives research funding from Aligos therapeutics for unrelated work. All other authors declare no competing interests.

Funding

Dr McLean received MRC funding and Dr Drake received CRUK funding.

Data availability statement

Data are available upon reasonable request.

Ethics approval statement

Formal institutional ethical approval was waived as this study was considered a service evaluation, otherwise involving routinely collected data.

References

1. Zarrinpar A, Busuttil RW. Liver transplantation: past, present and future. Nat Rev Gastroenterol Hepatol 2013 107. 2013 Jun 11;10(7):434–40.
2. National Health Service Blood and Transplant. Annual report on liver transplantation: Report for 2019/2020 (1 April 2010–31 March 2020). NHS. 2020;
3. Onghena L, Develtere W, Poppe C, Geerts A, Troisi R, Vanlander A, et al. Quality of life after liver transplantation: State of the art. World J Hepatol. 2016 Jun 28;8(18):749.
4. Cristin DJ, Forman LM, Jackson WE. Beyond Survival: Targeting Health-Related Quality of Life Outcomes After Liver Transplantation. Clin Liver Dis. 2021 May 1;17(5):359–64.
5. McLean KA, Drake TM, Sgrò A, Camilleri-Brennan J, Knight SR, Ots R, et al. The effect of liver transplantation on patient-centred outcomes: a propensity-score matched analysis. Transpl Int. 2019 Aug 1;32(8):808–19.
6. Telles-Correia D, Barbosa A, Mega I, Mateus E, Monteiro E. When Does Quality of Life Improve After Liver Transplantation? A Longitudinal Prospective Study. Transplant Proc. 2009 Apr 1;41(3):904–5.
7. Ratcliffe J, Longworth L, Young T, Bryan S, Burroughs A, Buxton M. Assessing health-related quality of life pre– and post–liver transplantation: A prospective multicenter study. Liver Transplant. 2002 Mar 1;8(3):263–70.
8. Tome S, Wells JT, Said A, Lucey MR. Quality of life after liver transplantation. A systematic review. J Hepatol. 2008 Apr 1;48(4):567–77.
9. Duffy JP, Kao K, Ko CY, Farmer DG, McDiarmid S V., Hong JC, et al. Long-term patient outcome and quality of life after liver transplantation: Analysis of 20-year survivors. Ann Surg. 2010 Oct;252(4):652–9.
10. Bona M De, Ponton P, Ermani M, Iemmolo RM, Feltrin A, Boccagni P, et al. The impact of liver disease and medical complications on quality of life and psychological distress before and after liver transplantation. J Hepatol. 2000 Oct 1;33(4):609–15.
11. Kousoulas L, Neipp M, Barg-Hock H, Jackobs S, Strassburg CP, Klempnauer J, et al. Health-related quality of life in adult transplant recipients more than 15 years after orthotopic liver transplantation.

Transpl Int. 2008 Nov 1;21(11):1052–8.

12. Shaw M, Gordon D, Dorling D, Mitchell R, Davey Smith G. Increasing mortality differentials by residential area level of poverty: Britain 1981–1997. Soc Sci Med. 2000 Jul 1;51(1):151–3.

13. Waitzman NJ, Smith KR. Phantom of the area: poverty-area residence and mortality in the United States. Am J Public Health. 1998;88(6):973.

14. Roux AVD, Merkin SS, Arnett D, Chambless L, Massing M, Nieto FJ, et al. Neighborhood of residence and incidence of coronary heart disease. N Engl J Med. 2001 Jul 12;345(2):99–106.

15. Drey N, Roderick P, Mullee M, Rogerson M. A population-based study of the incidence and outcomes of diagnosed chronic kidney disease. Am J Kidney Dis. 2003 Oct 1;42(4):677–84.

16. Adler JT, Yeh H. Social determinants in liver transplantation. Clin Liver Dis. 2016 Jan 1;7(1):15.

17. Stepanova M, Qahtani S Al, Mishra A, Younossi I, Venkatesan C, Younossi ZM. Outcomes of liver transplantation by insurance types in the United States. Am J Manag Care. 2020 Apr 1;26(4):E121–6.

18. Young Yoo H, Thuluvath PJ. Outcome of liver transplantation in adult recipients: Influence of neighborhood income, education, and insurance. Liver Transplant. 2004 Feb 1;10(2):235–43.

19. Wadhwani SI, Beck AF, Bucuvalas J, Gottlieb L, Kotagal U, Lai JC. Neighborhood socioeconomic deprivation is associated with worse patient and graft survival following pediatric liver transplantation. Am J Transplant. 2020 Jun 1;20(6):1597–605.

20. Dick AAS, Winstanley E, Ohara M, Blondet NM, Healey PJ, Perkins JD, et al. Do funding sources influence long-term patient survival in pediatric liver transplantation? Pediatr Transplant. 2021 Mar 1;25(2):e13887.

21. Serper M, Patzer RE, Reese PP, Przytula K, Koval R, Ladner DP, et al. Medication misuse, nonadherence, and clinical outcomes among liver transplant recipients. Liver Transplant. 2015 Jan 1;21(1):22–8.

22. Lieber SR, Volk ML. Non-adherence and graft failure in adult liver transplant recipients. Dig Dis Sci. 2013 Mar 2;58(3):824–34.

23. 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. J Clin Epidemiol. 2008;61(4):344–9.

24. Kanwal F, Spiegel BMR, Hays RD, Durazo F, Han SB, Saab S, et al. Prospective validation of the short form liver disease quality of life instrument. Aliment Pharmacol Ther. 2008 Nov 1;28(9):1088–101.

25. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A Brief Measure for Assessing Generalized Anxiety Disorder: The GAD-7. Arch Intern Med. 2006 May 22;166(10):1092–7.

26. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001 Sep 1;16(9):606–13.

27. Löwe B, Decker O, Müller S, Brähler E, Schellberg D, Herzog W, et al. Validation and standardization of the generalized anxiety disorder screener (GAD-7) in the general population. Med Care. 2008 Feb;46(3):266–74.

28. Levis B, Benedetti A, Thombs BD. Accuracy of Patient Health Questionnaire-9 (PHQ-9) for screening to detect major depression: individual participant data meta-analysis. BMJ. 2019 Apr 9;365.

29. Scottish Executive National Statistics. Scottish Index of Multiple Deprivation (SIMD): Technical Notes. 2016.

30. Rogal SS, Dew MA, Fontes P, Dimartini AF. Early Treatment of Depressive Symptoms and Long-Term Survival After Liver Transplantation. Am J Transplant. 2013 Apr 1;13(4):928–35.

31. Amanda Dew M, Rosenberger EM, Myaskovsky L, DiMartini AF, DeVito Dabbs AJ, Posluszny DM, et al. Depression and anxiety as risk factors for morbidity and mortality after organ transplantation: A systematic review and meta-analysis. Transplantation. 2016;100(5):988–1003.

32. Rogal SS, Landsittel D, Surman O, Chung RT, Rutherford A. Pretransplant depression, antidepressant use, and outcomes of orthotopic liver transplantation. Liver Transplant. 2011 Mar 1;17(3):251–60.

33. de Aguiar MIF, Braga VAB, Garcia JHP, de Lima CA, de Almeida PC, e Souza AMA, et al. Quality of life in liver transplant recipients and the influence of sociodemographic factors. Rev da Esc Enferm da USP. 2016;50(3):0411–8.

34. Zahn A, Seubert L, Jünger J, Schellberg D, Heinz Weiss K, Schemmer P, et al. Factors influencing long-term quality of life and depression in German liver transplant recipients: A single-centre cross-sectional study. Ann Transplant. 2013;18(1):327–35.

35. Saab S, Bownik H, Ayoub N, Younossi Z, Durazo F, Han S, et al. Differences in health-related quality of life scores after orthotopic liver transplantation with respect to selected socioeconomic factors. Liver

Transplant. 2011 May;17(5):580–90.

36. Estraviz B, Quintana JM, Valdivieso A, Bilbao A, Padierna A, de Urbina JO, et al. Factors influencing change in health-related quality of life after liver transplantation. Clin Transplant. 2007 Jul 1;21(4):481–99.

37. Åberg F, Höckerstedt K, Roine RP, Sintonen H, Isoniemi H. Influence of liver-disease etiology on long-term quality of life and employment after liver transplantation. Clin Transplant. 2012 Sep 1;26(5):729–35.

38. Desai R, Jamieson N V., Gimson AE, Watson CJ, Gibbs P, Bradley JA, et al. Quality of life up to 30 years following liver transplantation. Liver Transplant. 2008 Oct 1;14(10):1473–9.

39. Yang LS, Shan LL, Saxena A, Morris DL. Liver transplantation: a systematic review of long-term quality of life. Liver Int. 2014 Oct 1;34(9):1298–313.

40. Russell RT, Feurer ID, Wisawatapnimit P, Salomon RM, Pinson CW. The effects of physical quality of life, time, and gender on change in symptoms of anxiety and depression after liver transplantation. J Gastrointest Surg. 2008 Jan 23;12(1):138–44.

41. Van Ginneken BTJ, van den Berg-Emons RJG, van der Windt A, Tilanus HW, Metselaar HJ, Stam HJ, et al. Persistent fatigue in liver transplant recipients: a two-year follow-up study. Clin Transplant. 2010 Jan 1;24(1):E10–6.

42. Callaghan CJ, Charman SC, Muiesan P, Powell JJ, Gimson AE, Van Der Meulen JHP. Outcomes of transplantation of livers from donation after circulatory death donors in the UK: a cohort study. BMJ Open. 2013;3(9).

43. De Vera ME, Lopez-Solis R, Dvorchik I, Campos S, Morris W, Demetris AJ, et al. Liver Transplantation Using Donation After Cardiac Death Donors: Long-Term Follow-Up from a Single Center. Am J Transplant. 2009 Apr 1;9(4):773–81.

44. Xin L, Chen L, Ji Z, Zhang S, Wang J, Liu Y, et al. Risk Factors for Anxiety in Major Depressive Disorder Patients. Clin Psychopharmacol Neurosci. 2015;13(3):263–8.

45. Aadahl M, Hansen BA, Kirkegaard P, Groenvold M. Fatigue and physical function after orthotopic liver transplantation. Liver Transplant. 2002 Mar 1;8(3):251–9.

46. Collis I, Burroughs A, Rolles K, Lloyd G. Psychiatric and Social Outcome of Liver Transplantation.

Br J Psychiatry. 1995;166(4):521–4.

47. Annema C, Roodbol PF, Stewart RE, Porte RJ, Ranchor A V. Prevalence of psychological problems and associated transplant-related variables at different time periods after liver transplantation. Liver Transplant. 2015 Apr 1;21(4):524–38.

48. McLean J, Christie S, Hinchliffe S, Gray L, editors. Scottish Health Survey 2017: Volume 1: Main Report. Edinburgh, UK: The Scottish Government Health Directorate; 2018.

49. Krieger N. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. Am J Public Health. 1992;82(5):703–10.

50. Krieger N, Chen JT, Waterman PD, Soobader MJ, Subramanian S V., Carson R. Geocoding and Monitoring of US Socioeconomic Inequalities in Mortality and Cancer Incidence: Does the Choice of Area-based Measure and Geographic Level Matter?The Public Health Disparities Geocoding Project. Am J Epidemiol. 2002 Sep 1;156(5):471–82.

51. Xuan J, Kirchdoerfer LJ, Boyer JG, Norwood GJ. Effects of comorbidity on health-related quality-of-life scores: an analysis of clinical trial data. Clin Ther. 1999 Feb 1;21(2):383–403.

Figure legends

Figure 1. Flow diagram of patient inclusion

Abbreviations: SIMD: Scottish Index of Multiple Deprivation; SF-LDQOL: Short Form of Liver Disease Quality of Life; GAD-7: Generalised Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9

Figure 2. Forest plots of the effect size for socioeconomic deprivation on post-transplantation HR-QoL: A) reduced model; B) final model

Abbreviations: SF-LDQOL: Short Form of Liver Disease Quality of Life; SIMD: Scottish Index of Multiple Deprivation; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

Figure 3. Forest plots of the effect size for socioeconomic deprivation on post-transplantation anxiety: A) reduced model; B) final model

Abbreviations: SF-LDQOL: Short Form of Liver Disease Quality of Life; SIMD: Scottish Index of Multiple Deprivation; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death; GAD-7: Generalised Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9.

Figure 4. Forest plots of the effect size for socioeconomic deprivation on post-transplantation depression: A) reduced model; B) final model

Abbreviations: SF-LDQOL: Short Form of Liver Disease Quality of Life; SIMD: Scottish Index of Multiple Deprivation; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death; GAD-7: Generalised Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9.

Supplementary material

Table S1. Primary liver disease of patients in the cohort.

Table S2. Overall HR-QoL and in each SF-LDQOL domain

Table S3. Multiple linear regression: association of socioeconomic deprivation with post-transplantation HR-QoL.

Table S4. Multivariable logistic regression: association of socioeconomic deprivation with post-transplantation anxiety.

Table S5. Multivariable logistic regression: association of socioeconomic deprivation with post-transplantation depression.

Figure S1. Directed acyclic graph of the effect of socioeconomic deprivation on quality of life.

Figure S2. Directed acyclic graph of the effect of socioeconomic deprivation on anxiety/depression.

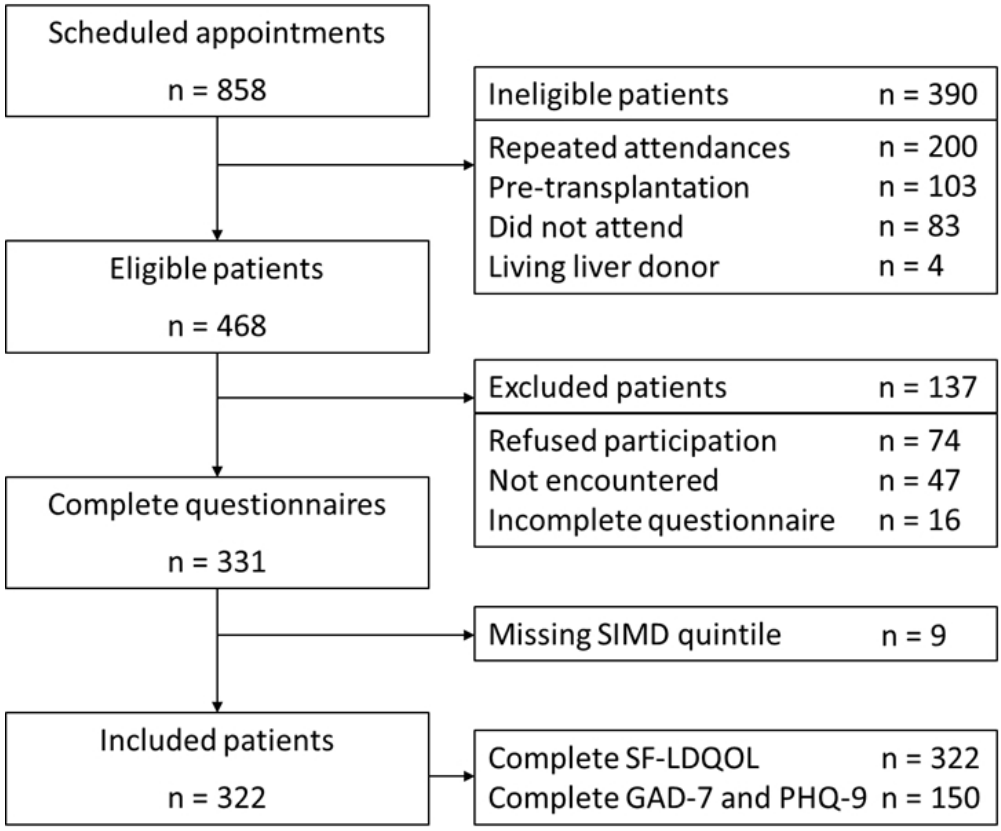


Figure 1

192x160mm (96 x 96 DPI)

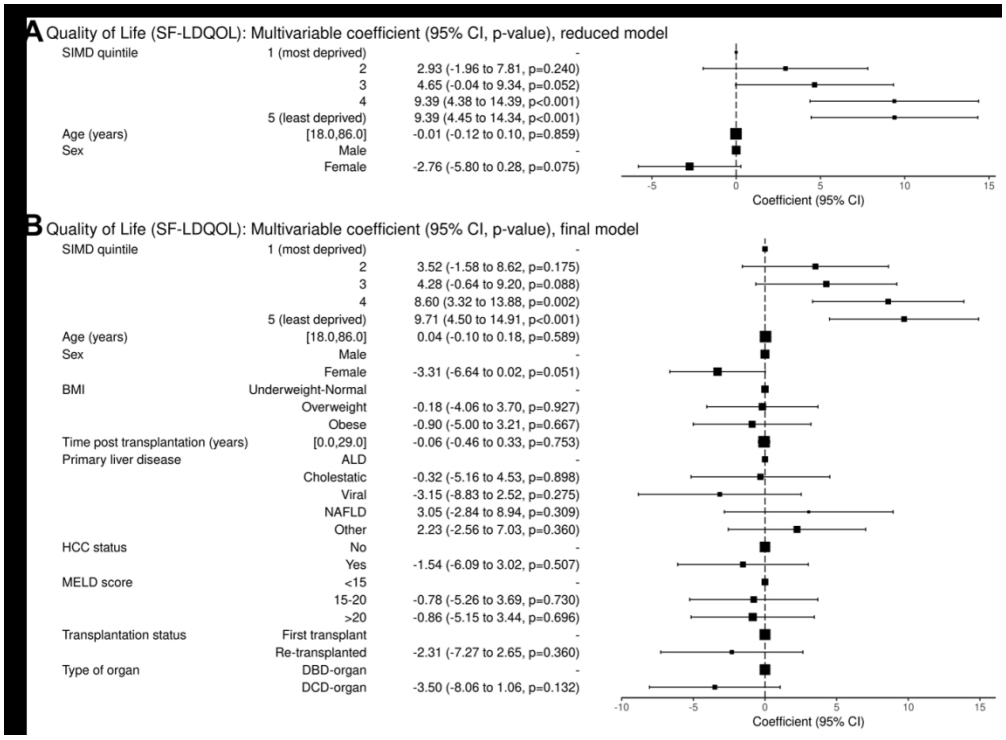


Figure 2

237x173mm (150 x 150 DPI)

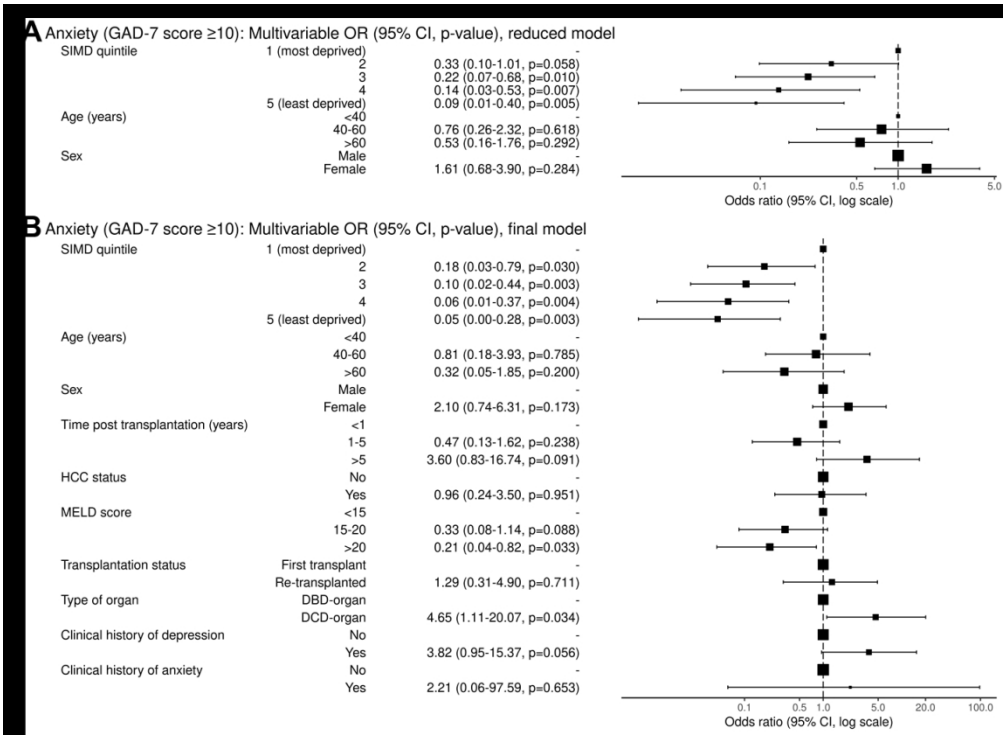


Figure 3

241x176mm (150 x 150 DPI)

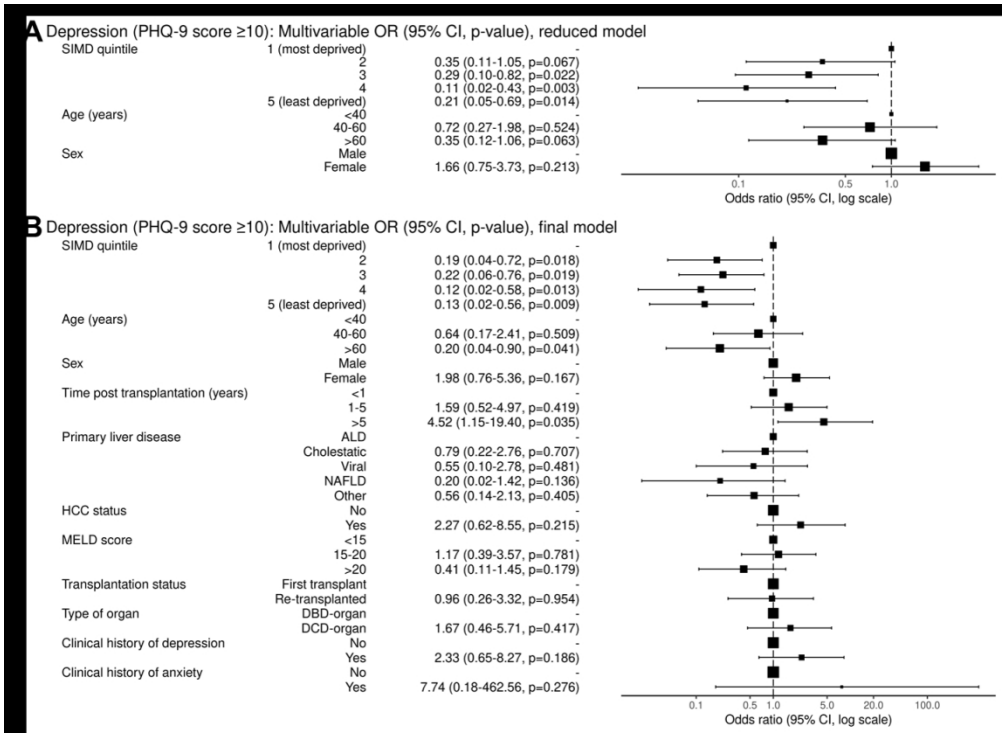


Figure 4

241x175mm (150 x 150 DPI)

Supplementary files

Table S1: Primary liver disease of patients in the cohort.

	(n=322)
Alcoholic liver disease	73
Non-alcoholic fatty liver disease (NAFLD)	32
Viral Hepatitis	
Acute hepatic failure - HBV	3
Hepatitis B cirrhosis	1
Hepatitis C cirrhosis	43
Cholestatic	
Biliary atresia	5
Primary biliary cirrhosis	38
Primary sclerosing cholangitis	30
Secondary biliary cirrhosis	1
Congenital biliary disease	1
Paediatric cholestatic liver disease	3
Other primary liver disease	
Acute hepatic failure - other drug toxicity	1
Acute hepatic failure - other	7
Acute hepatic failure - paracetamol hepatotoxicity	6
Acute hepatic failure - serologically indeterminate	4
Alpha-1-antitrypsin deficiency	2
Autoimmune chronic active liver disease	17
Budd-Chiari syndrome	1
Chronic rejection	6
Cryptogenic cirrhosis	16
Hepatic artery thrombosis	4
Hepatocellular carcinoma - cirrhotic	5
Hepatocellular carcinoma - non-cirrhotic	2
Hereditary haemachromatosis	7
Polycystic liver disease	3
Primary non-function	1
Recurrent disease	2
Wilsons disease	3
Other	5

Table S2: Overall health-related quality of life and in each SF-LDQOL domain

		Scottish Index of Multiple Deprivation (SIMD)						
		SIMD 1 (most deprived) (n=57)	SIMD 2 (n=66)	SIMD 3 (n=77)	SIMD 4 (n=60)	SIMD 5 (least deprived) (n=62)	Total (n=322)	p
Quality of Life (SF-LDQOL)	Median (IQR)	71.0 (62.0-82.0)	74.0 (60.8-82.8)	75.0 (66.0-86.0)	79.0 (73.0-85.0)	80.0 (69.8-87.8)	77.0 (66.0-84.0)	0.002
Symptoms of liver disease	Median (IQR)	67.0 (44.0-83.0)	72.0 (53.8-92.8)	75.0 (50.0-92.0)	81.0 (69.0-93.0)	82.0 (67.0-94.0)	78.0 (56.0-92.0)	0.010
Effects of liver disease	Median (IQR)	60.0 (33.0-80.0)	67.0 (33.0-87.0)	73.0 (53.0-100.0)	73.0 (51.0-93.0)	76.5 (41.8-100.0)	67.0 (40.0-93.0)	0.062
Concentration/memory	Median (IQR)	80.0 (60.0-95.0)	80.0 (65.0-93.8)	80.0 (70.0-95.0)	85.0 (78.8-100.0)	90.0 (80.0-98.8)	85.0 (70.0-95.0)	0.013
Health-related distress	Median (IQR)	80.0 (60.0-100.0)	90.0 (60.0-100.0)	90.0 (60.0-100.0)	100.0 (80.0-100.0)	100.0 (80.0-100.0)	90.0 (70.0-100.0)	0.124
Sexual function	Median (IQR)	100.0 (37.5-100.0)	100.0 (50.0-100.0)	100.0 (50.0-100.0)	100.0 (50.0-100.0)	100.0 (50.0-100.0)	100.0 (50.0-100.0)	0.693
Quality of sleep	Median (IQR)	60.0 (44.0-72.0)	64.0 (52.0-72.0)	64.0 (48.0-76.0)	68.0 (56.0-80.0)	72.0 (61.0-84.0)	66.0 (52.0-76.0)	0.004
Loneliness	Median (IQR)	84.0 (68.0-96.0)	84.0 (72.0-96.0)	92.0 (72.0-100.0)	96.0 (84.0-100.0)	96.0 (84.0-100.0)	88.0 (80.0-100.0)	0.002
Hopelessness	Median (IQR)	73.0 (53.0-87.0)	73.0 (54.8-93.0)	73.0 (67.0-93.0)	73.0 (67.0-100.0)	73.0 (67.0-93.0)	73.0 (60.0-93.0)	0.268
Social stigma of liver disease	Median (IQR)	90.0 (75.0-100.0)	100.0 (75.0-100.0)	95.0 (80.0-100.0)	95.0 (83.8-100.0)	100.0 (81.2-100.0)	95.0 (75.0-100.0)	0.525

Abbreviations: SIMD: Scottish Index of Multiple Deprivation; SF-LDQOL: Short Form of Liver Disease Quality of Life; IQR: Interquartile Range.

Table S3: Multiple linear regression: association of socioeconomic deprivation with post-transplantation HR-QoL.

				Quality of Life (SF-LDQOL)	
		Mean (SD)	Univariable coefficient (95% CI)	Multivariable coefficient (95% CI)[1]	Multivariable coefficient (95% CI)[2]
SIMD quintile	1 (most deprived)	69.6 (15.6)	-	-	-
	2	71.9 (15.4)	2.34 (-2.51 to 7.19, p=0.343)	2.93 (-1.96 to 7.81, p=0.240)	3.52 (-1.58 to 8.62, p=0.175)
	3	74.3 (13.3)	4.66 (-0.02 to 9.35, p=0.051)	4.65 (-0.04 to 9.34, p=0.052)	4.28 (-0.64 to 9.20, p=0.088)
	4	78.7 (10.9)	9.10 (4.14 to 14.06, p<0.001)	9.39 (4.38 to 14.39, p<0.001)	8.60 (3.32 to 13.88, p=0.002)
	5 (least deprived)	79.0 (12.4)	9.39 (4.47 to 14.31, p<0.001)	9.39 (4.45 to 14.34, p<0.001)	9.71 (4.50 to 14.91, p<0.001)
Age (years)	[18.0,86.0]	74.7 (14.0)	0.03 (-0.08 to 0.14, p=0.606)	-0.01 (-0.12 to 0.10, p=0.859)	0.04 (-0.10 to 0.18, p=0.589)
Sex	Male	76.0 (13.1)	-	-	-
	Female	73.1 (14.9)	-2.95 (-6.03 to 0.12, p=0.060)	-2.76 (-5.80 to 0.28, p=0.075)	-3.31 (-6.64 to 0.02, p=0.051)
BMI	Underweight-Normal	74.2 (15.0)	-	-	-
	Overweight	75.2 (13.1)	1.03 (-2.70 to 4.77, p=0.586)	-	-0.18 (-4.06 to 3.70, p=0.927)
	Obese	74.1 (14.1)	-0.05 (-3.92 to 3.83, p=0.982)	-	-0.90 (-5.00 to 3.21, p=0.667)
Time post transplantation (years)	[0.0,29.0]	0.2 (0.04)	-0.00 (-0.00 to 0.00, p=0.789)	-	-0.00 (-0.00 to 0.00, p=0.753)
Primary liver disease	ALD	75.2 (11.9)	-	-	-
	Cholestatic	73.7 (15.3)	-1.54 (-6.01 to 2.93, p=0.498)	-	-0.32 (-5.16 to 4.53, p=0.898)
	Viral	70.8 (15.1)	-4.44 (-9.68 to 0.80, p=0.097)	-	-3.15 (-8.83 to 2.52, p=0.275)
	NAFLD	78.1 (12.8)	2.86 (-2.96 to 8.68, p=0.334)	-	3.05 (-2.84 to 8.94, p=0.309)
	Other	75.8 (14.1)	0.54 (-3.74 to 4.81, p=0.805)	-	2.23 (-2.56 to 7.03, p=0.360)
HCC status	No	75.1 (14.1)	-	-	-
	Yes	73.1 (13.8)	-2.02 (-5.82 to 1.79, p=0.297)	-	-1.54 (-6.09 to 3.02, p=0.507)
MELD score	<15	75.1 (11.4)	-	-	-
	15-20	74.7 (14.9)	-0.40 (-4.62 to 3.82, p=0.853)	-	-0.78 (-5.26 to 3.69, p=0.730)
	>20	74.3 (14.9)	-0.74 (-4.48 to 2.99, p=0.695)	-	-0.86 (-5.15 to 3.44, p=0.696)
Transplantation status	First transplant	74.9 (14.2)	-	-	-
	Re-transplanted	73.5 (12.3)	-1.40 (-6.12 to 3.31, p=0.558)	-	-2.31 (-7.27 to 2.65, p=0.360)
Type of organ	DBD-organ	75.1 (13.5)	-	-	-
	DCD-organ	72.1 (16.2)	-3.04 (-7.42 to 1.34, p=0.173)	-	-3.50 (-8.06 to 1.06, p=0.132)

[1]Number in dataframe = 322, Number in model = 322, Missing = 0, Log-likelihood = -1293.93, AIC = 2603.9, R-squared = 0.075, Adjusted R-squared = 0.057
[2]Number in dataframe = 322, Number in model = 306, Missing = 16, Log-likelihood = -1225.31, AIC = 2490.6, R-squared = 0.1, Adjusted R-squared = 0.047
Data are percentages unless otherwise stated.
Abbreviations: SF-LDQOL: Short Form of Liver Disease Quality of Life; SIMD: Scottish Index of Multiple Deprivation; IQR: Interquartile Range; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

Table S4: Multivariable logistic regression: association of socioeconomic deprivation with post-transplantation anxiety

		Anxiety (GAD-7 score ≥10)				
		No (n=132)	Yes (n=18)	Univariable OR (95% CI)	Multivariable OR (95% CI)[1]	Multivariable OR (95% CI)[2]
SIMD quintile	1 (most deprived)	16 (53.3)	14 (46.7)	-	-	-
	2	22 (75.9)	7 (24.1)	0.36 (0.11-1.08, p=0.075)	0.33 (0.10-1.01, p=0.058)	0.18 (0.03-0.79, p=0.030)
	3	31 (83.8)	6 (16.2)	0.22 (0.07-0.66, p=0.009)	0.22 (0.07-0.68, p=0.010)	0.10 (0.02-0.44, p=0.003)
	4	26 (89.7)	3 (10.3)	0.13 (0.03-0.48, p=0.004)	0.14 (0.03-0.53, p=0.007)	0.06 (0.01-0.37, p=0.004)
	5 (least deprived)	23 (92.0)	2 (8.0)	0.10 (0.01-0.42, p=0.005)	0.09 (0.01-0.40, p=0.005)	0.05 (0.00-0.28, p=0.003)
Age (years)	<40	18 (69.2)	8 (30.8)	-	-	-
	40-60	48 (76.2)	15 (23.8)	0.70 (0.26-2.00, p=0.496)	0.76 (0.26-2.32, p=0.618)	0.81 (0.18-3.93, p=0.785)
	>60	52 (85.2)	9 (14.8)	0.39 (0.13-1.18, p=0.091)	0.53 (0.16-1.76, p=0.292)	0.32 (0.05-1.85, p=0.200)
Sex	Male	69 (80.2)	17 (19.8)	-	-	-
	Female	49 (76.6)	15 (23.4)	1.24 (0.56-2.73, p=0.588)	1.61 (0.68-3.90, p=0.284)	2.10 (0.74-6.31, p=0.173)
BMI	Underweight-Normal	38 (74.5)	13 (25.5)	-	-	-
	Overweight	44 (86.3)	7 (13.7)	0.47 (0.16-1.26, p=0.140)	-	-
	Obese	36 (75.0)	12 (25.0)	0.97 (0.39-2.42, p=0.955)	-	-
Time post transplantation (years)	<1	43 (81.1)	10 (18.9)	-	-	-
	1-5	48 (82.8)	10 (17.2)	0.90 (0.34-2.38, p=0.824)	-	0.47 (0.13-1.62, p=0.238)
	>5	27 (69.2)	12 (30.8)	1.91 (0.73-5.12, p=0.189)	-	3.60 (0.83-16.74, p=0.091)
Primary liver disease	ALD	28 (77.8)	8 (22.2)	-	-	-
	Cholestatic	29 (74.4)	10 (25.6)	1.21 (0.42-3.59, p=0.729)	-	-
	Viral	15 (78.9)	4 (21.1)	0.93 (0.22-3.50, p=0.920)	-	-
	NAFLD	15 (88.2)	2 (11.8)	0.47 (0.06-2.16, p=0.372)	-	-
	Other	31 (79.5)	8 (20.5)	0.90 (0.29-2.77, p=0.857)	-	-
HCC status	No	91 (77.8)	26 (22.2)	-	-	-
	Yes	27 (81.8)	6 (18.2)	0.78 (0.27-1.98, p=0.617)	-	0.96 (0.24-3.50, p=0.951)
MELD score	<15	42 (75.0)	14 (25.0)	-	-	-
	15-20	34 (81.0)	8 (19.0)	0.71 (0.26-1.85, p=0.486)	-	0.33 (0.08-1.14, p=0.088)
	>20	36 (81.8)	8 (18.2)	0.67 (0.24-1.74, p=0.416)	-	0.21 (0.04-0.82, p=0.033)
Transplantation status	First transplant	100 (79.4)	26 (20.6)	-	-	-
	Re-transplanted	18 (75.0)	6 (25.0)	1.28 (0.43-3.41, p=0.633)	-	1.29 (0.31-4.90, p=0.711)
Type of organ	DBD-organ	96 (80.0)	24 (20.0)	-	-	-
	DCD-organ	16 (69.6)	7 (30.4)	1.75 (0.61-4.61, p=0.270)	-	4.65 (1.11-20.07, p=0.034)
Clinical history of depression	No	110 (84.0)	21 (16.0)	-	-	-
	Yes	8 (42.1)	11 (57.9)	7.20 (2.62-20.74, p<0.001)	-	3.82 (0.95-15.37, p=0.056)
Clinical history of anxiety	No	117 (79.6)	30 (20.4)	-	-	-
	Yes	1 (33.3)	2 (66.7)	7.80 (0.72-171.18, p=0.098)	-	2.21 (0.06-97.59, p=0.653)

[1]Number in dataframe = 150, Number in model = 150, Missing = 0, AIC = 153.1, C-statistic = 0.745, H&L = Chi-sq(8) 3.37 (p=0.909)
[2]Number in dataframe = 150, Number in model = 140, Missing = 10, AIC = 142.3, C-statistic = 0.828, H&L = Chi-sq(8) 6.73 (p=0.566)
Data are percentages unless otherwise stated.
Abbreviations: GAD-7: Generalised Anxiety Disorder-7; SIMD: Scottish Index of Multiple Deprivation; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

Table S5: Multivariable logistic regression: association of socioeconomic deprivation with post-transplantation depression

				Depression (PHQ-9 score ≥10)		
		No (n=108)	Yes (n=42)	Univariable OR (95% CI)	Multivariable OR (95% CI)[1]	Multivariable OR (95% CI)[2]
SIMD quintile	1 (most deprived)	14 (46.7)	16 (53.3)	-	-	-
	2	20 (69.0)	9 (31.0)	0.39 (0.13-1.12, p=0.086)	0.35 (0.11-1.15, p=0.067)	0.19 (0.04-0.72, p=0.018)
	3	28 (75.7)	9 (24.3)	0.28 (0.10-0.78, p=0.017)	0.29 (0.09-0.92, p=0.022)	0.22 (0.06-0.76, p=0.019)
	4	26 (89.7)	3 (10.3)	0.10 (0.02-0.36, p=0.001)	0.11 (0.02-0.43, p=0.003)	0.12 (0.02-0.58, p=0.013)
	5 (least deprived)	20 (80.0)	5 (20.0)	0.22 (0.06-0.70, p=0.014)	0.21 (0.06-0.79, p=0.014)	0.13 (0.02-0.56, p=0.009)
Age (years)	<40	15 (57.7)	11 (42.3)	-	-	-
	40-60	42 (66.7)	21 (33.3)	0.68 (0.27-1.76, p=0.424)	0.72 (0.27-1.98, p=0.524)	0.64 (0.17-2.41, p=0.509)
	>60	51 (83.6)	10 (16.4)	0.27 (0.09-0.75, p=0.012)	0.35 (0.12-1.06, p=0.063)	0.20 (0.04-0.90, p=0.041)
Sex	Male	64 (74.4)	22 (25.6)	-	-	-
	Female	44 (68.8)	20 (31.2)	1.32 (0.64-2.71, p=0.445)	1.66 (0.77-3.63, p=0.213)	1.98 (0.76-5.36, p=0.167)
BMI	Underweight-Normal	34 (66.7)	17 (33.3)	-	-	-
	Overweight	40 (78.4)	11 (21.6)	0.55 (0.22-1.32, p=0.186)	-	-
	Obese	34 (70.8)	14 (29.2)	0.82 (0.35-1.93, p=0.655)	-	-
Time post transplantation (years)	<1	42 (79.2)	11 (20.8)	-	-	-
	1-5	41 (70.7)	17 (29.3)	1.58 (0.67-3.87, p=0.302)	-	1.59 (0.52-4.97, p=0.419)
	>5	25 (64.1)	14 (35.9)	2.14 (0.85-5.53, p=0.110)	-	4.52 (1.15-19.40, p=0.035)
Primary liver disease	ALD	26 (72.2)	10 (27.8)	-	-	-
	Cholestatic	25 (64.1)	14 (35.9)	1.46 (0.55-3.96, p=0.452)	-	0.79 (0.22-2.76, p=0.707)
	Viral	14 (73.7)	5 (26.3)	0.93 (0.25-3.18, p=0.908)	-	0.55 (0.10-2.78, p=0.481)
	NAFLD	15 (88.2)	2 (11.8)	0.35 (0.05-1.54, p=0.207)	-	0.20 (0.02-1.42, p=0.136)
	Other	28 (71.8)	11 (28.2)	1.02 (0.37-2.84, p=0.967)	-	0.56 (0.14-2.13, p=0.405)
HCC status	No	84 (71.8)	33 (28.2)	-	-	-
	Yes	24 (72.7)	9 (27.3)	0.95 (0.39-2.21, p=0.916)	-	2.27 (0.62-8.55, p=0.215)
MELD score	<15	42 (75.0)	14 (25.0)	-	-	-
	15-20	27 (64.3)	15 (35.7)	1.67 (0.70-4.03, p=0.252)	-	1.17 (0.39-3.57, p=0.781)
	>20	33 (75.0)	11 (25.0)	1.00 (0.40-2.49, p=1.000)	-	0.41 (0.11-1.45, p=0.179)
Transplantation status	First transplant	91 (72.2)	35 (27.8)	-	-	-
	Re-transplanted	17 (70.8)	7 (29.2)	1.07 (0.39-2.72, p=0.890)	-	0.96 (0.26-3.32, p=0.954)
Type of organ	DBD-organ	86 (71.7)	34 (28.3)	-	-	-
	DCD-organ	16 (69.6)	7 (30.4)	1.11 (0.40-2.84, p=0.838)	-	1.67 (0.46-5.71, p=0.417)
Clinical history of depression	No	100 (76.3)	31 (23.7)	-	-	-
	Yes	8 (42.1)	11 (57.9)	4.44 (1.65-12.42, p=0.003)	-	2.33 (0.65-8.27, p=0.186)
Clinical history of anxiety	No	107 (72.8)	40 (27.2)	-	-	-
	Yes	1 (33.3)	2 (66.7)	5.35 (0.50-117.00, p=0.176)	-	7.74 (0.18-462.56, p=0.276)

[1]Number in dataframe = 150, Number in model = 150, Missing = 0, AIC = 172.8, C-statistic = 0.736, H&L = Chi-sq(8) 4.13 (p=0.845)
[2]Number in dataframe = 150, Number in model = 140, Missing = 10, AIC = 176.2, C-statistic = 0.806, H&L = Chi-sq(8) 9.60 (p=0.295)
Data are percentages unless otherwise stated.
Abbreviations: PHQ-9: Patient Health Questionnaire-9; SIMD: Scottish Index of Multiple Deprivation; BMI: Body Mass Index; ALD: Alcoholic Liver Disease; NAFLD: Non-alcoholic Fatty Liver Disease; HCC: Hepatocellular Carcinoma; MELD: Model for End-Stage Liver Disease; DBD: Donation after Brainstem Death; DCD: Donation after Circulatory Death.

Figure S1: Directed acyclic graph of the effect of socioeconomic deprivation on quality of life.

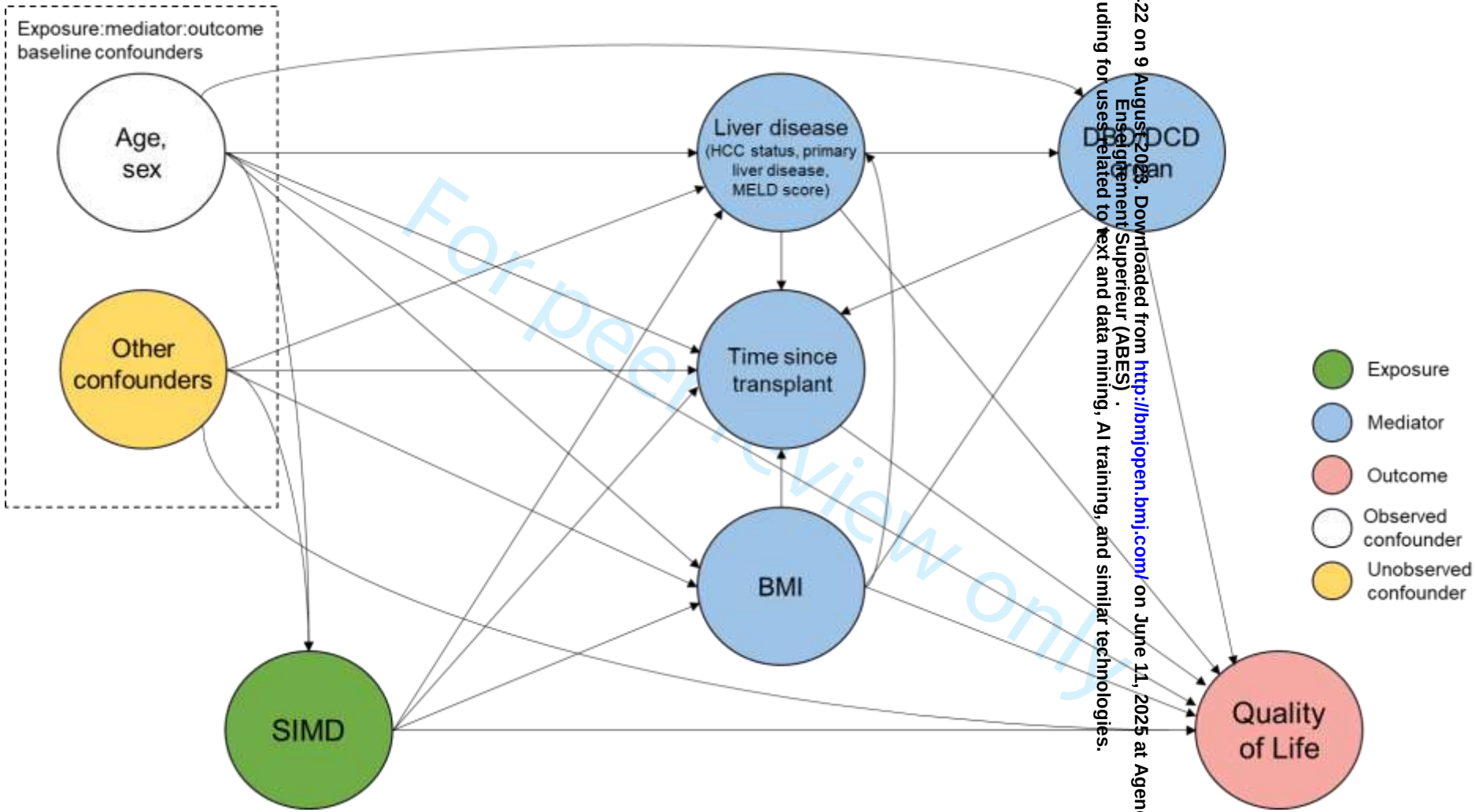
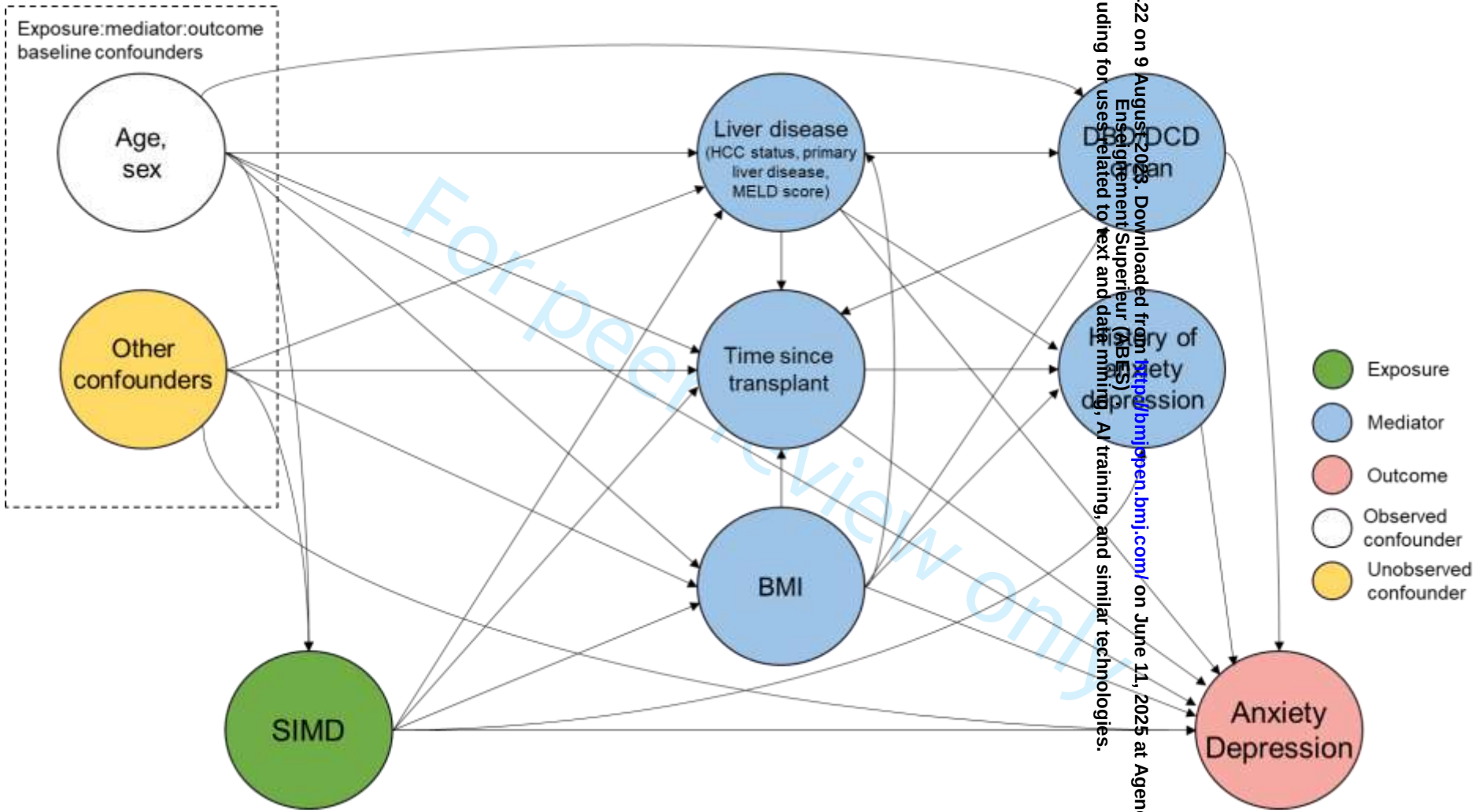


Figure S2: Directed acyclic graph of the effect of socioeconomic deprivation on anxiety/depression.



STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	N/A
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	7
Outcome data	15*	Report numbers of outcome events or summary measures	7/8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7/8

		(*b*) Report category boundaries when continuous variables were categorized	7/8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11/12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11/12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.