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Citation for published version:

Sgro, A, Cambridge, WA, Mclean, KA, Drake, TM, Camilleri-Brennan, J, Knight, S, Pius, R, Wu, DA, Wigmore, SJ & Harrison, EM 2023, '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', *BMJ Open*, vol. 13, no. 8, e070422. <https://doi.org/10.1136/bmjopen-2022-070422>

Digital Object Identifier (DOI):

[10.1136/bmjopen-2022-070422](https://doi.org/10.1136/bmjopen-2022-070422)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Publisher's PDF, also known as Version of record

Published In:

BMJ Open

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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

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To cite: Sgrò A, Cambridge WA, McLean KA, *et al.* 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. *BMJ Open* 2023;**13**:e070422. doi:10.1136/bmjopen-2022-070422

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2022-070422>).

Received 23 November 2022
Accepted 02 June 2023



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ABSTRACT

Objective To identify whether socioeconomic deprivation is associated with worse health-related quality of life (HR-QoL), anxiety and 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 Quality of Life' Questionnaire, the Generalised Anxiety Disorder-7 (GAD-7) Questionnaire and the Patient Health Questionnaire-9 (PHQ-9). The aggregate HR-QoL Score (range 0–100) was derived, and multivariable linear regression was performed based on sociodemographic and clinical variables to estimate its independent association with Scottish Index of Multiple Deprivation (SIMD) quintiles. The GAD-7 Questionnaire and PHQ-9 were used to screen respondents for anxiety and depression, and multivariable logistic regression was 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 to 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 to 0.28, $p = 0.003$) or depression (OR 0.13, 95% CI: 0.02 to 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.

INTRODUCTION

Liver transplantation (LT) is the only curative treatment for end-stage liver disease. Over the course of the last 50 years, advances

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Large sample size with a high response rate.
- ⇒ The validated and disease-specific Short Form of Liver Disease Quality of Life Questionnaire was used.
- ⇒ Association between Scottish Index of Multiple Deprivation and outcomes not adjusted for comorbidities.
- ⇒ Lack of pretransplantation Health-Related Quality of Life scores.

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 with pretransplantation 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} Pretransplantation and post-transplantation variables, such as primary liver disease, retransplantation 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 USA, inferior insurance cover is linked with greater mortality in adult recipients.^{17 18} Similarly, greater socio-economic 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) LT recipients attending the Scottish Liver Transplant Unit for an outpatient clinic in two different periods (16 July–3 September 2015; 15 August–14 September 2017) were enrolled on a voluntary basis. This analysis was performed according to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) 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 0–100, with higher scores denoting better QoL).

Patients recruited in the second period were also invited to complete the Generalised Anxiety Disorder-7 (GAD-7) Questionnaire and Patient Health Questionnaire-9 (PHQ-9).^{25 26} The total GAD-7 Score ranges from 0 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 0–27 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 on 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 summarised 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 χ^2 or Fisher's exact tests. All SF-LDQOL Questionnaire responses were assigned to a value based on 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, viral (hepatitis B or C) or other aetiology); hepatocellular carcinoma status (present, absent); pretransplantation Model for End-stage Liver Disease (MELD) category (< 15 , $15–20$, ≥ 21); transplantation status (first transplant, retransplanted) 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 (online supplemental figures S1 and S2). The threshold of statistical significance was set at $p < 0.05$ a priori. Statistical analyses were conducted in R V.3.3.4 (R Foundation for

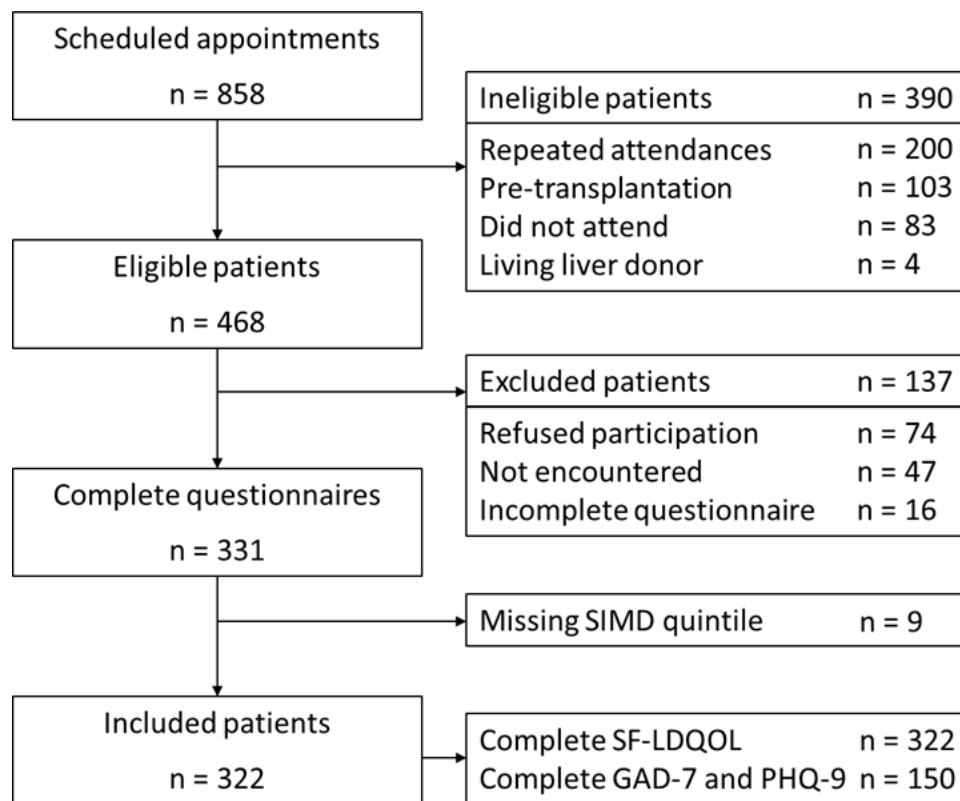


Figure 1 Flow diagram of patient inclusion. GAD-7, Generalised Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9; SF-LDQOL, Short Form of Liver Disease Quality of Life; SIMD, Scottish Index of Multiple Deprivation.

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 (figure 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, 9 had an invalid postcode and could not be allocated to an 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/PHQ-9 subgroup are summarised in tables 1 and 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 groups and greater prevalence of retransplantation in recipients living in areas of least deprivation in the GAD-7/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 online supplemental table S1. The scores of the nine SF-LDQOL domains are presented in online supplemental 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 to 14.9, $p < 0.001$) between the most and least deprived quintiles (figure 2, online supplemental 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 (online supplemental table S3).

Multivariable logistic regression

In the GAD-7/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 to 0.28, $p = 0.003$) and depression (OR 0.13, 95% CI: 0.02 to 0.56, $p = 0.009$) (figures 3 and 4, online supplemental tables S4 and S5). Pretransplantation MELD Scores > 20 were found to be

Table 1 Patients' demographics for the overall cohort

	Scottish Index of Multiple Deprivation (SIMD)					Total (n=322)	P value
	SIMD 1 (most deprived) (n=57)	SIMD 2 (n=66)	SIMD 3 (n=77)	SIMD 4 (n=60)	SIMD 5 (least deprived) (n=62)		
Quality of Life (SF- LDQOL)	71.0 (62.0–82.0)	74.0 (60.8–82.8)	75.0 (66.0–86.0)	79.0 (73.0–87.5)	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 (55.0–66.2)	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 (24.8–31.3)	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)	16 (26.7)	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)	14 (23.3)	16 (25.8)	95 (29.5)	0.906
HCC status	No 44 (77.2)	51 (77.3)	64 (83.1)	48 (80.0)	49 (79.0)	256 (79.5)	
	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)	26 (43.3)	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
	Retransplanted 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)	50 (83.3)	49 (79.0)	269 (83.5)	0.596
	DCD-organ 6 (10.5)	9 (13.6)	10 (13.0)	8 (13.3)	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.

ALD, alcoholic liver disease; BMI, body mass index; DBD, donation after brainstem death; DCD, donation after circulatory death; HCC, hepatocellular carcinoma; MELD, Model for End-stage Liver Disease; NAFLD, non-alcoholic fatty liver disease; SF-LDQOL, Short Form of Liver Disease Quality of Life; SIMD, Scottish Index of Multiple Deprivation.

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

		Scottish Index of Multiple Deprivation (SIMD)					Total (n=150)	P value
		SIMD 1 (most deprived) (n=30)	SIMD 2 (n=29)	SIMD 3 (n=37)	SIMD 4 (n=29)	SIMD 5 (least deprived) (n=25)		
Anxiety (GAD-7 Score \geq 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 \geq 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)	
	\geq 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
	Retransplanted	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.

ALD, alcoholic liver disease; BMI, body mass index; DBD, donation after brainstem death; DCD, donation after circulatory death; GAD-7, Generalised Anxiety Disorder-7; HCC, hepatocellular carcinoma; MELD, Model for End-stage Liver Disease; NAFLD, non-alcoholic fatty liver disease; PHQ-9, Patient Health Questionnaire-9; SIMD, Scottish Index of Multiple Deprivation.

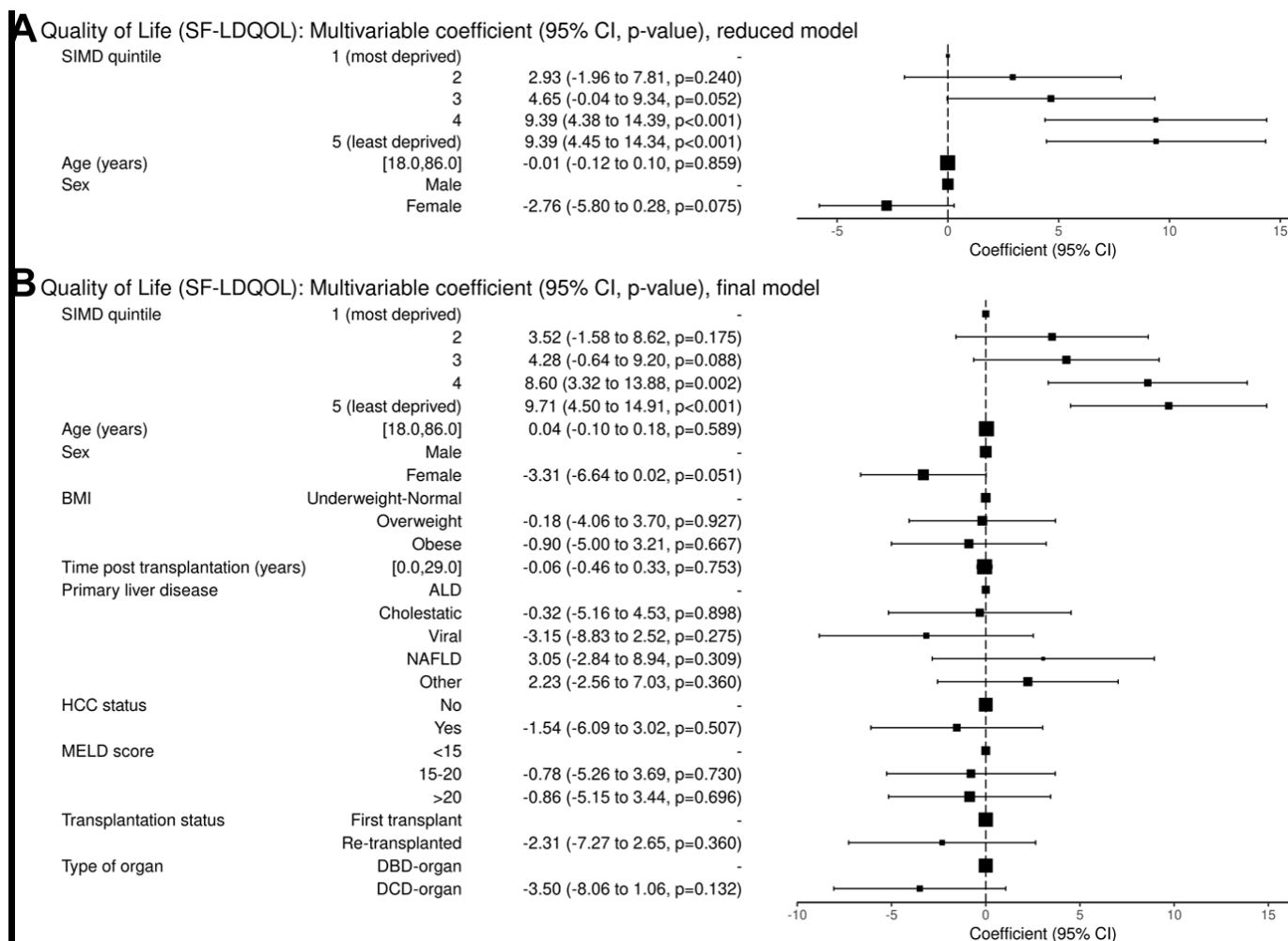


Figure 2 Forest plots of the effect size for socioeconomic deprivation on post-transplantation HR-QoL: (A) reduced model; (B) final model. ALD, alcoholic liver disease; BMI, body mass index; DBD, donation after brainstem death; DCD, donation after circulatory death; HCC, hepatocellular carcinoma; MELD, Model for End-stage Liver Disease; NAFLD, non-alcoholic fatty liver disease; SF-LDQOL, Short Form of Liver Disease Quality of Life; SIMD, Scottish Index of Multiple Deprivation.

protective towards post-transplantation anxiety (OR 0.21, 95% CI: 0.04 to 0.82, $p=0.033$), whereas receipt of a DCD-organ was associated with greater anxiety (OR 4.65, 95% CI: 1.11 to 20.07, $p=0.034$) (online supplemental table S4). Although a post-transplantation survival time greater than 5 years was associated with worse depression (OR 4.52, 95% CI: 1.15 to 19.40, $p=0.035$), recipients older than 60 years of age were found to be less likely to suffer from depressive disorders (OR 0.20, 95% CI: 0.04 to 0.90, $p=0.041$) (online supplemental table S5).

DISCUSSION

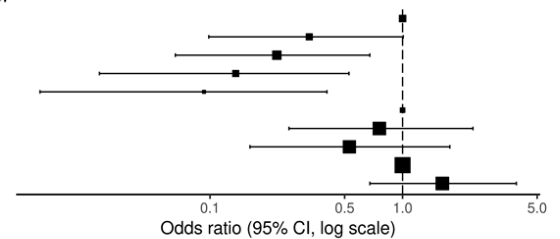
Most LT recipients experience a significant improvement in HR-QoL after transplantation, but it is not completely understood why they do not achieve HR-QoL scores comparable with the healthy general population.⁶⁸ There is a paucity of data on the factors that may influence HR-QoL outcomes after LT. This 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

A Anxiety (GAD-7 score ≥ 10): Multivariable OR (95% CI, p-value), reduced model

SIMD quintile	1 (most deprived)	-
	2	0.33 (0.10-1.01, p=0.058)
	3	0.22 (0.07-0.68, p=0.010)
	4	0.14 (0.03-0.53, p=0.007)
Age (years)	5 (least deprived)	0.09 (0.01-0.40, p=0.005)
	<40	-
Sex	40-60	0.76 (0.26-2.32, p=0.618)
	>60	0.53 (0.16-1.76, p=0.292)
Sex	Male	-
	Female	1.61 (0.68-3.90, p=0.284)


B Anxiety (GAD-7 score ≥ 10): Multivariable OR (95% CI, p-value), final model

SIMD quintile	1 (most deprived)	-
	2	0.18 (0.03-0.79, p=0.030)
	3	0.10 (0.02-0.44, p=0.003)
	4	0.06 (0.01-0.37, p=0.004)
Age (years)	5 (least deprived)	0.05 (0.00-0.28, p=0.003)
	<40	-
Sex	40-60	0.81 (0.18-3.93, p=0.785)
	>60	0.32 (0.05-1.85, p=0.200)
Sex	Male	-
	Female	2.10 (0.74-6.31, p=0.173)
Time post transplantation (years)	<1	-
	1-5	0.47 (0.13-1.62, p=0.238)
	>5	3.60 (0.83-16.74, p=0.091)
HCC status	No	-
	Yes	0.96 (0.24-3.50, p=0.951)
MELD score	<15	-
	15-20	0.33 (0.08-1.14, p=0.088)
	>20	0.21 (0.04-0.82, p=0.033)
Transplantation status	First transplant	-
	Re-transplanted	1.29 (0.31-4.90, p=0.711)
Type of organ	DBD-organ	-
	DCD-organ	4.65 (1.11-20.07, p=0.034)
Clinical history of depression	No	-
	Yes	3.82 (0.95-15.37, p=0.056)
Clinical history of anxiety	No	-
	Yes	2.21 (0.06-97.59, p=0.653)

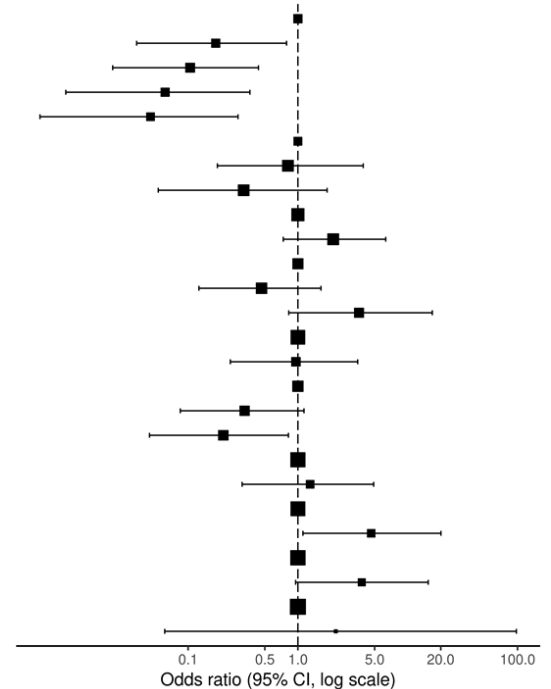


Figure 3 Forest plots of the effect size for socioeconomic deprivation on post-transplantation anxiety: (A) reduced model; (B) final model. ALD, alcoholic liver disease; BMI, body mass index; DBD, donation after brainstem death; DCD, donation after circulatory death; GAD-7, Generalised Anxiety Disorder-7; HCC, hepatocellular carcinoma; MELD, Model for End-stage Liver Disease; NAFLD, non-alcoholic fatty liver disease; PHQ-9, Patient Health Questionnaire-9; SF-LDQOL, Short Form of Liver Disease Quality of Life; SIMD, Scottish Index of Multiple Deprivation.

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 retransplantation 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%) were in line with prevalence rates described by other studies (range 20%–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 pretransplantation 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

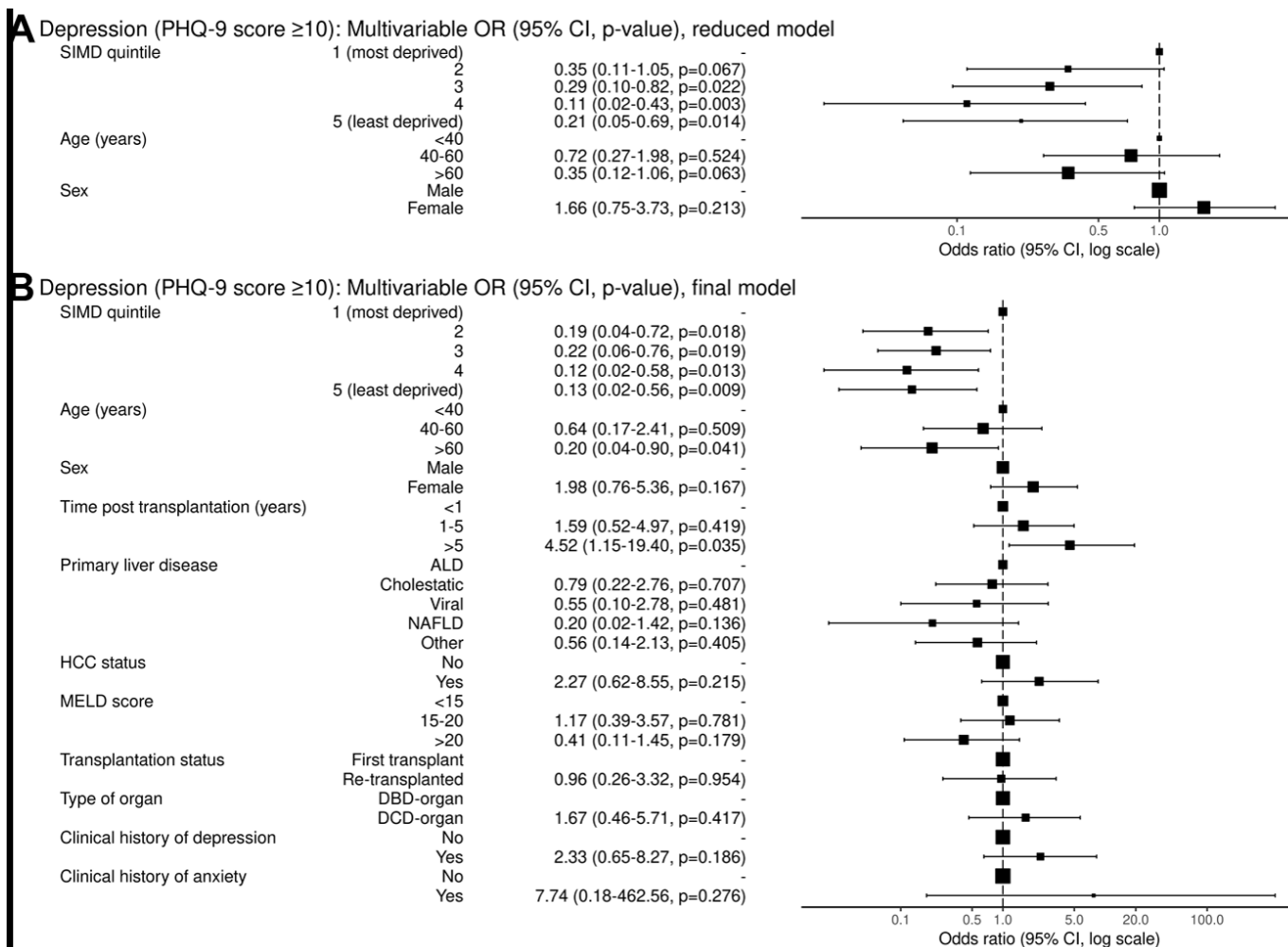


Figure 4 Forest plots of the effect size for socioeconomic deprivation on post-transplantation depression: (A) reduced model; (B) final model. ALD, alcoholic liver disease; BMI, body mass index; DBD, donation after brainstem death; DCD, donation after circulatory death; GAD-7, Generalised Anxiety Disorder-7; HCC, hepatocellular carcinoma; MELD, Model for End-stage Liver Disease; NAFLD, non-alcoholic fatty liver disease; PHQ-9, Patient Health Questionnaire-9; SF-LDQOL, Short Form of Liver Disease Quality of Life; SIMD, Scottish Index of Multiple Deprivation.

Depressive symptoms were more prevalent in our sample (28.0%) than in other studies (range 15%–20%).^{40 45 46} A possible explanation is that most studies have focused on the first 5 years after LT, while in our study over one-fourth of patients who completed the PHQ-9 questionnaire were over 5 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 5 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. Second, 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. Third, 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 pretransplantation HR-QoL scores. It is plausible that the lower HR-QoL scores in more deprived recipients could be explained by lower pretransplantation 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: KM, AS, EH and RP. Data collection: KM, AS, WAC and JC-B. Analysis and interpretation of the data: KM, AS, TMD and EH. Drafting of the article: AS. Critical revision of the article for important intellectual content; final approval of the article: AS, WAC, KM, TMD, JC-B, SRK, RP, WAD, SJW and EH. EH is responsible for the overall content of the research as the guarantor.

Funding KM received MRC funding, and TMD received CRUK funding.

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

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Participants gave informed consent to participate in the study before taking part.

Ethics approval 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 exempted this study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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REFERENCES

- Zarrinpar A, Busuttil RW. Liver transplantation: past, present and future. *Nat Rev Gastroenterol Hepatol* 2013;10:434–40.
- National Health Service Blood and Transplant. Annual report on liver transplantation: report For2019/2020 (1 April 2010–31 March 2020). NHS; 2020.
- Onghena L, Develtere W, Poppe C, *et al*. Quality of life after liver transplantation: state of the art. *World J Hepatol* 2016;8:749–56.
- Cristin DJ, Forman LM, Jackson WE. Beyond survival: targeting health-related quality of life outcomes after liver transplantation. *Clin Liver Dis (Hoboken)* 2021;17:359–64.
- McLean KA, Drake TM, Sgrò A, *et al*. The effect of liver transplantation on patient-centred outcomes: a propensity-score matched analysis. *Transpl Int* 2019:808–19.
- Telles-Correia D, Barbosa A, Mega I, *et al*. When does quality of life improve after liver transplantation? A longitudinal prospective study. *Transplant Proc* 2009;41:904–5.
- Ratcliffe J, Longworth L, Young T, *et al*. Assessing health-related quality of life pre- and post-liver transplantation: A prospective multicenter study. *Liver Transplantation* 2002;8:263–70.
- Tome S, Wells JT, Said A, *et al*. Quality of life after liver transplantation. A systematic review. *J Hepatol* 2008;48:567–77.
- Duffy JP, Kao K, Ko CY, *et al*. Long-term patient outcome and quality of life after liver transplantation: analysis of 20-year survivors. *Ann Surg* 2010;252:652–61.
- De Bona M, Ponton P, Ermani M, *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;33:609–15.
- Kousoulas L, Neipp M, Barg-Hock H, *et al*. Health-related quality of life in adult transplant recipients more than 15 years after orthotopic liver transplantation. *Transpl Int* 2008;21:1052–8.
- Shaw M, Gordon D, Dorling D, *et al*. Increasing mortality differentials by residential area level of poverty: Britain 1981–1997. *Soc Sci Med* 2000;51:151–3.
- Waitzman NJ, Smith KR. Phantom of the area: poverty-area residence and mortality in the United States. *Am J Public Health* 1998;88:973–6.
- Roux AVD, Merkin SS, Arnett D, *et al*. Neighborhood of residence and incidence of coronary heart disease. *N Engl J Med* 2001;345:99–106.
- Drey N, Roderick P, Mullee M, *et al*. A population-based study of the incidence and outcomes of diagnosed chronic kidney disease. *Am J Kidney Dis* 2003;42:677–84.
- Adler JT, Yeh H. Social determinants in liver transplantation. *Clin Liver Dis (Hoboken)* 2016;7:15–7.
- Stepanova M, Al Qahtani S, Mishra A, *et al*. Outcomes of liver transplantation by insurance types in the United States. *Am J Manag Care* 2020;26:e121–6.
- Yoo HY, Thuluvath PJ. Outcome of liver transplantation in adult recipients: influence of neighborhood income, education, and insurance. *Liver Transpl* 2004;10:235–43.
- Wadhvani SI, Beck AF, Bucuvalas J, *et al*. Neighborhood socioeconomic deprivation is associated with worse patient and graft survival following pediatric liver transplantation. *Am J Transplant* 2020;20:1597–605.



- 20 Dick AAS, Winstanley E, Ohara M, *et al.* Do funding sources influence long-term patient survival in pediatric liver transplantation *Pediatr Transplant* 2021;25:e13887.
- 21 Serper M, Patzer RE, Reese PP, *et al.* Medication misuse, Nonadherence, and clinical outcomes among liver transplant recipients. *Liver Transpl* 2015;21:22–8.
- 22 Lieber SR, Volk ML. Non-adherence and graft failure in adult liver transplant recipients. *Dig Dis Sci* 2013;58:824–34.
- 23 von Elm E, Altman DG, Egger M, *et al.* The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Journal of Clinical Epidemiology* 2008;61:344–9.
- 24 Kanwal F, Spiegel BMR, Hays RD, *et al.* Prospective validation of the short form liver disease quality of life instrument. *Aliment Pharmacol Ther* 2008;28:1088–101.
- 25 Spitzer RL, Kroenke K, Williams JBW, *et al.* A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006;166:1092–7.
- 26 Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–13.
- 27 Löwe B, Decker O, Müller S, *et al.* Validation and standardization of the generalized anxiety disorder Screener (GAD-7) in the general population. *Med Care* 2008;46:266–74.
- 28 Levis B, Benedetti A, Thombs BD, *et al.* Accuracy of patient health Questionnaire-9 (PHQ-9) for screening to detect major depression: individual participant data meta-analysis. *BMJ* 2019;365:l1476.
- 29 Scottish Executive National Statistics. *Scottish Index of Multiple Deprivation (SIMD): Technical Notes*. 2016.
- 30 Rogal SS, Dew MA, Fontes P, *et al.* Early treatment of depressive symptoms and long-term survival after liver transplantation. *Am J Transplant* 2013;13:928–35.
- 31 Dew MA, Rosenberger EM, Myaskovsky L, *et al.* Depression and anxiety as risk factors for morbidity and mortality after organ transplantation: A systematic review and meta-analysis. *Transplantation* 2016;100:988–1003.
- 32 Rogal SS, Landsittel D, Surman O, *et al.* Pretransplant depression, antidepressant use, and outcomes of orthotopic liver transplantation. *Liver Transpl* 2011;17:251–60.
- 33 Aguiar MIF de, Braga VAB, Garcia JHP, *et al.* Quality of life in liver transplant recipients and the influence of Sociodemographic factors. *Rev Esc Enferm USP* 2016;50:411–8.
- 34 Zahn A, Seubert L, Jünger J, *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;18:327–35.
- 35 Saab S, Bownik H, Ayoub N, *et al.* Differences in health-related quality of life scores after orthotopic liver transplantation with respect to selected socioeconomic factors. *Liver Transpl* 2011;17:580–90. 10.1002/lt.22268 Available: <http://doi.wiley.com/10.1002/lt.v17.5>
- 36 Estraviz B, Quintana JM, Valdivieso A, *et al.* Factors influencing change in health-related quality of life after liver transplantation. *Clin Transplant* 2007;21:481–99.
- 37 Aberg F, Höckerstedt K, Roine RP, *et al.* Influence of liver-disease etiology on long-term quality of life and employment after liver transplantation. *Clin Transplant* 2012;26:729–35.
- 38 Desai R, Jamieson NV, Gimson AE, *et al.* Quality of life up to 30 years following liver transplantation. *Liver Transpl* 2008;14:1473–9.
- 39 Yang LS, Shan LL, Saxena A, *et al.* Liver transplantation: a systematic review of long-term quality of life. *Liver Int* 2014;34:1298–313.
- 40 Russell RT, Feurer ID, Wisawatapnimit P, *et al.* 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;12:138–44.
- 41 van Ginneken BTJ, van den Berg-Emons RJG, van der Windt A, *et al.* Persistent fatigue in liver transplant recipients: a two-year follow-up study. *Clin Transplant* 2010;24:E10–6.
- 42 Callaghan CJ, Charman SC, Muiesan P, *et al.* Outcomes of transplantation of livers from donation after circulatory death donors in the UK: a cohort study. *BMJ Open* 2013;3:e003287.
- 43 de Vera ME, Lopez-Solis R, Dvorchik I, *et al.* Liver transplantation using donation after cardiac death donors: long-term follow-up from a single center. *Am J Transplant* 2009;9:773–81.
- 44 Xin L-M, Chen L, Ji Z-P, *et al.* Risk factors for anxiety in major depressive disorder patients. *Clin Psychopharmacol Neurosci* 2015;13:263–8.
- 45 Aadahl M, Hansen BA, Kirkegaard P, *et al.* Fatigue and physical function after orthotopic liver transplantation. *Liver Transplantation* 2002;8:251–9.
- 46 Collis I, Burroughs A, Rolles K, *et al.* Psychiatric and social outcome of liver transplantation. *Br J Psychiatry* 1995;166:521–4.
- 47 Annema C, Roodbol PF, Stewart RE, *et al.* Prevalence of psychological problems and associated transplant-related variables at different time periods after liver transplantation. *Liver Transpl* 2015;21:524–38.
- 48 McLean J, Christie S, Hinchliffe S, *et al.*, eds. In: *Scottish Health Survey 2017*. 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;82:703–10.
- 50 Krieger N, Chen JT, Waterman PD, *et al.* 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;156:471–82.
- 51 Xuan J, Kirchoerfer LJ, Boyer JG, *et al.* Effects of Comorbidity on health-related quality-of-life scores: an analysis of clinical trial data. *Clin Ther* 1999;21:383–403.