Socioeconomic deprivation and survival after heart transplantation in England: an analysis of the United Kingdom Transplant Registry.

Evans *et al*: Deprivation and heart transplant survival

Jonathan D. W. Evans MBChB[1,2], Stephen Kaptoge PhD[2], Rishi Caleyachetty MBBS[3], Emanuele Di Angelantonio PhD[2], Clive Lewis PhD[1], K. Jayan Parameshwar MD[1], Stephen J. Pettit PhD[1].

[1.] Transplant Unit, Papworth Hospital NHS Foundation Trust, Papworth Everard, Cambridge, UK

[2.] Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK

[3.] Department of Public Health, Epidemiology, and Biostatistics, University of Birmingham, Birmingham, UK.

Word count: 5993

Corresponding author

Dr Jonathan D. W. Evans

Transplant Unit

Papworth Hospital NHS Foundation Trust

Papworth Everard

Cambridge, UK

Email: jonathanevans3@nhs.net

Phone: +44-1480-830541

Fax: +44-1480-831315

Abstract

Background

Socioeconomic deprivation (SED) is associated with shorter survival across a range of cardiovascular and non-cardiovascular 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 1995-2014. We used the United Kingdom Index of Multiple Deprivation (UK IMD), a neighbourhood 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 one 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 and heart failure aetiology. 2384 patients underwent heart transplantation. There were 1,101 deaths during 17,040 patient years follow-up. Median overall survival was 12.6 years and conditional survival was 15.6 years. Comparing the most deprived versus 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 and conditional survival was 3.4 years shorter in the most deprived quintile compared with 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 centres. Future research should seek to identify modifiable mediators of this association.

Introduction

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]. Over 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 that survive the first year[3].

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 (US). Greater SED was associated with an increased risk of graft failure and an increased risk of acute rejection in adult[7] and paediatric recipients[8, 9]. In addition, health insurance status was associated with survival after heart transplantation in the US. 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 healthcare 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 health care systems such as the NHS are thought to reduce socio-economic inequalities in health[11]. There are socioeconomic gradients in the incidence, prevalence and case-fatality rates of heart failure in England, but the magnitude of these gradients has reduced in the last decade[12]. Importantly, use of evidence-based treatments for heart failure appear 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 United Kingdom (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 seven specialist centers in England in 1995 and five centers remain active in 2014. Any patient entitled to NHS treatment may be referred for transplant assessment, irrespective of gender, socio-economic 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 UNOS 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. Non-urgent 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 standardised 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 and above who received a heart transplant from 1995-2014 and were resident in England at the time of transplant. This study was approved by an institutional review committee. Prior to April 2010, the UK Transplant Registry data was 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 seven 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 (LSOAs) in England (each of which has approximately 1,000-1,500 residents) and used to rank the relative deprivation of LSOAs. We obtained the IMD rank for each patient using their postcode at the time of transplantation and the 2010 UK IMD dataset[14]. Patients were categorized into five quintiles of deprivation based on the rank of the LSOA in which they lived at the time of transplantation, with group 1 being most deprived and group 5 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, one-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 summarised as counts and percentages. Continuous variables were summarised as either median [interquartile range] or mean (standard deviation) 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 centre.

The association of SED with 30-day post transplant mortality was assessed using logistic regression. The model was adjusted for age, sex, ethnicity (white/non-white), diabetes, heart disease aetiology (dilated cardiomyopathy, ischaemic heart disease, congenital heart disease, other), pre-transplant serum creatinine, previous cardiac surgery, inpatient or outpatient prior to 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 was assessed using multivariable adjusted Cox Proportional Hazards models stratified by transplant center. These models were adjusted for age, sex, recipient ethnicity, heart disease aetiology (as above), recipient diabetes, pre-transplant serum creatinine, donor sex and donor age. For Cox PH models, individuals alive at last follow up were censored at that time. Patients who died on the day of transplant (n=23) were assigned a follow up duration of 0.001 years for inclusion in Cox models.

IMD rank was modelled as a categorical variable grouped in quintiles, using the least deprived quintile as the reference group, as well as continuously after verified absence of non-linear 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.

In order to assess the association of SED with graft failure and death with a functioning graft independently, we modelled IMD rank as a continuous variable in a multivariable adjusted competing risk regression model treating the other outcome as a competing risk. Endpoints 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 four subgroups by adding an interaction term to the adjusted Cox PH models. Subgroups included recipient age, sex, heart failure aetiology (ischaemic/non-ischaemic) and ethnicity (white/non-white).

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.

A two sided p-value <0.05 was considered significant throughout. All analysis was performed in STATA (version 14; StataCorp, USA).

Results

A total of 2961 heart transplants were performed in the UK between 1995-2014. We included 2391 patients who were resident in England at the time of transplantation. We excluded 7 patients that did not have outcome data recorded and 2384 patients remained as the cohort analysed in this study. The characteristics of the cohort overall and by SED quintile are shown in **Table 1**. Median [IQR] recipient age was 51 [41-57] years and 79% were male. Recipients in the more deprived quintiles were slightly younger, more likely to be black or South Asian and had a lower serum creatinine.

30-day mortality

30-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 one-year survival was 80.6 (95% CI 78.9-82.1)% for the cohort as a whole. SED was not associated with any difference in one-year survival **(Table 3).**

Long-term survival

The median (IQR) 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% CI) 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 and conditional survival was 3.4 years shorter in the most deprived compared with 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 (1.05-1.24), p=0.001) and death with a functioning graft (1.10 (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 aetiology **(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 and conditional survival was 3.4 years shorter for those who live in the most deprived compared with 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 programme within a universal healthcare system.

A number of studies have examined the association between SED and outcomes after heart transplantation in adults, most of which have been conducted in the US. In a small study of 44 patients at a single center in Brazil from 2000-2005, 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 four transplant centers in the US from 1996-2005 did not find an association between SED and survival to discharge, but those living in more deprived neighbourhoods had a greater incidence of acute rejection and allograft loss during long term follow-up[7]. While 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 (UNOS) database from 1997-2008 showed shorter survival after heart transplantation in patients with Medicaid or Medicare insurance, who tend to have lower socio-economic status, compared with patients with private medical insurance.[10]. It has been suggested that Medicaid and Medicare co-payments for immunosuppressive medications might adversely affect compliance and lead to worse outcomes after heart transplantation.

In contrast to the US, the NHS in England provides universal healthcare 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 healthcare 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 myocardial infarction have been observed more frequently in more deprived Medicare beneficiaries in the US[19]. In addition, more deprived individuals have been reported to have higher rates of medication non-adherence[20]. Our findings suggest that the association between SED and post-transplant adverse events in the US and UK 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 healthcare, compliance and health behaviours, 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 appears to be driven by a higher risk of both graft failure and death from other causes. Cardiac allograft vasculopathy (CAV) is present in over 50% of recipients at ten years after transplantation and is an important cause of allograft failure and death[21]. Conventional risk factors for atherosclerosis such as smoking, dyslipidaemia, diabetes and obesity all increase the risk of CAV[22, 23], and are more prevalent in areas of socioeconomic deprivation[24, 25]. Abstinence from tobacco smoking is required before listing for heart transplantation in the UK. However, around 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 CAV 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 (CMV) seropositivity is more common in low-income households[27], and has been associated with a greater risk of CAV[28]. Malignancy is another important cause of death after heart transplantation and the incidence is 2.5 times 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 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. Socio-demographic data for all recipients should be collected at both the individual and neighbourhood 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 centres. In the UK, risk adjustment models are used to allow continuous performance monitoring in each centre. By stratifying our analyses by transplant centre 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 >99.5% of all heart transplant recipients in England over a 19-year period with a median follow up time of over 6 years, use of a hard clinical endpoint (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 while 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 dataset for analysis. It is possible that relative deprivation of an area could change, although most areas of the UK have remained in the same quintile of IMD scores over 25 years[38]. We defined SED by post-code at the time of transplantation, but individuals may move during follow up. Finally, there may be residual confounding from unmeasured variables such as HLA-matching and pre-transplant factors such as a history of smoking and hypertension.

In conclusion, we have demonstrated that socioeconomic deprivation is associated with shorter survival after heart transplantation in England. Socioeconomic deprivation 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

All authors declare no conflicts of interest

Funding sources

No direct funding was provided for the conduct of this study. JE completed part of this work as part of an academic clinical fellowship, where he spent time at the University of Cambridge, Cardiovascular Epidemiology Unit receiving training on research methods, supported by SK and EDA. The Cardiovascular Epidemiology Unit is funded by the UK Medical Research Council (G0800270), British Heart Foundation (SP/09/002), British Heart Foundation Cambridge Cardiovascular Centre of Excellence, and UK National Institute for Health Research Cambridge Biomedical Research Centre.

Acknowledgments

We would like to thank all UK cardiothoracic transplant centres for access to outcome data. We would like to thank the staff at NHSBT for their assistance in extracting the data from UKTR and performing linkage of postcodes to IMD data.

References

1. Banner NR, Rogers CA, Bonser RS and United Kingdom Cardiothoracic Transplant Audit Steering G. Effect of heart transplantation on survival in ambulatory and decompensated heart failure. *Transplantation*. 2008; 86:1515-22.

2. Kugler C, Tegtbur U, Gottlieb J, Bara C, Malehsa D, Dierich M, Simon A and Haverich A. Health-related quality of life in long-term survivors after heart and lung transplantation: a prospective cohort study. *Transplantation*. 2010; 90:451-7.

3. Lund LH, Edwards LB, Kucheryavaya AY, Benden C, Dipchand AI, Goldfarb S, Levvey BJ, Meiser B, Rossano JW, Yusen RD and Stehlik J. The Registry of the International Society for Heart and Lung Transplantation: Thirty-second Official Adult Heart Transplantation Report-2015; Focus Theme: Early Graft Failure. *J Heart Lung Transplant*. 2015;34:1244-54.

4. Havranek EP, Mujahid MS, Barr DA, Blair IV, Cohen MS, Cruz-Flores S, Davey-Smith G, Dennison-Himmelfarb CR, Lauer MS, Lockwood DW, Rosal M, Yancy CW, American Heart Association Council on Quality of C, Outcomes Research CoE, Prevention CoC, Stroke Nursing CoL, Cardiometabolic H and Stroke C. Social Determinants of Risk and Outcomes for Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation*. 2015;132:873-98.

5. Pujades-Rodriguez M, Timmis A, Stogiannis D, Rapsomaniki E, Denaxas S, Shah A, Feder G, Kivimaki M and Hemingway H. Socioeconomic deprivation and the incidence of 12 cardiovascular diseases in 1.9 million women and men: implications for risk prediction and prevention. *PLoS One*. 2014;9:e104671.

6. Hawkins NM, Jhund PS, McMurray JJ and Capewell S. Heart failure and socioeconomic status: accumulating evidence of inequality. *Eur J Heart Fail*. 2012;14:138-46.

7. Singh TP, Givertz MM, Semigran M, Denofrio D, Costantino F and Gauvreau K. Socioeconomic position, ethnicity, and outcomes in heart transplant recipients. *Am J Cardiol*. 2010;105:1024-9.

8. Davies RR, Russo MJ, Reinhartz O, Maeda K, Rosenthal DN, Chin C, Bernstein D and Mallidi HR. Lower socioeconomic status is associated with worse outcomes after both listing and transplanting children with heart failure. *Pediatr Transplant*. 2013;17:573-81.

9. Singh TP, Naftel DC, Addonizio L, Mahle W, Foushee MT, Zangwill S, Blume ED, Kirklin JK, Singh R, Johnston JK and Chinnock R. Association of race and socioeconomic position with outcomes in pediatric heart transplant recipients. *Am J Transplant*. 2010;10:2116-23.

10. Allen JG, Weiss ES, Arnaoutakis GJ, Russell SD, Baumgartner WA, Shah AS and Conte JV. Insurance and education predict long-term survival after orthotopic heart transplantation in the United States. *J Heart Lung Transplant*. 2012;31:52-60.

11. Asaria M, Ali S, Doran T, Ferguson B, Fleetcroft R, Goddard M, Goldblatt P, Laudicella M, Raine R and Cookson R. How a universal health system reduces inequalities: lessons from England. *J Epidemiol Community Health*. 2016, published online 19 January 2016. DOI: 10.1136/jech-2015-206742.

12. Hawkins NM, Scholes S, Bajekal M, Love H, O'Flaherty M, Raine R and Capewell S. Community care in England: reducing socioeconomic inequalities in heart failure. *Circulation*. 2012;126:1050-7.

13. Banner NR, Bonser RS, Clark AL, Clark S, Cowburn PJ, Gardner RS, Kalra PR, McDonagh T, Rogers CA, Swan L, Parameshwar J, Thomas HL and Williams SG. UK guidelines for referral and assessment of adults for heart transplantation. *Heart*. 2011;97:1520-7.

14. UK Index of Multiple Deprivation. Published by Department for Communities and Local Government, UK. https://data.gov.uk/dataset/index-of-multiple-deprivation. Accessed 19th Feb 2015.

15. Parra AV, Rodrigues V, Cancella S, Cordeiro JA and Bestetti RB. Impact of socioeconomic status on outcome of a Brazilian heart transplant recipients cohort. *Int J Cardiol*. 2008;125:142-3.

16. Adler NE and Newman K. Socioeconomic disparities in health: pathways and policies. *Health Aff*. 2002;21:60-76.

17. Jacobs EA, Shepard DS, Suaya JA and Stone EL. Overcoming language barriers in health care: costs and benefits of interpreter services. *Am J Public Health*. 2004;94:866-9.

18. McAlister FA, Murphy NF, Simpson CR, Stewart S, MacIntyre K, Kirkpatrick M, Chalmers J, Redpath A, Capewell S and McMurray JJ. Influence of socioeconomic deprivation on the primary care burden and treatment of patients with a diagnosis of heart failure in general practice in Scotland: population based study. *BMJ*. 2004;328:1110.

19. Sheifer SE, Rathore SS, Gersh BJ, Weinfurt KP, Oetgen WJ, Breall JA and Schulman KA. Time to presentation with acute myocardial infarction in the elderly: associations with race, sex, and socioeconomic characteristics. *Circulation*. 2000;102:1651-6.

20. Wamala S, Merlo J, Bostrom G, Hogstedt C and Agren G. Socioeconomic disadvantage and primary non-adherence with medication in Sweden. *Int J Qual Health Care*. 2007;19:134-40.

21. Stehlik J, Edwards LB, Kucheryavaya AY, Aurora P, Christie JD, Kirk R, Dobbels F, Rahmel AO and Hertz MI. The Registry of the International Society for Heart and Lung Transplantation: twenty-seventh official adult heart transplant report--2010. *J Heart Lung Transplant*. 2010;29:1089-103.

22. Valantine H. Cardiac allograft vasculopathy after heart transplantation: risk factors and management. *J Heart Lung Transplant*. 2004;23:S187-93.

23. Costanzo MR, Naftel DC, Pritzker MR, Heilman JK, 3rd, Boehmer JP, Brozena SC, Dec GW, Ventura HO, Kirklin JK, Bourge RC and Miller LW. Heart transplant coronary artery disease detected by coronary angiography: a multiinstitutional study of preoperative donor and recipient risk factors. Cardiac Transplant Research Database. *J Heart Lung Transplant*. 1998;17:744-53.

24. Scholes S, Bajekal M, Love H, Hawkins N, Raine R, O'Flaherty M and Capewell S. Persistent socioeconomic inequalities in cardiovascular risk factors in England over 1994-2008: a time-trend analysis of repeated cross-sectional data. *BMC Public Health*. 2012;12:129.

25. Sundquist J, Malmstrom M and Johansson SE. Cardiovascular risk factors and the neighbourhood environment: a multilevel analysis. *Int J Epidemiol*. 1999;28:841-5.

26. Botha P, Peaston R, White K, Forty J, Dark JH and Parry G. Smoking after cardiac transplantation. *Am J Transplant*. 2008;8:866-71.

27. Dowd JB, Aiello AE and Alley DE. Socioeconomic disparities in the seroprevalence of cytomegalovirus infection in the US population: NHANES III. *Epidemiol Infect*. 2009;137:58-65.

28. Grattan MT, Moreno-Cabral CE, Starnes VA, Oyer PE, Stinson EB and Shumway NE. Cytomegalovirus infection is associated with cardiac allograft rejection and atherosclerosis. *JAMA*. 1989;261:3561-6.

29. Collett D, Mumford L, Banner NR, Neuberger J and Watson C. Comparison of the incidence of malignancy in recipients of different types of organ: a UK Registry audit. *Am J Transplant*. 2010;10:1889-96.

30. S R. Trends in cancer incidence by deprivation, England and Wales, 1990-2002. *Health Statistics Quarterly*. 2007:24-35.

31. Rachet B, Ellis L, Maringe C, Chu T, Nur U, Quaresma M, Shah A, Walters S, Woods L, Forman D and Coleman MP. Socioeconomic inequalities in cancer survival in England after the NHS cancer plan. *Br J Cancer*. 2010;103:446-53.

32. Vedanthan R, Bansilal S, Soto AV, Kovacic JC, Latina J, Jaslow R, Santana M, Gorga E, Kasarskis A, Hajjar R, Schadt EE, Bjorkegren JL, Fayad ZA and Fuster V. Family-Based Approaches to Cardiovascular Health Promotion. *J Am Coll Cardiol*. 2016;67:1725-37.

33. Galobardes B, Smith GD and Lynch JW. Systematic review of the influence of childhood socioeconomic circumstances on risk for cardiovascular disease in adulthood. *Ann Epidemiol*. 2006;16:91-104.

34. Allen JG, Arnaoutakis GJ, Orens JB, McDyer J, Conte JV, Shah AS and Merlo CA. Insurance status is an independent predictor of long-term survival after lung transplantation in the United States. *J Heart Lung Transplant*. 2011;30:45-53.

35. Goldfarb-Rumyantzev AS, Koford JK, Baird BC, Chelamcharla M, Habib AN, Wang BJ, Lin SJ, Shihab F and Isaacs RB. Role of socioeconomic status in kidney transplant outcome. *Clin J Am Soc Nephrol*. 2006;1:313-22.

36. Yoo HY and Thuluvath PJ. Outcome of liver transplantation in adult recipients: influence of neighborhood income, education, and insurance. *Liver Transpl*. 2004;10:235-43.

37. Begaj I, Khosla S, Ray D and Sharif A. Socioeconomic deprivation is independently associated with mortality post kidney transplantation. *Kidney Int.* 2013;84:803-9.

38. Bajekal M, Scholes S, O'Flaherty M, Raine R, Norman P and Capewell S. Unequal trends in coronary heart disease mortality by socioeconomic circumstances, England 1982-2006: an analytical study. *PLoS One*. 2013;8:e59608.

Table 1. Characteristics of patients in the cohort

Data presented for the cohort as a whole and for each SED quintile. Data presented as mean (SD), median [IQR] or count (%).

	Overall	Quintile 1 (most deprived)	Quintile 2	Quintile 3	Quintile 4	Quintile 5 (least deprived)	p-value
Number 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)							
Male	1879 (78.8)	387 (76.0)	386 (77.0)	393 (79.6)	361 (81.7)	352 (79.3)	0.071
Female	505 (21.2)	122 (24.0)	109 (22.0)	101 (20.45)	81 (18.3)	92 (20.7)	
Ethnicity (n=2314)							
Caucasian	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
Aetiology (n=2365)							
Ischaemic heart disease	718 (30.4)	180 (35.7)	137 (27.9)	138 (28.2)	144 (32.9)	119 (26.9)	0.264
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)	
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 (n=2218)	207 (9.3)	45 (9.5)	52 (11.4)	35 (7.6)	44 (10.6)	31 (7.5)	0.242
In hospital pre-transplant (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
Ischaemic time (n=2125)							
<120 minutes	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)							
Male	787 (33.0)	158 (31.0)	170 (34.3)	173 (35.0)	142 (32.1)	144 (32.4)	0.449
Female	1597 (67.0)	351 (69.0)	325 (65.7)	321 (65.0)	300 (67.9)	300 (67.6)	
Donor diabetes (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, years (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

Table 2. Association between socioeconomic deprivation and 30-day mortality.

Unadjusted and risk adjusted odds ratios (95% confidence interval) for 30-day mortality by SED quintile.

SED Quintile	Number of patients	Deaths at 30 days	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

*Adjusted for age, sex, ethnicity, diabetes, heart disease aetiology (dilated cardiomyopathy, ischaemic heart disease, congenital heart disease, other), pre-transplant serum creatinine, previous cardiac surgery, inpatient or outpatient prior to transplantation, ventilation status at registration (ventilated/not ventilated), donor age and donor sex.

Table 3. Association between socioeconomic deprivation and one-year mortality.

Unadjusted and risk adjusted hazard ratios (95% confidence interval) for death during the first year by SED quintile. One year mortality generated using unadjusted Kaplan Meier estimates.

SED Quintile	One-year 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

*Adjusted for age, sex, ethnicity, diabetes, heart disease aetiology (dilated cardiomyopathy, ischaemic heart disease, congenital heart disease, other), pre-transplant serum creatinine, previous cardiac surgery, inpatient or outpatient prior to transplantation, ventilation status at registration (ventilated/not ventilated), donor age and donor sex.

Table 4. Association between socioeconomic deprivation and long-term survival.

Unadjusted and risk-adjusted hazard ratios (95% confidence interval) by SED quintile and for IMD rank as a continuous variable per quintile increase (indicates increase in relative SED).

Overall Survival					
SED Quintile	**Unadjusted HR (95% CI)**	**P-value**	**Risk-adjusted* HR (95% CI)**	**P-value**	**Median Survival (95% CI)**
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					
SED Quintile	**Unadjusted HR (95% CI)**	**P-value**	**Risk-adjusted HR* (95% CI)**	**P-value**	**Median Survival (95% CI)**
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	-

*Adjusted for age, sex, ethnicity, diabetes, pre-transplant creatinine, heart failure aetiology, donor age and donor sex

Table 5. Association of Index of Multiple Deprivation domains with long-term survival.

Risk-adjusted hazard ratios (95% confidence interval) per quintile increase in rank in each of the 7 IMD domains. Increase in IMD rank indicates increase in relative SED.

Overall Survival		
IMD Domain	**Risk-adjusted HR* (95% CI)**	**P-value**
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		
IMD Domain	**Risk-adjusted HR* (95% CI)**	**P-value**
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

*Adjusted for age, sex, ethnicity, diabetes, pre-transplant creatinine, heart failure aetiology, donor age and donor sex

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).

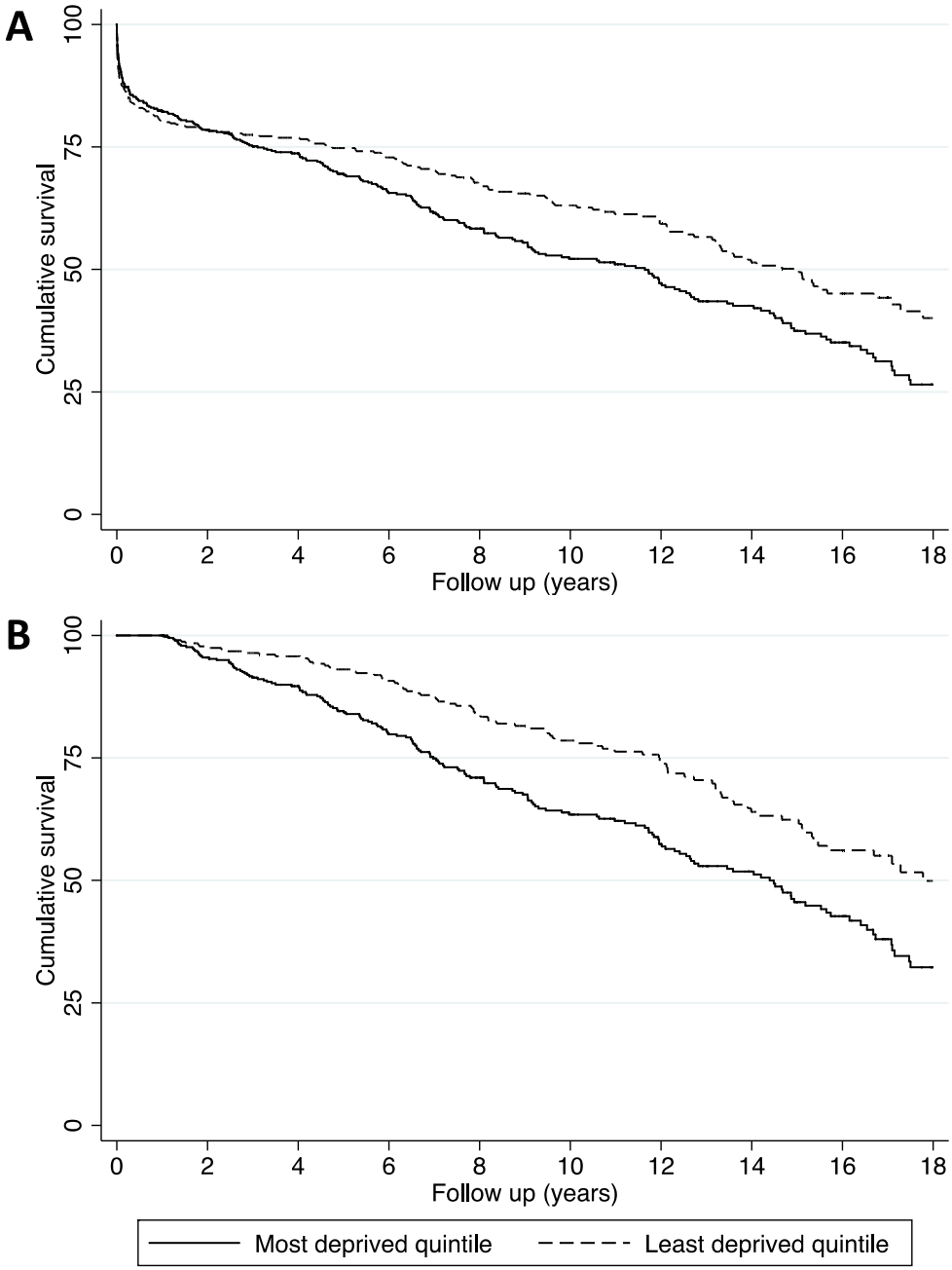

Figure 2. Subgroup analysis

Association of SED and A) Overall and B) conditional survival, by age at transplant, sex, ethnicity and heart failure aetiology. P-values presented for interaction between subgroups.