Original Article

Socioeconomic Deprivation and Survival After Heart Transplantation in England
An Analysis of the United Kingdom Transplant Registry

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Background—Socioeconomic deprivation (SED) is associated with shorter survival across a range of cardiovascular and noncardiovascular diseases. The association of SED with survival after heart transplantation in England, where there is universal healthcare provision, is unknown.

Methods and Results—Long-term follow-up data were obtained for all patients in England who underwent heart transplantation between 1995 and 2014. We used the United Kingdom Index of Multiple Deprivation (UK IMD), a neighborhood level measure of SED, to estimate the relative degree of deprivation for each recipient. Cox proportional hazard models were used to examine the association between SED and overall survival and conditional survival (dependant on survival at 1 year after transplantation) during follow-up. Models were stratified by transplant center and adjusted for donor and recipient age and sex, ethnicity, serum creatinine, diabetes mellitus, and heart failure cause. A total of 2384 patients underwent heart transplantation. There were 1101 deaths during 17 040 patient-year follow-up. Median overall survival was 12.6 years, and conditional survival was 15.6 years. Comparing the most deprived with the least deprived quintile, adjusted hazard ratios for all-cause mortality were 1.27 (1.04–1.55; *P*=0.021) and 1.59 (1.22–2.09; *P*=0.001) in the overall and conditional models, respectively. Median overall survival and conditional survival were 3.4 years shorter in the most deprived quintile than in the least deprived.

Conclusions—Higher SED is associated with shorter survival in heart transplant recipients in England and should be considered when comparing outcomes between centers. Future research should seek to identify modifiable mediators of this association. (***Circ Cardiovasc Qual Outcomes***. 2016;9:695-703. DOI: 10.1161/CIRCOUTCOMES.116.002652.)

Key Words: England ■ heart failure ■ heart transplantation ■ proportional hazards models

Patients with advanced heart failure have a poor prognosis and quality of life. Heart transplantation remains the definitive treatment for advanced heart failure that is refractory to conventional medical and surgical therapy. Heart transplantation offers improved survival[1] and quality of life.[2] More than 110 000 heart transplants have been performed worldwide and recorded in the Registry of the International Society for Heart and Lung Transplantation. Survival is excellent with a median survival from transplantation of 11 years, and 13 years for patients who survive the first year.[3]

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Socioeconomic deprivation (SED) refers to the social and economic conditions in which an individual or group of individuals live. Determinants of SED include wealth and income, education, employment and occupation, access to services and local environmental factors such as crime.[4] SED has been associated with increased incidence, earlier presentation, and shorter survival in a range of cardiovascular diseases,[5] including heart failure.[6] Socioeconomic gradients in outcomes after heart transplantation have been described in the United States. Greater SED was associated with an increased risk of graft failure and an increased risk of acute rejection in adult[7] and pediatric recipients.[8,9] In addition, health insurance status was associated with survival after heart transplantation in the United States. Recipients with Medicaid or Medicare insurance had shorter post-transplant survival than recipients with private insurance.[10]

The National Health Service (NHS) in England provides universal health care to all residents, free at the point of delivery. There is a small charge for prescribed medications (a set fee, not dependent on the drug dispensed), but some patients with long-term conditions or those living in low-income households are exempt from these charges. Universal healthcare systems such as the NHS are thought to reduce socioeconomic inequalities in health.[11] There are socioeconomic

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WHAT IS KNOWN

- Socioeconomic deprivation is associated with adverse outcomes across a range of cardiovascular and noncardiovascular diseases.
- In the United States, various indicators of socioeconomic deprivation including insurance status and level of education have been associated with survival after heart transplantation.
- Whether such an association exists in systems with universal access to health care, provided free of charge, is unknown.

WHAT THE STUDY ADDS

- In England, where health care is provided free of charge to all residents, socioeconomic deprivation is associated with shorter survival after heart transplantation.
- This suggests that the disparities in survival observed in the United States are unlikely to be explained by variations in access to healthcare services alone.

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gradients in the incidence, prevalence, and case-fatality rates of heart failure in England, but the magnitude of these gradients has reduced in the past decade.[12] Importantly, the use of evidence-based treatments for heart failure seem to be independent of SED within the NHS in England. The association between SED and outcomes after heart transplantation has not been examined in a country with a universal healthcare system. We have used data from the UK Transplant Registry to examine the association between SED and survival after heart transplantation in England.

Methods

Study Population

The UK Transplant Registry, maintained by NHS Blood and Transplant, was established in April 1995 to monitor overall and center-specific outcomes. Heart transplantation was performed in 7 specialist centers in England in 1995 and 5 centers remain active in 2014. Any patient entitled to NHS treatment may be referred for transplant assessment, irrespective of sex, socioeconomic status, or ethnicity. All centers apply national consensus guidelines to select patients for heart transplantation.[13] Patients requiring continuous inotropic support or temporary mechanical circulatory support are given priority in organ allocation (equivalent to United Network for Organ Sharing Status I). Patients are placed on a national waiting list. Organs are allocated to patients on the urgent list nationally according to blood group and waiting time. For the last financial year, 80% of patients receiving a transplant were on the urgent list. Nonurgent listed patients are offered a heart if no suitable patient is found on the urgent list, and centers have some latitude in allocating these donor hearts. Post-transplant care is not standardized between transplant centers. Each center collects individual patient data at the time of listing, at the time of transplantation, and at regular intervals until death. Data are monitored and subjected to periodic external validation. We included all patients aged ≥18 years who received a heart transplant from 1995 to 2014 and were resident in England at the time of transplant. This study was approved by an institutional review committee. Before April 2010, the UK Transplant Registry data were collected for audit purposes with presumed consent. Since April 2010, all patients have provided written consent.

Socioeconomic Deprivation

The UK index of multiple deprivation (IMD) was used to measure SED. The UK IMD is a local area-based model with 7 domains: (1) income, (2) employment, (3) health and disability, (4) education, skills and training, (5) barriers to housing and services, (6) living environment, and (7) crime. Each domain is assessed for 32 482 lower layer super output areas in England (each of which has ≈1000–1500 residents) and used to rank the relative deprivation of lower super output areas. We obtained the IMD rank for each patient using their postcode at the time of transplantation and the 2010 UK IMD data set.[14] Patients were categorized into 5 quintiles of deprivation based on the rank of the layer super output areas in which they lived at the time of transplantation, with group 1 being the most deprived and group 5 the least deprived.

Outcomes

The primary outcome measure was time to all-cause mortality during follow-up (overall survival). Secondary outcome measures were 30-day post-transplant mortality, 1-year post-transplant mortality, and time to all-cause mortality during long-term follow-up in those who survived the first year post transplant (conditional survival). Graft outcome was recorded as graft failure, death with functioning graft, or death-only recorded.

Statistical Analysis

Categorical variables were summarized as counts and percentages. Continuous variables were summarized as either median (interquartile range) or mean (SD) as deemed appropriate after graphical examination of their distribution. Baseline characteristics were assessed for a trend across quintiles of SED using logistic, ordinal, or linear regression as appropriate. These regression models were adjusted for transplant center.

The association of SED with 30-day post-transplant mortality was assessed using logistic regression. The model was adjusted for age, sex, ethnicity (white/nonwhite), diabetes mellitus, heart disease cause (dilated cardiomyopathy, ischemic heart disease, congenital heart disease, and other), pretransplant serum creatinine, previous cardiac surgery, inpatient or outpatient before transplantation, ventilation status at registration (ventilated/not ventilated), donor age, donor sex, and transplant center. One-year post-transplant mortality was assessed using a multivariable-adjusted Cox proportional hazards model stratified by transplant center adjusted for the same variables as the model for 30-day mortality. Overall survival and conditional survival were assessed using multivariable-adjusted Cox proportional hazards models stratified by transplant center. These models were adjusted for age, sex, recipient ethnicity, heart disease cause (as above), recipient diabetes mellitus, pretransplant serum creatinine, donor sex, and donor age. For Cox proportional hazards models, individuals alive at last follow-up were censored at that time. Patients who died on the day of the transplant (n=23) were assigned a follow-up duration of 0.001 years for inclusion in Cox models.

IMD rank was modeled as a categorical variable grouped in quintiles, using the least deprived quintile as the reference group, as well as continuously after verified absence of nonlinear associations. The proportional hazard assumption was satisfied for overall and conditional survival models. Survival curves were generated using Kaplan–Meier method by SED quintiles and compared using the log-rank test. Estimates of median survival times by quintiles of SED and differences thereof were also presented as additional summary statistics.

To assess the association of SED with graft failure and death with a functioning graft independently, we modeled IMD rank as a continuous variable in a multivariable-adjusted competing risk regression model treating the other outcome as a competing risk. End points were recorded as graft failure or death with a functioning graft in all patients included in the conditional model compared with 38.6% in the overall model because the majority of events recorded as death-only recorded occurred in the first year post transplant. For this reason, the competing risk regression analysis was performed only for conditional survival.

The association between SED and overall and conditional survival was examined for 4 subgroups by adding an interaction term to the adjusted Cox proportional hazards models. Subgroups included recipient age, sex, heart failure cause (ischemic/nonischemic), and ethnicity (white/nonwhite).

For categorical variables with missing data, an indicator variable was assigned for missing data points to allow inclusion of patients with missing data points in the multivariable-adjusted models. For creatinine, the only continuous variable with missing data, the 260 (10.9%) missing data points were imputed as the mean value across the cohort.

Two-sided $P<0.05$ was considered significant throughout. All analysis was performed in STATA (version 14; StataCorp).

Results

A total of 2961 heart transplants were performed in the United Kingdom between 1995 and 2014. We included 2391 patients who were resident in England at the time of transplantation. We excluded 7 patients who did not have outcome data recorded, and 2384 patients remained as the cohort analyzed in this study. The characteristics of the cohort overall and by SED quintile are shown in Table 1. Median (interquartile range) recipient age was 51 (41–57) years, and 79% were men. Recipients in the more deprived quintiles were slightly

Table 1. Characteristics of Patients in the Cohort

	Overall	Quintile 1 (Most Deprived)	Quintile 2	Quintile 3	Quintile 4	Quintile 5 (Least Deprived)	P Value
No. of patients	2384	509 (21.3)	495 (20.8)	494 (20.7)	442 (18.5)	444 (18.6)	
Age (n=2384)	51 [41–57]	49 [38–55]	49 [40–56]	51 [42–57]	51 [42–57]	52 [44–58]	<0.001
Sex (n=2384)							
Men	1879 (78.8)	387 (76.0)	386 (77.0)	393 (79.6)	361 (81.7)	352 (79.3)	0.071
Women	505 (21.2)	122 (24.0)	109 (22.0)	101 (20.45)	81 (18.3)	92 (20.7)	
Ethnicity (n=2314)							
White	2110 (91.2)	424 (85.5)	430 (90.0)	442 (92.3)	406 (94.4)	408 (95.1)	<0.001
Black	39 (1.7)	20 (4.0)	11 (2.3)	6 (1.3)	2 (0.5)	0 (0)	
South Asian	138 (6.0)	43 (8.7)	32 (6.6)	30 (6.3)	13 (3)	20 (4.7)	
Other	27 (1.2)	9 (1.8)	7 (1.4)	1 (0.2)	9 (2.1)	1 (0.2)	
BMI (n=2333)	25.4 (4.0)	25.5 (4.1)	25.6 (4.0)	25.5 (3.9)	25.3 (4.2)	25.2 (3.8)	0.320
Cause (n=2365)							
Ischemic heart disease	718 (30.4)	180 (35.7)	137 (27.9)	138 (28.2)	144 (32.9)	119 (26.9)	
Cardiomyopathy	1293 (54.7)	258 (51.2)	272 (55.4)	272 (55.6)	240 (54.8)	251 (56.7)	
Congenital	109 (4.6)	20 (4.0)	33 (6.7)	22 (4.5)	15 (3.4)	19 (4.3)	0.264
Other	245 (10.4)	46 (9.1)	49 (10.0)	57 (11.7)	39 (8.9)	54 (12.2)	
Previous open heart surgery (n=2215)	159 (7.2)	31 (8.7)	40 (8.7)	32 (7.0)	25 (6.0)	31 (7.6)	0.516
Diabetes mellitus (n=2218)	207 (9.3)	45 (9.5)	52 (11.4)	35 (7.6)	44 (10.6)	31 (7.5)	0.242
In hospital pretransplant (n=2326)	847 (36.4)	185 (37.2)	179 (37.1)	165 (34.2)	149 (34.6)	169 (39.1)	0.450
Serum creatinine (n=2124)	112 [91–135]	103 [87–128]	113 [91–137]	110 [93–132]	116 [95–139]	115 [93–140]	0.015
Ischemic time (n=2125), min							
<120	196 (9.2)	31 (6.9)	43 (9.6)	35 (8.0)	43 (10.9)	44 (11.1)	0.106
120–179	645 (30.4)	130 (29)	133 (29.7)	128 (29.2)	128 (32.5)	126 (31.7)	
180–239	819 (38.5)	183 (40.9)	180 (40.2)	173 (39.5)	143 (36.3)	140 (35.3)	
>240	465 (21.9)	104 (23.2)	92 (20.5)	102 (23.3)	80 (20.3)	87 (21.9)	
Ventilated at registration (n=1448)	40 (2.8)	10 (3.1)	6 (2.0)	9 (3.0)	9 (3.5)	6 (2.2)	0.819
Donor age (n=2384)	37 [25–46]	36 [24–46]	35 [25–45]	38 [25–47]	37 [25–47]	37 [27–45]	0.327
Donor sex (n=2384)							
Men	787 (33.0)	158 (31.0)	170 (34.3)	173 (35.0)	142 (32.1)	144 (32.4)	0.449
Women	1597 (67.0)	351 (69.0)	325 (65.7)	321 (65.0)	300 (67.9)	300 (67.6)	
Donor diabetes mellitus (n=2076)	55 (2.7)	7 (1.6)	13 (3.1)	13 (2.9)	13 (3.3)	9 (2.3)	0.911
Follow-up duration, y (n=2384)	6.1 [1.0–12.1]	5.9 [1.0–11.7]	6.0 [1.0–12.0]	6.9 [1.0–12.0]	6.9 [1.0–13.0]	6.0 [0.9–12.1]	0.368

Data presented for the cohort as a whole and for each socioeconomic deprivation quintile. Data presented as mean (SD), median [interquartile range] or count (%). BMI indicates body mass index.

Table 2.   Association Between SED and 30-Day Mortality

SED Quintile	No. of Patients	Deaths at 30 d, n (%)	Unadjusted OR (95% CI)	P Value	Risk-Adjusted* OR (95% CI)	P Value
5 (least deprived)	444	50 (11.3)	1.00	…	1.00	…
4	442	58 (13.1)	1.19 (0.80–1.78)	0.398	1.25 (0.82–1.89)	0.294
3	494	55 (11.1)	0.99 (0.66–1.48)	0.951	0.95 (0.62–1.45)	0.813
2	495	61 (12.3)	1.11 (0.74–1.65)	0.615	1.09 (0.72–1.65)	0.674
1 (most deprived)	509	48 (9.4)	0.82 (0.54–1.25)	0.354	0.83 (0.53–1.29)	0.403

Unadjusted and risk-adjusted ORs (95% CI) for 30-day mortality by SED quintile. CI indicates confidence interval; OR, odds ratio; and SED, socioeconomic deprivation.

*Adjusted for age, sex, ethnicity, diabetes mellitus, heart disease cause (dilated cardiomyopathy, ischemic heart disease, congenital heart disease, and other), pretransplant serum creatinine, previous cardiac surgery, inpatient or outpatient before transplantation, ventilation status at registration (ventilated/not ventilated), donor age, and donor sex.

younger, more likely to be black or South Asian, and had a lower serum creatinine.

Thirty-Day Mortality

Thirty-day mortality was 11.4% (272 deaths) for the cohort as a whole and was 9.4%, 12.3%, 11.1%, 13.1%, and 11.3% for quintile 1 (most deprived) to quintile 5 (least deprived) of SED respectively. There was no significant difference in 30-day mortality between SED quintiles (Table 2).

One-Year Survival

Kaplan–Meier–predicted 1-year survival was 80.6% (95% confidence interval, 78.9–82.1) for the cohort as a whole. SED was not associated with any difference in 1-year survival (Table 3).

Long-Term Survival

The median (interquartile range) duration of follow-up was 6.13 (1.00–12.1) years. There were 1101 deaths during 17 040 patient years at risk. Median (95% confidence interval) overall survival was 12.6 (11.9–13.5) years, and conditional survival was 15.6 (14.9–16.4) years.

A higher level of SED was associated with a higher risk of death in the long term (Table 4). Median overall survival and conditional survival were 3.4 years shorter in the most deprived than in the least deprived quintile (Table 4). Survival curves for the most deprived and least deprived quintiles are shown in Figure 1. The association between deprivation in each of the seven IMD domains and survival is shown in Table 5. In competing risks regression models for conditional survival, hazard

ratios per quintile increase in IMD rank (indicating greater SED) were similar for both graft failure (1.14 [95% confidence interval, 1.05–1.24]; P=0.001) and death with a functioning graft (1.10 [95% confidence interval, 1.02–1.18]; P=0.012). There was no significant interaction between the association of SED and survival with sex, ethnicity, or heart failure cause (Figure 2). In the conditional survival model, there was a significant interaction with age such that the association between higher levels of SED and worse outcome was stronger in younger recipients. Hazard ratios were unchanged when using alternative approaches to stratification in Cox regression models to account for center effect, including adjusting for center as a covariate (fixed effect) or estimating a shared frailty variance by center (random effect).

Discussion

We have demonstrated that a higher level of SED is associated with shorter survival after heart transplantation in patients in England. Median overall survival and conditional survival were 3.4 years shorter for those who live in the most deprived compared with those who live in the least deprived areas. However, there was no association between SED and either 30-day or 1-year mortality. Our study is the first to demonstrate an association between SED and long-term survival after heart transplantation in a country with universal provision of healthcare. These findings may be relevant to other countries that have a heart transplantation program within a universal healthcare system.

Table 3.   Association Between SED and 1-Year Mortality

SED Quintile	1-y Mortality % (95% CI)	Unadjusted HR (95% CI)	P Value	Risk-Adjusted* HR (95% CI)	P Value
5 (least deprived)	20.1 (16.6–24.2)	1.00	…	1.00	…
4	19.9 (16.5–24.0)	1.03 (0.76–1.38)	0.870	1.04 (0.77–1.41)	0.779
3	19.3 (16.0–23.1)	0.98 (0.73–1.31)	0.883	0.90 (0.67–1.22)	0.503
2	19.8 (16.5–23.6)	1.00 (0.75–1.34)	0.989	0.99 (0.73–1.33)	0.941
1 (most deprived)	18.2 (15.1–21.9)	0.92 (0.68–1.25)	0.613	0.91 (0.66–1.24)	0.534

Unadjusted and risk-adjusted HRs (95% CI) for death during the first year by SED quintile. One-year mortality generated using unadjusted Kaplan–Meier estimates. CI indicates confidence interval; HR, hazard ratio; and SED, socioeconomic deprivation.

*Adjusted for age, sex, ethnicity, diabetes mellitus, heart disease cause (dilated cardiomyopathy, ischemic heart disease, congenital heart disease, and other), pretransplant serum creatinine, previous cardiac surgery, inpatient or outpatient before transplantation, ventilation status at registration (ventilated/not ventilated), donor age, and donor sex.

Table 4. Association Between SED and Long-Term Survival

SED Quintile	Unadjusted HR (95% CI)	P Value	Risk-adjusted* HR (95% CI)	P Value	Median Survival (95% CI)
Overall survival					
5 (least deprived)	1.00	…	1.00	…	15.0 (13.2–17.1)
4	1.11 (0.91–1.36)	0.295	1.14 (0.93–1.39)	0.217	14.1 (12.1–15.2)
3	1.11 (0.91–1.35)	0.319	1.11 (0.91–1.35)	0.321	12.3 (11.2–13.9)
2	1.24 (1.02–1.51)	0.030	1.27 (1.05–1.55)	0.016	11.3 (10.0–13.5)
1 (most deprived)	1.22 (1.00–1.49)	0.047	1.27 (1.04–1.55)	0.021	11.6 (9.1–12.6)
Per quintile increase in SED	1.05 (1.00–1.09)	0.032	1.06 (1.01–1.10)	0.012	…
Conditional survival					
5 (least deprived)	1.00	…	1.00	…	17.8 (15.4–20.3)
4	1.21 (0.92–1.59)	0.174	1.24 (0.94–1.64)	0.124	15.8 (14.6–17.0)
3	1.23 (0.94–1.62)	0.129	1.26 (0.96–1.65)	0.097	16.2 (13.4–19.0)
2	1.48 (1.94–1.92)	0.004	1.55 (1.19–2.03)	0.001	14.8 (13.1–18.0)
1 (most deprived)	1.51 (1.15–1.97)	0.003	1.59 (1.22–2.09)	0.001	14.4 (12.3–15.6)
Per quintile increase in SED	1.09 (1.03–1.15)	0.002	1.11 (1.05–1.17)	<0.001	…

Unadjusted and risk-adjusted HRs (95% CI) by SED quintile and for Index of Multiple Deprivation rank as a continuous variable per quintile increase (indicates increase in relative SED). CI indicates confidence interval; HR, hazard ratio; and SED, socioeconomic deprivation.

*Adjusted for age, sex, ethnicity, diabetes mellitus, pretransplant creatinine, heart failure cause, donor age, and donor sex

Many studies have examined the association between SED and outcomes after heart transplantation in adults, most of which have been conducted in the United States. In a small study of 44 patients at a single center in Brazil from 2000 to 2005, no association was observed between SED and survival after heart transplantation.[15] However, SED was not clearly defined, and there was no attempt to separate the effect of SED from other risk factors for mortality. A larger retrospective study of 520 patients at 4 transplant centers in the United States from 1996 to 2005 did not find an association between SED and survival to discharge, but those living in more deprived neighborhoods had a greater incidence of acute rejection and allograft loss during long term follow-up.[7] Although all patients in their analysis had medical insurance, the type of insurance varied according to socioeconomic status. Analysis of the United Network for Organ Sharing database from 1997 to 2008 showed shorter survival after heart transplantation in patients with Medicaid or Medicare insurance, who tend to have lower socioeconomic status, than in patients with private medical insurance.[10] It has been suggested that Medicaid and Medicare copayments for immunosuppressive medications might adversely affect compliance and lead to worse outcomes after heart transplantation.

In contrast to the United States, the NHS in England provides universal health care to all residents. We have shown that SED has an adverse effect on post-transplant survival despite universal healthcare provision, but the reasons for this finding are uncertain. Uptake of healthcare services and engagement with healthcare providers may be lower in areas of greater SED.[16] Language barriers may deter non-English–speaking ethnic minorities from accessing healthcare.[17] Individuals under financial pressure may be unable to afford time off work to access health care or be unable to afford travel costs to distant heart transplant centers. In Scotland,

patients with heart failure who were more socioeconomically deprived were less likely to have regular contact with their general practitioner[18] and delays in presentation with acute
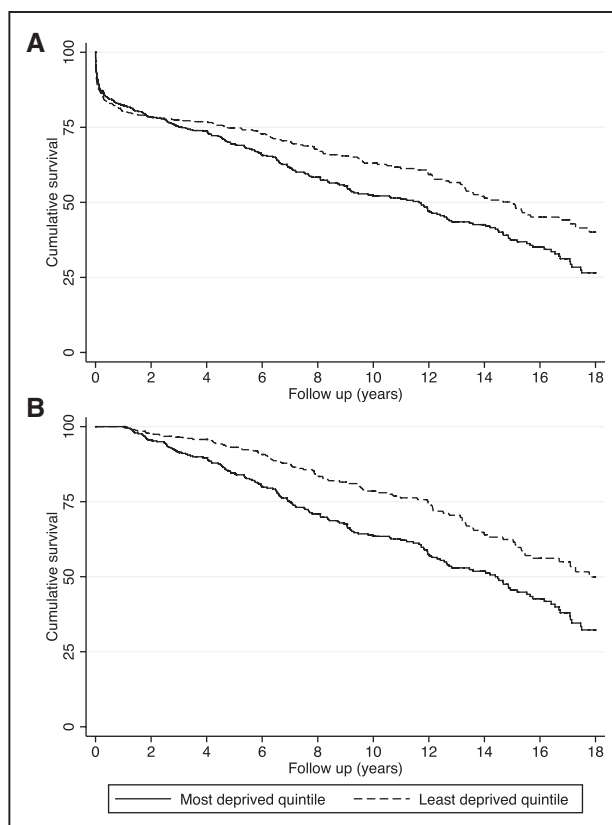

Figure 1. Survival curves by socioeconomic deprivation quintile. Kaplan–Meier survival curves comparing patients in the most deprived and least deprived quintiles. **A**, Overall survival (*P*=0.008) and **B**, conditional survival (*P*<0.001).

Table 5.   Association of IMD Domains With Long-Term Survival

IMD Domain	Risk-Adjusted HR* (95% CI)	P Value
Overall survival		
Income	1.06 (1.01–1.11)	0.011
Employment	1.06 (1.01–1.11)	0.012
Health	1.06 (1.01–1.11)	0.019
Education	1.05 (1.01–1.09)	0.029
Housing	0.99 (0.94–1.03)	0.554
Crime	1.03 (0.99–1.07)	0.198
Environment	1.06 (1.01–1.10)	0.015
Conditional survival		
Income	1.12 (1.06–1.18)	<0.001
Employment	1.11 (1.05–1.18)	<0.001
Health	1.12 (1.05–1.19)	<0.001
Education	1.11 (1.05–1.17)	<0.001
Housing	0.96 (0.91–1.02)	0.228
Crime	1.06 (1.00–1.12)	0.037
Environment	1.09 (1.03–1.15)	0.004

Risk-adjusted HRs (95% CI) per quintile increase in rank in each of the 7 IMD domains. Increase in IMD rank indicates increase in relative socioeconomic deprivation. CI indicates confidence interval; HR, hazard ratio; and IMD, Index of Multiple Deprivation.

*Adjusted for age, sex, ethnicity, diabetes mellitus, pretransplant creatinine, heart failure cause, donor age, and donor sex.

myocardial infarction have been observed more frequently in more deprived Medicare beneficiaries in the United States.[19] In addition, more deprived individuals have been reported to have higher rates of medication nonadherence.[20] Our findings suggest that the association between SED and post-transplant adverse events in the United States and United Kingdom is complex and not wholly explained by inequitable access to post-transplant healthcare and expensive immunosuppression. It is likely that factors such as engagement with health care, compliance, and health behaviors, all of which display socioeconomic gradients, may be important. As such, our findings are relevant to transplant programmes across the world, regardless of the healthcare system.

There are numerous other potential mediators of the association between greater SED and shorter survival after heart transplantation. Shorter survival seems to be driven by a higher risk of both graft failure and death from other causes. Cardiac allograft vasculopathy is present in >50% of recipients at 10 years after transplantation and is an important cause of allograft failure and death.[21] Conventional risk factors for atherosclerosis such as smoking, dyslipidemia, diabetes mellitus, and obesity all increase the risk of cardiac allograft vasculopathy[22,23] and are more prevalent in areas of SED.[24,25] Abstinence from tobacco smoking is required before listing for heart transplantation in the United Kingdom. However, ≈25% of heart transplant recipients were smoking during follow-up when assessed by urinary cotinine screening, and these individuals had an increased risk of death from cardiac allograft vasculopathy and malignancy.[26] Socioeconomic gradients in the prevalence of smoking were not assessed, but could mediate the effect of SED on survival if such gradients reflect those in wider society.[24] Cytomegalovirus seropositivity is more common in low-income households[27] and has been associated with a greater risk of cardiac allograft vasculopathy.[28] Malignancy is another important cause of death after heart transplantation, and the incidence is 2.5× greater than in the general population.[29] There are socioeconomic inequalities in both the incidence[30] and survival[31] from a wide variety of cancers, and these may apply equally to patients who have undergone heart transplantation.

These findings should not deter clinicians from listing individuals from more deprived areas for transplantation. Instead, strategies to reduce the disparity in outcomes should be explored. Potential interventions include the use of electronic dossette boxes to measure compliance, closer monitoring of immunosuppressive drug levels, education about post-transplant care, and support with lifestyle modifications such as smoking, diet, and exercise. Use of the family or other social support networks may be beneficial.[32] It is important to note that exposure to adverse socioeconomic conditions during childhood has been associated with poor cardiovascular health in later life.[33] Some of the observed disparity in survival after heart transplantation may not be modifiable. Nevertheless, heart transplant recipients have life-long follow-up, and there are numerous opportunities for intervention. Sociodemographic data for all recipients should be collected at both the individual and neighborhood level to allow this subject to be studied further. Such data would allow targeting and evaluation of the potential interventions described above. This should be an area for future research in other types of solid organ transplant, where similar disparities in outcomes exist with SED.[34–37]

The association between SED and post-transplant survival may be relevant for performance monitoring of heart transplant centers. In the United Kingdom, risk-adjustment models are used to allow continuous performance monitoring in each center. By stratifying our analyses by transplant center and thus accounting for any differences in the baseline hazard for death between centers, we have demonstrated that the association between SED and survival is not a result of differences in care between centers. Incorporation of SED into the risk adjustment used for performance monitoring should be evaluated to account for variation in the relative deprivation of patient cohorts at different centers.

The strengths of our study are inclusion of >99.5% of all heart transplant recipients in England over a 19-year period with a median follow-up time of >6 years, use of a hard clinical end point (all-cause mortality), and use of a standardized measure (UK IMD) to assess SED. There are several limitations of our study. The UK Transplant Registry does not currently collect socioeconomic data at the individual level, and although the IMD is an area-based index that permits meaningful comparisons and monitoring of national, regional, and local socioeconomic gradients in health over time, it is only a proxy for individual-level socioeconomic data. We included patients who underwent transplantation between 1995 and 2014, but used the 2010 IMD data set for analysis. It is possible that relative deprivation of an area could change although
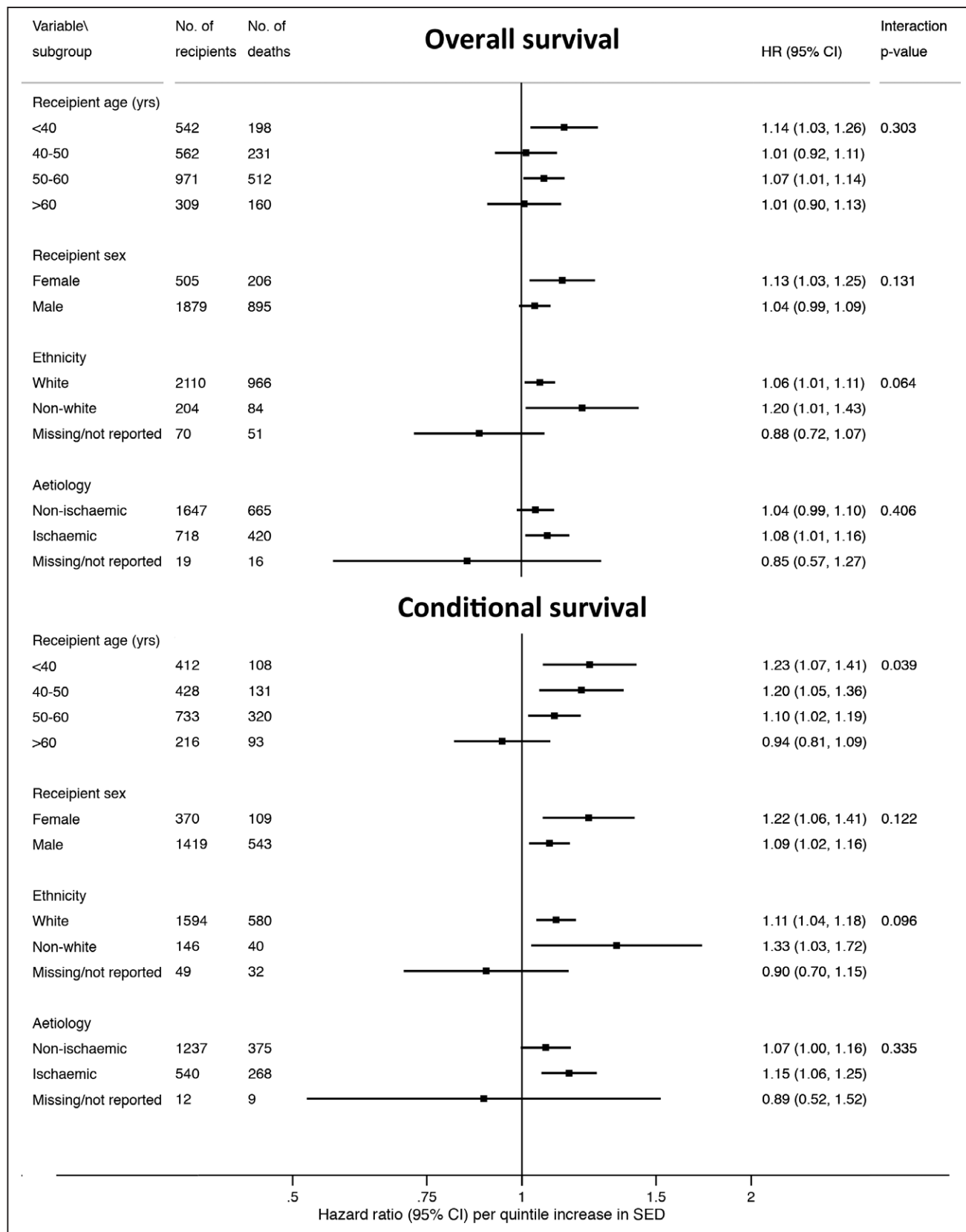
Figure 2. Subgroup analysis. Association of socioeconomic deprivation (SED) and overall survival and conditional survival, by age at transplant, sex, ethnicity, and heart failure cause. *P* values presented for interaction between subgroups.

most areas of the United Kingdom have remained in the same quintile of IMD scores for >25 years.[38] We defined SED by postcode at the time of transplantation, but individuals may move during follow-up. Finally, there may be residual confounding from unmeasured variables such as human leukocyte antigen (HLA)-matching and pretransplant factors such as a history of smoking and hypertension.

In conclusion, we have demonstrated that SED is associated with shorter survival after heart transplantation in England. SED of recipients should be evaluated as a potential risk factor in adjustment of survival data for performance monitoring of individual transplant centers. More importantly, research is required to identify and develop strategies to address modifiable mediators of the association between SED and shorter survival, with a view to improving outcomes for more deprived patients undergoing heart transplantation.

Disclosures

None.

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