Table S1

Table S1: Estimated proportions of the sample in various labour market outcomes the year after transplantation and dialysis, and treatment effects.

	Employment	Labour force	Labour income (ln)[a], unconditioned	Early retirement[b]	Months early retirement[a]
Haemodialysis	0.34*** [0.28 – 0.40]	0.36*** [0.31 – 0.42]	5.20*** [4.59 – 5.81]	0.51*** [0.45 – 0.56]	4.54*** [4.14 – 4.94]
Peritoneal dialysis	0.29*** [0.24 – 0.35]	0.33*** [0.27 – 0.39]	4.66*** [4.05 – 5.27]	0.62*** [0.56 – 0.68]	5.06*** [4.45 – 5.67]
Transplantation	0.54*** [0.52 – 0.55]	0.59*** [0.58 – 0.61]	7.22*** [7.03 – 7.42]	0.44*** [0.43 – 0.46]	3.97*** [3.75 – 4.19]
Average Treatment Effect PD vs. HD	-0.05 [-0.13 – 0.03]	-0.04 [-0.12 – 0.04]	-0.54 [-1.39 – 0.30]	0.11*** [0.03 – 0.19]	0.52 [-0.16 – 1.19]
Average Treatment Effect Tx vs. HD	0.19*** [0.13 – 0.26]	0.23*** [0.17 – 0.29]	2.02*** [1.41 – 2.63]	-0.06** [-0.12 – -0.01]	-0.57*** [-0.94 – -0.21]
Average Treatment Effect Tx vs. PD	0.25*** [0.19 – 0.30]	0.27*** [0.21 – 0.33]	2.56*** [1.94 – 3.18]	-0.17*** [-0.23 – -0.12]	-1.09*** [-1.68 – -0.50]
Observations	4302	4302[d]	4302	4269[c]	2366

Statistical significance is indicated at 5% (**) and 1% (***) levels. The following variables are controlled for in the outcome models: gender, age, civil status, education, disposable income before start of RRT, the dependent variable before start of RRT, and number of risk factors. [a] Outcome model OLS. [b] Controlling for early retirement 2 years before treatment instead of 1 as in the other models due to collinearity. [c] Only covers the period 2003-2012. [d] Information on unemployment is only available for the period 1998-2012.

The treatment effect of transplantation compared to haemodialysis is generally as compared to the whole group of dialysis with the largest change in relation to early retirement. No significant treatment effect of peritoneal dialysis compared to haemodialysis was found except an increased risk of early retirement. These results should be interpreted with caution as the treatment selection model is specified to balance covariates between transplantation and dialysis and not between modalities within dialysis.

SDC, Materials and Methods

Estimating the Average Treatment Effect

Controlling for nonrandom selection into treatment is of particular importance in the field of RRT due to the scarcity of kidneys available for transplantation. This can be done by conditioning on factors that determine treatment assignment, which ideally would result in that treatment assignment and outcome are independent and the treatment effect simply the difference in average outcomes between the treatments.[1] There are several approaches available in order to accomplish this. One approach is the Regression Adjustment (RA) estimator that uses a regression model to predict potential outcomes adjusted for covariates. One outcome model for each treatment assignment is estimated and the average treatment effect is the difference in potential outcome means over the full sample. Another approach is the Inverse-Probability Weighting (IPW) estimator that uses weights to correct the estimate for observable differences between the treatment groups. A treatment model is estimated where observed treatment assignment is a function of individuals' characteristics; the weights are the inverse probability of being in the observed treatment group. More weight is thus given to those least likely to be in the observed group when the mean outcomes of the treatment groups are calculated. In the current study, we will combine these approaches into the IPWRA approach where weighted regression coefficients correct for possible model misspecification using the estimated inverse probability weights. The weighted regression coefficients are used to calculate average potential outcome of each treatment. The difference in average potential outcome between treatments is the Average Treatment Effect (ATE), showing the treatment effect of getting one treatment over another for the same sample of patients. Failure to control for all factors that influences treatment assignment and the outcome might lead to biased estimates which highlight the importance of careful model specification and access to extensive data material.[1]

The purpose of the inverse probability weighting approach is thus to deal with the problem of covariates being related to both the treatment assignment and the outcome of interests by

balancing the covariates so that the distributions do not vary over treatment choice. It is therefore important to test if the specification of the treatment model accomplishes this. We will do this by calculating the standardised differences and variance ratio where a perfect balance after weighting is indicated by a standardised difference of 0 and variance ratio of 1.[2] A standardised difference below |0.1| is considered to indicate a balanced covariate and thus that the treatment specification has resulted a balanced distribution. An overidentification test for balance of covariates will also be applied.[3]

The overlap assumption requires all individuals in the sample to have a positive probability of receiving treatment. A minimum probability of 0.001% will be used which is the default limit in Stata.[4] This assumption will be further studied by graphically plot estimated densities of the probability of getting the different treatments. If the estimated densities largely overlap this indicates that the groups are comparable and the estimated treatment effect is credible in terms of reducing the estimation bias. Limiting the estimation to those treated with transplantation, so called average treatment effect of the treated requires less restrictive forms of the conditional-independence and the overlap assumptions compared to average treatment effect (also known as strong ignorability). We will therefore also estimate the average treatment effect of the treated as a check for potential problems with the assumption in the ATE estimates, especially the overlap assumption. A large difference between the estimates could indicate a problem with the overlap assumption. Another approach to increase overlap between treatments is choosing patients that already from the start are similar. Patients who at any time has been on the waiting list for a kidney transplantation are more likely to be comparable as it excludes those in dialysis that, under current allocation rules, never will be considered for transplantation. We will therefore check the overlap in the baseline results by also estimate the average treatment effect for those on the waiting list.

Estimation models

Beside medical factors such as contraindications and existing risk factors, several socio-economic factors have been found to be related to the treatment choice between kidney transplantation and dialysis.[5] Based on prior research, a logistic treatment model is specified controlling for civil status, education, individual disposable income before start of RRT adjusted for household equivalence scale[7], primary disease, and diabetes, cancer and heart disease comorbidity. Employment status has previously been shown to be associated with treatment choice/allocation in RRT which raises a concerns regarding an endogenous relationship between employment status and treatment modality.[5] We therefore also control for the employment status before start of RRT and the final logistic treatment model is specified as:

$$\begin{aligned} Tx_{i\,T>t} = {} & \alpha_i + \beta_1 Gender_{i\,t} + \beta_2 Age_{i\,t} + \beta_3 Marital\ status_{i\,t} + \beta_4 Education_{i\,t} \\ & + \beta_5 Ln(Disposable\ Income)_{i\,t-1} + \beta_6 Ln(Disposable\ Income)^2_{i\,t-1} \\ & + \beta_7 Primary\ disease_{i\,t} + \beta_8 Diabetes_{i\,t} + \beta_9 Cancer_{i\,t} + \beta_{10} Heart\ disease_{i\,t} \\ & + \beta_{11} Employment_{i\,t-1} + \varepsilon_i \end{aligned}$$

Where Tx is the intention to treat choice of transplantation (=1) over dialysis (=0) of the i:th individual, and ε is the error term. Independent variables are either measured at the start of RRT, indicated by t, or the year before start of RRT, indicated by t-1. Marital status is defined as married, single, divorced or widowed. Education is following the current Swedish educational system and is categorised as up to 9 years (mandatory school), 9-12 years (secondary school), and more than 12 years (higher education). The individual disposable income is derived from the family's total disposable income, adjusted for household equivalence scale.[7] Primary disease is categorised into diabetic nephropathy, adult polycystic kidney disease, glomerulonephritis, hypertension, pyelonephritis, unspecified kidney disease, and other diseases. Comorbidities controlled for are diabetes, cancers, and heart diseases (hypertension, cerebrovascular-, peripheral vascular-, and ischemic heart disease). History of abuse is defined as having a health care contact with a F10-19

ICD-10 diagnosis (psychoactive substance use) up to 10 years prior to start of RRT. This variable is included in the treatment model in a sensitivity analysis as this information is only available for a subset of the sample. Natural logarithms (Ln) are created after setting negative values to zero and adding 1SEK to all values in order to achieve a more normal distribution.

The labour market outcomes to be investigated are employment, labour force participation, labour income, early retirement, months in early retirement, and participation in educational activities. All variables are based on register data. Both employment and labour force participation status are defined according to the status during the month of November for each year by Statistics Sweden. Employment includes both full and part time employment while labour force participation combines employed and unemployed. Labour income is defined as individual income from employment plus nonnegative business income and analysed conditioned on employment and earning at least SEK100 000 (€11561).[9] Early retirement is a binary variable whether the individual is considered to have permanent or long-term reduced work ability and receives benefits for this reason. Early retirement can be granted on full or part time and an additional variable shows the net months, ie, includes both the length and magnitude of the reduced ability to work. Finally, an individual is considered to participate in educational activity if s/he was registered in any education during the fall semester, including some labour market policy initiatives.

The weighted outcome model, estimated separately for each treatment, were either logistic or OLS models depending on the nature of the outcome variable. The following patient characteristics were controlled for: gender, age, civil status, education, disposable income before start of RRT, and total number of risk factors. The following specification was applied, using the variable definitions above with Y as the studied labour market outcome:

$$Y_{i\,T>t} = \alpha_i + \beta_1 Gender_{i\,t} + \beta_2 Age_{i\,t} + \beta_3 Marital\ status_{i\,t} + \beta_4 Education_{i\,t} + \beta_5 Ln(Disposable\ Income)_{i\,t-1} + \beta_6 Number\ of\ risk\ factors_{i\,t} + \beta_{7i} Y_{i\,t-1} + \varepsilon_i$$

We lacked a generic measure of health status. Instead, as a proxy, we used the total number of risk factors at start of RRT with the assumption that presence of more risk factors indicates worse health status. The lag t-1 (ie, the year before start of RRT) of the labour market outcome under study (Y) was also added to the equation as this has previously been shown to be one of the strongest predictors of a positive outcome in terms of employment.[8] After estimation, the outcome model was used to predict the potential outcome of each treatment for the full sample.

Weighting performance

RTRs are compared to patients in the sample who do not receive a transplant during the study period but remain on dialysis. The reason for why they do not receive a transplant is expected to vary substantially, eg, being too sick to go through surgery, low adherence, and bad luck. Having such a diverse comparison group increases the risk of not being able to balance the covariates (ie, create comparable groups through inverse probability weighting) and achieve overlap in the individual probability of getting a transplantation (ie, common support). Thus, a number of checks are performed in order to determine if the results are credible in reducing estimation bias.

The specification of the treatment equation is successful in obtaining covariate distributions that do not vary substantially between treatment levels (Table S2). Standardised differences are all below the applied threshold of |0.1| and the variance ratio is close to 1 with the exception of one category of the primary disease. As the overidentification test for covariate balance soundly fails to reject the null hypothesis that the model balances all covariates we conclude that we have obtained a balanced sample over treatment choice. However, it is possible that the sample is unbalanced over treatment choice in terms of important unobserved variables and causality therefore cannot be established. The results should be interpreted as a reduced bias estimate compared to naïve model that fail to adjust for treatment selection on the variables included in Table S2.

Table S2: Covariate balance after inverse probability weighting

	Standardised differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
Gender				
Woman	-0.02	-0.04	0.99	0.98
Age	-0.76	-0.05	1.61	1.04
Civil status				
Single	0.04	0.05	1.02	1.03
Divorced	-0.20	-0.05	0.70	0.91
Widow	-0.13	0.00	0.38	0.96
Education				
Secondary education	0.04	-0.02	1.00	1.00
Higher education	0.37	0.05	1.73	1.07
Primary disease				
Adult polycystic kidney disease	0.26	-0.02	2.00	0.96
Glomerulonephritis	0.43	0.07	1.83	1.08
Hypertension	-0.10	-0.02	0.67	0.93
Pyelonephritis	0.06	0.03	1.42	1.17
Unspecified kidney disease	-0.07	0.01	0.81	1.04
Other kidney diseases	0.00	-0.05	1.00	0.93
Comorbidity diabetes	-0.58	-0.02	0.62	0.98
Comorbidity cancer	-0.24	-0.01	0.28	0.96
Comorbidity heart disease	-0.46	-0.01	0.30	0.96
Ln(Disposable income before treatment)	0.14	0.01	1.30	1.06
Ln(Disposable income before treatment)^2	0.15	0.01	1.23	0.98
Employment before treatment	0.73	0.06	1.16	0.99
Overidentification test for covariate balance			Prob>chi2	0.95

The graphical plot of the estimated densities of the probability of getting a transplantation for patients receiving dialysis and transplantation respectively are shown in Fig S1. Although potentially problematic at high and low propensity scores, most of the 2 densities' respective masses are in regions where they overlap. For patients receiving transplantation, the overlap assumption appears to be satisfied indicating that the average treatment of the treated will supply unbiased estimates. Results regarding the effect of receiving transplantation for patients currently on dialysis and with low probability of receiving transplantation could potentially suffer from lack of overlap. We deal

with this uncertainty in 2 ways: 1) we compare the average treatment effect to the average treatment effect of the treated as described above, and 2) restrict our sample to patients on the waiting list only. The overlap graph of the latter is shown in Fig S2, indicating a satisfying overlap. We will therefore also estimate the average treatment effect based a sample of patients on the waiting list and compare to the baseline results. Stable and similar results between all 3 estimations average treatment effects (baseline, of the treated and waiting list sample) will be interpreted as sufficient overlap in the baseline sample.

Sensitivity analyses

Seven different sensitivity analyses are presented here:

- As the effect size of employment the year before start of RRT was very large, employment status prior to treatment for transplanted was redefined as the year before transplantation. This reduced the average treatment effect on employment posttransplantation by 1 percentage point (20% vs. 21% at baseline).
- A subsample (n=2029) where information was available on history of diagnosed abuse showed that prior abuse is strongly associated with reduced chance of getting a transplantation (OR=0.25 P<0.00). The average treatment effect on employment increased to 23 percentage points (P<0.00) compared to 21 percentage points at baseline.
- The rules and regulations regarding early retirement has been substantially revised during the study period and the rate of early retirement is expected to fall over time. Controlling for start year of RRT in the early retirement model increased the average treatment effect of transplantation by 3 percentage points (-15 vs. -12 at baseline). The start year was significantly negatively associated with the likelihood of early retirement in the outcome models for both transplantation and dialysis.

- The average disposable income of the last 5 years before start of RRT was used instead of the year before start of RRT. This had a minor effect on the average treatment effect on employment estimate, increasing it to 22 percentage points (21% at baseline).
- Dividing RTR into 2 groups based on waiting shorter or longer than 1 year for a transplant showed a higher treatment effect with shorter waiting time. Transplantation was associated with 16 percentage points higher employment rate compared to dialysis for those waiting longer than 1 year. The corresponding figure for those waiting less than 1 year was 24 percentage points. In addition, the estimated average outcomes were lower for both treatments with a longer waiting time. Reduced waiting times thus seem to be important in order to achieve increased levels of return to work.
- Limiting the dialysis group to only patients in in-center dialysis, ie, excluding home-HD and different PD modalities, did not change the results compared to the baseline.
- Excluding the pretreatment variables in the outcome model strengthened the estimated average treatment effect in all estimations (1 – 6 percentage points) and in 1 case gained statistical significance at the 95% level (likelihood of early retirement for the waiting list sample).

Figure S1: Estimated densities of the probability of getting treatment after inverse probability weighting

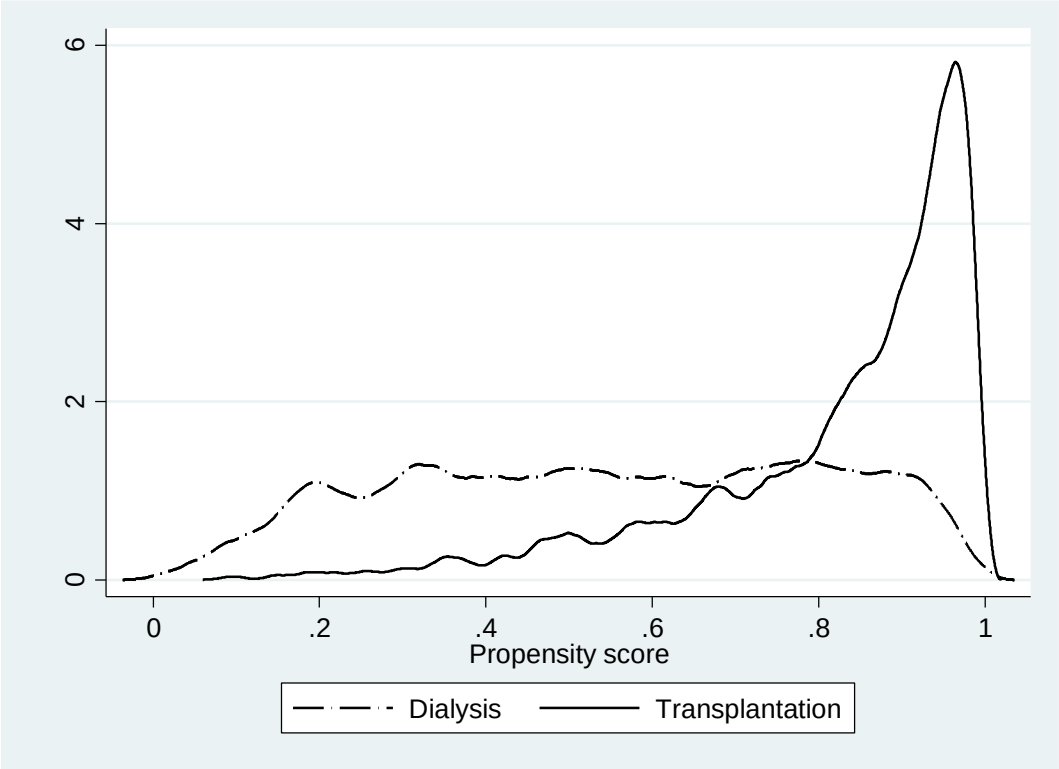
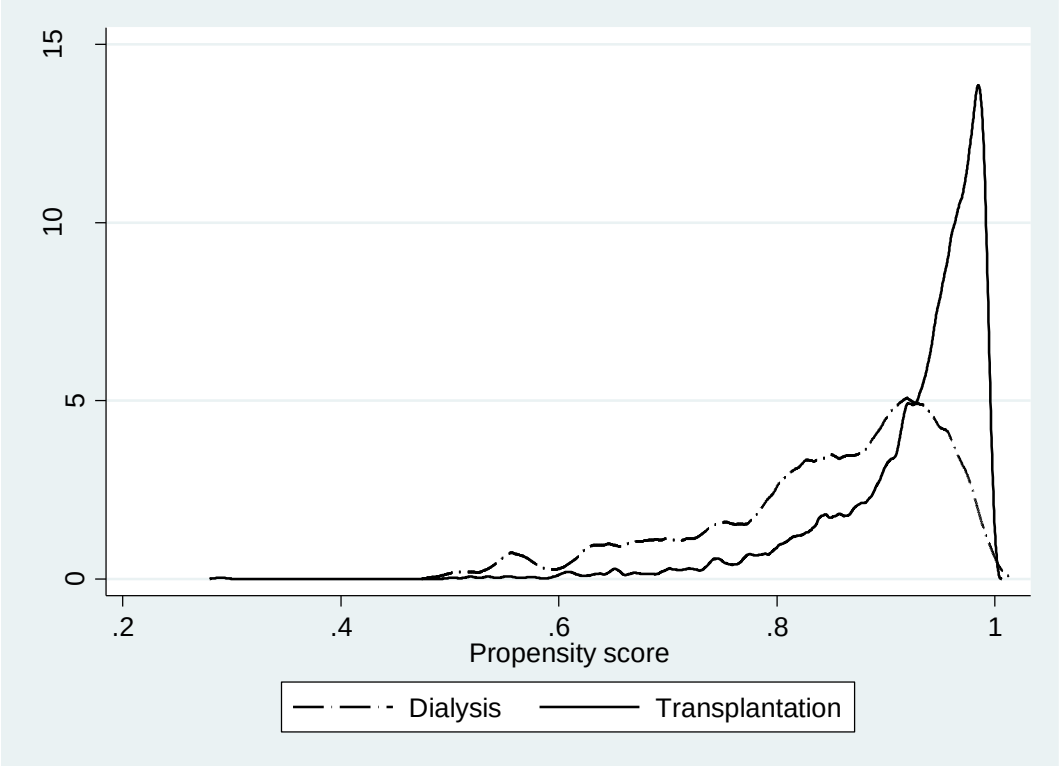


Figure S2: Estimated densities of the probability of getting treatment after inverse probability weighting for patients on the waiting list only



References

1. Wooldridge J. Econometric analysis of cross section and panel data. Cambridge, Massachusetts 2002.
2. Rubin DB. Using Propensity Scores to Help Design Observational Studies: Application to the Tobacco Litigation. Health Services and Outcomes Research Methodology. 2001;2(3):169-88.
3. Imai K, Ratkovic M. Covariate balancing propensity score. Journal of the Royal Statistical Society: Series B (Statistical Methodology). 2014;76(1):243-63.
4. StatCorp. Stata treatment effects reference manual: Potential outcomes/counterfactual outcomes. College Station, Texas: Stata Press; 2015.
5. Hod T, Goldfarb-Rumyantzev AS. The role of disparities and socioeconomic factors in access to kidney transplantation and its outcome. Renal Failure. 2014;36(8):1193-9.
6. Böhlke M. Dialysis and Kidney Transplantation: Why Have Our Rehabilitation Hopes Not Been Achieved Fully? American Journal of Kidney Diseases. 2012;59(5):598-600.
7. SCB. Longitudinell integrationsdatabas för Sjukförsäkrings- och Arbetsmarknadsstudier (LISA)1990–2013. Örebro: Statistics Sweden; 2016.
8. Nour N, Heck CS, Ross H. Factors related to participation in paid work after organ transplantation: perceptions of kidney transplant recipients. Journal of occupational rehabilitation. 2015;25(1):38-51.
9. Antelius J, Björklund A. How reliable are register data for studies of the return to schooling? An examination of Swedish data. Scandinavian Journal of Educational Research. 2000;44(4):341-55.