

SUPPLEMENTAL DIGITAL CONTENT

SUPPLEMENTARY MATERIALS AND METHODS

Potential confounders and mediators

Potential confounders

- (i) Age at the time of transplantation. In France in 2017, the median age of renal graft recipients was 51.4 years [4-85] for preemptive kidney transplantation (PKT) versus 55.1 years [1.8-87] for non-PKT.⁵⁴ Age under 60 years is associated with quintile 5 of the EDI.¹⁶ Moreover, age is independently associated with deceased-donor PKT.⁵⁵
- (ii) Gender. In France in 2017, 35.7% of PKT was performed in women versus 64.3% in men.⁵⁴ Female gender is associated with quintile 5 of the EDI.¹⁶ Female gender is also associated with deceased-donor PKT.⁵⁵
- (iii) Diabetes. We assumed that a chronic disease, such as diabetes mellitus, increases social inequalities in health, but social deprivation is also a known risk factor for diabetes mellitus.⁵⁶ Moreover, diabetes is associated with a reduced risk of PKT.⁵⁷
- (iv) The underlying nephropathy. We assumed that underlying nephropathies, such as diabetic or vascular nephropathies, are associated with the most deprived patients and affect access to PKT.⁵⁵

Potential mediators

We hypothesized that the association between deprivation and PKT could be affected by the following mediators:

- (i) Living-donor kidney source. In France, LDKT represents 12% of the non-PKT, and 37% of PKT. The most deprived patients are less likely to receive a living-donor kidney and consequently less likely to undergo preemptive transplantation.⁷ Living donor transplantation was considered as a proxy of organ donation process.
- (ii) Positive cytomegalovirus (CMV) serology. Lower socioeconomic status is associated with positive CMV serology.⁵⁸ CMV is independently associated with an increased risk of cardiovascular disease.⁵⁰
- (iii) Positive human leukocyte antigens (HLA) antibodies. The most deprived recipients have an increased risk of HLA immunization.⁵⁹ HLA antibodies increase the time spent on the transplant waiting list and reduce the likelihood of preemptive transplantation.^{60,61}
- (iv) Blood group. In France, blood groups A and O represent 44% and 42% of the general population respectively, whereas only 10% of the population has group B. However, ABO blood group distribution differs according to country and continent. The non-European population more frequently belongs to the most deprived group and has blood group B than the European population.⁶² In 2018, the ABM reported that patients with blood groups B and O patients have a more difficult access to transplantation in France. The non-O blood groups are associated with deceased-donor PKT.⁵⁵
- (v) Hepatitis C virus (HCV) infection. HCV infection is more frequent in socially deprived patients.⁵¹ We hypothesized that positive hepatitis C serology was associated with PKT.^{7,55}

SUPPLEMENTARY RESULTS

Table S1. Patient characteristics (complete cohort, quintile 5 of the European Deprivation Index versus others).

	Quintiles 1 to 4 (N=5883)	Quintile 5 (N=2818)
Patient characteristics		
Age (years)		
[18-30]	439 (7%)	246 (9%)
[30-60]	3167 (54%)	1672 (59%)
> 60	2277 (39%)	900 (32%)
Gender (male)	3837 (65%)	1714 (61%)
BMI (kg/m²)		
< 20	166 (3%)	81 (3%)
[20-25]	2886 (49%)	1317 (47%)
> 25	2831 (48%)	1420 (50%)
Underlying nephropathy		
Diabetic	527 (9%)	368 (13%)
Glomerulonephritis	1430 (24%)	549 (19%)
Interstitial nephritis	526 (9%)	263 (9%)
PKD (ref)	1267 (22%)	383 (14%)
Systemic disease	210 (4%)	92 (3%)
Uropathy	149 (3%)	55 (2%)
Vascular	530 (9%)	336 (12%)
Miscellaneous	304 (5%)	173 (6%)
Unknown	940 (16%)	599 (21%)
Diabetes	912 (16%)	554 (20%)
Cardiovascular disease	1376 (23%)	665 (24%)
Tobacco (smoker)	3030 (52%)	1351 (48%)
Hypertension	4001 (68%)	1947 (69%)

(Continues)

Table S1. Patient characteristics (complete cohort, quintile 5 of the European Deprivation Index versus others).

	Quintiles 1 to 4 (N=5883)	Quintile 5 (N=2818)
Positive hepatitis C serology	120 (3%)	102 (4%)
Positive CMV serology	3105 (53%)	2042 (72%)
Positive EBV serology	5616 (95%)	2713 (96%)
HLA antibody class I and/or II > 0%	1275 (22%)	701 (25%)
Blood group		
B	617 (10%)	426 (15%)
Others	5266 (90%)	2392 (85%)
Transplantation characteristics		
Donor source (living donor)	899 (15%)	326 (12%)
<i>Preemptive living donor transplantation</i>	371 (41%)	107 (33%)
Preemptive registration	2236 (38%)	790 (28%)
Preemptive transplantation	1067 (18%)	330 (12%)

Table S2. Bivariate analysis (logistic regression). Factors associated with each quintile of the European Deprivation Index.

	Quintile 1*	Quintile 2*	Quintile 3*	Quintile 4*	Quintile 5*
Patient characteristics (N=2818)	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]
Age (years)					
[18-30]	ref	ref	ref	ref	ref
[30-60]	1.07 [0.85-1.37]	1.17 [0.93-1.47]	1.07 [0.86-1.33]	0.86 [0.71-1.06]	0.94 [0.80-1.11]
> 60	1.34 [1.06-1.72]	1.13 [0.90-1.44]	1.20 [0.96-1.50]	0.98 [0.80-1.21]	0.71 [0.59-0.84]
Gender (female)	0.90 [0.79-1.02]	0.88 [0.78-0.99]	0.94 [0.84-1.06]	0.98 [0.88-1.10]	1.21 [1.10-1.33]
BMI (kg/m ²)					
< 20	0.95 [0.65-1.35]	0.86 [0.59-1.23]	1.11 [0.79-1.53]	0.97 [0.70-1.33]	1.07 [0.81-1.40]
[20-25]	ref	ref	ref	ref	ref
> 25	0.91 [0.81-1.03]	1.00 [0.89-1.12]	1.05 [0.94-1.18]	0.90 [0.81-1.00]	1.10 [1.00-1.20]
Underlying nephropathy					
Diabetic	0.59 [0.46-0.75]	0.63 [0.50-0.79]	0.76 [0.61-0.94]	0.92 [0.75-1.13]	2.31 [1.94-2.75]
Glomerulonephritis	0.87 [0.73-1.04]	0.89 [0.75-1.05]	0.95 [0.80-1.12]	1.00 [0.85-1.18]	1.27 [1.09-1.48]
Interstitial nephritis	0.70 [0.55-0.89]	0.79 [0.63-0.99]	0.93 [0.74-1.15]	0.94 [0.76-1.16]	1.65 [1.37-1.99]
PKD	ref	ref	ref	ref	ref
Systemic disease	0.78 [0.55-1.10]	0.77 [0.55-1.07]	1.03 [0.75-1.39]	0.96 [0.70-1.29]	1.45 [1.10-1.89]
Uropathy	0.78 [0.51-1.16]	0.91 [0.61-1.31]	0.89 [0.60-1.29]	1.18 [0.83-1.66]	1.22 [0.87-1.69]
Vascular	0.85 [0.68-1.07]	0.63 [0.50-0.79]	0.75 [0.60-0.93]	0.82 [0.66-1.01]	2.10 [1.75-2.51]
Miscellaneous	0.85 [0.64-1.12]	0.63 [0.47-0.84]	0.84 [0.64-1.09]	0.88 [0.67-1.14]	1.88 [1.51-2.34]
Unknown	0.68 [0.56-0.83]	0.62 [0.51-0.75]	0.79 [0.66-0.95]	0.95 [0.79-1.13]	2.11 [1.81-2.46]
Diabetes	0.85 [0.72-1.00]	0.96 [0.82-1.12]	0.84 [0.72-0.98]	0.90 [0.78-1.04]	1.33 [1.19-1.50]
Cardiovascular disease	1.01 [0.88-1.16]	1.01 [0.88-1.15]	1.05 [0.92-1.19]	0.93 [0.81-1.05]	1.01 [0.91-1.12]
Tobacco (smoker)	0.99 [0.88-1.11]	1.00 [0.89-1.12]	0.97 [0.87-1.08]	1.07 [0.96-1.19]	0.98 [0.89-1.07]
Hypertension	1.05 [0.93-1.20]	1.00 [0.89-1.14]	0.98 [0.87-1.10]	0.91 [0.81-1.02]	1.05 [0.95-1.16]

Positive hepatitis C serology	0.77 [0.50-1.14]	0.98 [0.67-1.40]	0.41 [0.24-0.64]	0.93 [0.65-1.30]	1.80 [1.38-2.36]
Positive CMV serology	0.57 [0.51-0.64]	0.66 [0.59-0.74]	0.76 [0.68-0.85]	0.94 [0.84-1.05]	2.35 [2.14-2.60]
HLA antibody class I and/or II > 0%	0.91 [0.79-1.04]	0.91 [0.79-1.03]	0.96 [0.85-1.09]	0.96 [0.85-1.08]	1.19 [1.07-1.31]
Blood group					
B	0.84 [0.69-1.02]	0.86 [0.71-1.03]	0.92 [0.77-1.09]	0.73 [0.61-0.87]	1.52 [1.33-1.73]
Others	ref	ref	ref	ref	ref
Donor source (living donor)	1.24 [1.05-1.46]	1.18 [1.00-1.38]	1.03 [0.88-1.20]	1.08 [0.92-1.25]	0.73 [0.63-0.83]
Preemptive kidney transplantation	1.36 [1.16-1.58]	1.31 [1.13-1.51]	1.12 [0.96-1.29]	1.06 [0.92-1.22]	0.60 [0.52-0.68]

* For each quintile, reference class was the other quintiles.

Table S3. Bivariate analysis (logistic regression). Factors associated with preemptive registration.

Preemptive registration	
N = 3026	
Patient characteristics	OR [95% CI]
Age (years)	
[18-30]	ref
[30-60]	1.01 [0.85-1.19]
> 60	0.75 [0.63-0.89]
Gender (female)	1.26 [1.15-1.38]
BMI (kg/m ²)	
< 20	1.13 [0.87-1.47]
[20-25]	ref
> 25	0.89 [0.82-0.98]
Underlying nephropathy	
Diabetic	0.23 [0.19-0.28]
Glomerulonephritis	0.50 [0.44-0.57]
Interstitial nephritis	0.62 [0.52-0.73]
PKD	ref
Systemic disease	0.18 [0.13-0.25]
Uropathy	0.79 [0.59-1.06]
Vascular	0.30 [0.25-0.35]
Miscellaneous	0.39 [0.31-0.49]
Unknown	0.34 [0.29-0.39]
Diabetes	0.52 [0.45-0.59]
Cardiovascular disease	0.48 [0.43-0.54]
Tobacco (smoker)	0.80 [0.73-0.88]
Hypertension	0.88 [0.80-0.96]
Positive hepatitis C serology	0.40 [0.28-0.56]
Positive CMV serology	0.75 [0.68-0.81]

HLA antibody class I and/or II > 0%	0.95 [0.86-1.05]
Blood group	
B	0.86 [0.74-0.98]
Others	ref
Donor source (living donor)	2.69 [2.38-3.04]
EDI (quintile 5)	0.64 [0.58-0.70]

Table S4. Mediation analyses: effects of social deprivation on preemptive registration (one mediator at a time).

	Living-donor transplantation		Positive CMV serology		HLA immunization		Positive hepatitis C serology		Blood group B	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Natural Direct Effect	0.71	[0.65-0.79]**	0.70	[0.63-0.78]**	0.69	[0.62-0.76]**	0.69	[0.62-0.77]**	0.69	[0.62-0.76]**
Natural Indirect Effect	0.96	[0.94-0.98]**	0.98	[0.96-0.99]*	1.00	[0.99-1.00]	0.99	[0.99-1.00]*	1.00	[0.99-1.00]
Total Effect	0.68	[0.62-0.76]**	0.68	[0.62-0.76]**	0.68	[0.62-0.76]**	0.68	[0.62-0.76]**	0.68	[0.62-0.75]**

The analyses were adjusted for confounders: age, sex, diabetes and underlying nephropathy.

* $p < 0.05$

** $p < 0.001$

Table S5. Sequential mediation analyses: effects of social deprivation on preemptive registration.

	Model 1		Model 2		Model 3		Model 4		Model 5	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Natural Direct Effect	0.71	[0.64-0.79]**	0.73	[0.66-0.81]**	0.73	[0.66-0.81]**	0.73	[0.66-0.81]**	0.74	[0.67-0.82]**
Natural Indirect Effect	0.96	[0.95-0.98]**	0.94	[0.92-0.96]*	0.94	[0.92-0.96]	0.93	[0.91-0.96]*	0.93	[0.91-0.95]
Total Effect	0.69	[0.62-0.76]**	0.69	[0.62-0.76]**	0.69	[0.62-0.76]**	0.69	[0.62-0.76]**	0.69	[0.62-0.76]**

The analyses were adjusted for confounders: age, sex, diabetes and underlying nephropathy.

Model 1: mediation analysis with a single mediator – living-donor transplantation.

Model 2: mediation analysis with two mediators – living-donor transplantation and positive CMV serology.

Model 3: mediation analysis with three mediators – living-donor transplantation, positive CMV serology and HLA immunization.

Model 4: mediation analysis with four mediators – living-donor transplantation, positive CMV serology, HLA immunization and positive hepatitis C serology.

Model 5: complete mediation analysis with the five mediators described in the DAG – living-donor transplantation, positive CMV serology, HLA immunization, positive hepatitis C serology and blood group.

Table S6. Multivariable analyses stratified by donor type.

	Complete cohort N = 8701		Living donor kidney transplantation N = 1225 (14%)		Deceased donor kidney transplantation N = 7476 (86%)	
	Preemptive registration N = 3026 (35%)	Preemptive transplantation N = 1397 (16%)	Preemptive registration N = 676 (55%)	Preemptive transplantation N = 478 (39%)	Preemptive registration N = 2350 (31%)	Preemptive transplantation N = 919 (12%)
Patient characteristics	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]
Age (years)						
[18-30]	ref	ref	ref	ref	ref	ref
[30-60]	1.04 [0.87-1.25]	0.79 [0.64-0.98]	1.33 [0.96-1.84]	1.06 [0.76-1.84]	1.18 [0.94-1.48]	1.07 [0.78-1.49]
> 60	0.91 [0.75-1.10]	0.84 [0.67-1.06]	1.13 [0.72-1.76]	1.04 [0.66-1.64]	1.14 [0.90-1.45]	1.46 [1.06-2.06]
Gender (female)	0.85 [0.77-0.95]	0.90 [0.79-1.03]	0.90 [0.69-1.17]	0.96 [0.74-1.25]	0.82 [0.73-0.92]	0.82 [0.70-0.96]
BMI (kg/m ²)						
< 20	1.15 [0.87-1.51]	0.97 [0.67-1.36]	1.47 [0.79-2.76]	1.24 [0.66-2.28]	1.10 [0.80-1.51]	0.84 [0.51-1.32]
[20-25]	ref	ref	ref	ref	ref	ref
> 25	1.02 [0.93-1.12]	1.04 [0.92-1.17]	1.24 [0.96-1.61]	1.31 [1.01-1.70]	0.99 [0.89-1.11]	0.98 [0.85-1.14]
Underlying nephropathy						
Diabetic	0.34 [0.26-0.44]	0.66 [0.47-0.92]	0.35 [0.16-0.79]	0.62 [0.27-1.42]	0.34 [0.26-0.44]	0.69 [0.47-1.02]
Glomerulonephritis	0.52 [0.45-0.60]	0.70 [0.59-0.83]	0.37 [0.25-0.53]	0.51 [0.36-0.72]	0.53 [0.46-0.62]	0.73 [0.59-0.90]
Interstitial nephritis	0.64 [0.54-0.77]	0.97 [0.79-1.20]	0.67 [0.39-1.14]	0.97 [0.60-1.59]	0.66 [0.55-0.80]	1.09 [0.84-1.39]
PKD	ref	ref	ref	ref	ref	ref
Systemic disease	0.18 [0.13-0.25]	0.31 [0.19-0.47]	0.26 [0.13-0.51]	0.39 [0.19-0.78]	0.15 [0.10-0.22]	0.24 [0.12-0.42]
Uropathy	0.75 [0.55-1.01]	1.12 [0.78-1.57]	0.55 [0.29-1.06]	0.77 [0.42-1.41]	0.75 [0.53-1.07]	1.20 [0.75-1.86]
Vascular	0.36 [0.30-0.44]	0.55 [0.43-0.71]	0.22 [0.13-0.38]	0.38 [0.21-0.66]	0.39 [0.32-0.48]	0.64 [0.48-0.84]
Miscellaneous	0.43 [0.34-0.53]	0.73 [0.55-0.96]	0.30 [0.17-0.51]	0.38 [0.21-0.66]	0.44 [0.34-0.56]	0.89 [0.64-1.22]
Unknown	0.38 [0.33-0.44]	0.58 [0.47-0.70]	0.25 [0.17-0.39]	0.36 [0.24-0.55]	0.41 [0.34-0.48]	0.66 [0.53-0.84]
Diabetes	0.88 [0.73-1.05]	0.73 [0.56-0.93]	0.81 [0.43-1.51]	0.77 [0.39-1.47]	0.91 [0.74-1.10]	0.74 [0.56-0.98]
Cardiovascular disease	0.56 [0.40-0.82]	0.59 [0.50-0.70]	0.57 [0.40-0.82]	0.64 [0.43-0.93]	0.57 [0.50-0.65]	0.62 [0.51-0.75]
Tobacco (smoker)	0.91 [0.83-1.00]	0.88 [0.78-0.99]	0.88 [0.69-1.12]	0.88 [0.69-1.12]	0.92 [0.83-1.03]	0.90 [0.77-1.04]
Hypertension	1.04 [0.94-1.15]	1.03 [0.91-1.18]	1.05 [0.81-1.35]	0.91 [0.70-1.17]	1.04 [0.93-1.17]	1.09 [0.94-1.28]
Positive hepatitis C serology	0.47 [0.33-0.67]	0.53 [0.31-0.84]	0.86 [0.32-2.25]	0.63 [0.20-1.72]	0.44 [0.29-0.64]	0.53 [0.28-0.91]
Positive CMV serology	0.88 [0.80-0.97]	0.88 [0.78-0.99]	0.94 [0.74-1.21]	0.86 [0.67-1.10]	0.87 [0.77-0.97]	0.90 [0.78-1.04]

HLA antibody class I and/or II > 0%	0.91 [0.81-1.01]	0.75 [0.65-0.87]	0.92 [0.69-1.23]	0.91 [0.67-1.21]	0.93 [0.83-1.05]	0.75 [0.63-0.89]
Blood group B Others	0.92 [0.80-1.06] ref	0.80 [0.66-0.97] ref	0.85 [0.60-1.20] ref	0.96 [0.67-1.36] ref	0.91 [0.77-1.07] ref	0.68 [0.53-0.87] ref
EDI (quintile 5)	0.71 [0.64-0.78]	0.66 [0.57-0.76]	0.82 [0.63-1.08]	0.78 [0.59-1.04]	0.71 [0.64-0.80]	0.67 [0.57-0.79]

SUPPLEMENTARY REFERENCES (*only related to the supplementary Materials and Methods paragraph*)

54. Agence de la Biomedecine. Registre Épidémiologie et Information en Néphrologie. Rapport annuel REIN 2017. <https://www.agence-biomedecine.fr/IMG/pdf/rapportrein2017.pdf>. Accessed April, 2019.
55. Grams ME, Chen BP-H, Coresh J, Segev DL. Preemptive deceased donor kidney transplantation: Considerations of equity and utility. *Clin J Am Soc Nephrol*. 2013;8(4):575–582.
56. Agardh E, Allebeck P, Hallqvist J, Moradi T, Sidorchuk A. Type 2 diabetes incidence and socio-economic position: A systematic review and meta-analysis. *Int J Epidemiol*. 2011;40(3):804–818.
57. Jay CL, Dean PG, Helmick RA, Stegall MD. Reassessing preemptive kidney transplantation in the United States: Are we making progress? *Transplantation*. 2016;100(5):1120–1127.
58. Cannon MJ, Schmid DS, Hyde TB. Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. *Rev Med Virol*. 2010;20(4):202–213.
59. Axelrod DA, Dzebisashvili N, Schnitzler MA, et al. The interplay of socioeconomic status, distance to center, and interdonor service area travel on kidney transplant access and outcomes. *Clin J Am Soc Nephrol*. 2010;5(12):2276–2288.
60. Heemann U, Oberbauer R, Sprangers B, Gökalp C, Bemelman F. Deceased donor kidney allocation schemes and international exchange. *Curr Opin Organ Transplant*. 2020;25(1):66–73.

61. Lim WH, Chapman JR, Wong G. Peak panel reactive antibody, cancer, graft, and patient outcomes in kidney transplant recipients. *Transplantation*. 2015;99(5):1043–1050.
62. Laging M, Kal-van Gestel JA, van de Wetering J, Ijzermans JNM, Weimar W, Roodnat JJ. Understanding the influence of ethnicity and socioeconomic factors on graft and patient survival after kidney transplantation. *Transplantation*. 2014;98(9):974–978.