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**Access to the waiting list and to kidney transplantation for people living with HIV: a
national registry study**

Short title: “Access to kidney transplantation for people living with HIV”

Jérôme Tourret^{1*}, Marguerite Guiguet², Mathilde Lassalle³, Sophie Grabar⁴, Laurence Lièvre²,
Corinne Isnard-Bagnis⁵, Benoit Barrou⁵, Dominique Costagliola², Cécile Couchoud⁶, Sophie
Abgrall⁷ and Sophie Tézenas Du Montcel⁸

¹Sorbonne Université, INSERM UMR1138, Assistance Publique – Hôpitaux de Paris AP-HP, Hôpitaux Universitaires Pitié Salpêtrière - Charles Foix, Département d’urologie, néphrologie et transplantation, Paris, France.

²Sorbonne Université, INSERM, Institut Pierre Louis d’épidémiologie et de Santé Publique, IPLESP UMR-S1136, Paris, France

³REIN registry, Agence de la biomédecine, Saint Denis La Plaine, France.

⁴Université Paris Descartes, Sorbonne Paris Cité, INSERM, Institut Pierre Louis d’épidémiologie et de Santé Publique, IPLESP UMR-S1136, Assistance Publique – Hôpitaux de Paris AP-HP, Hôpitaux Universitaires Cochin Broca Hôtel-Dieu, Unité de Biostatistique et d’épidémiologie Paris, FR 75005

⁵Sorbonne Université, Assistance Publique – Hôpitaux de Paris AP-HP, Hôpitaux Universitaires Pitié Salpêtrière - Charles Foix, Département d’urologie, néphrologie et transplantation, Paris, France

⁶REIN registry, Agence de la biomédecine, Saint Denis La Plaine, Université Claude Bernard Lyon I, UMR CNRS 5558, Laboratoire de Biostatistique en Santé, France.

⁷Université Paris-Saclay, Univ. Paris Sud, INSERM, Institut Pierre Louis d'épidémiologie et de Santé Publique, IPLESP UMR-S1136, Paris, UVSQ, CESP INSERM U1018, Le Kremlin-Bicêtre, Assistance Publique – Hôpitaux de Paris AP-HP, Hôpital Antoine Bécère, Service de Médecine interne, Clamart, France.

⁸Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique IPLESP, Assistance Publique – Hôpitaux de Paris AP-HP, Hôpitaux Universitaires Pitié Salpêtrière - Charles Foix, Paris, France

*Corresponding author:

Département d'urologie, néphrologie et transplantation, Hôpital Pitié Salpêtrière, 83 Bd de l'Hôpital, 75013 PARIS

Phone: +33 1 42 17 71 79

Fax: +33 1 42 17 72 92

Email: jerome.tourret@aphp.fr

ORCID number: 0000-0003-2998-6531

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ABSTRACT

We compared access to a kidney transplantation (KT) waiting list (WL) and to KT between people living with HIV (PLHIV) and HIV-uninfected controls. Using the REIN (the national Renal Epidemiology and Information Network registry), we included all PLHIV initiating dialysis in France throughout 2006-2010 and HIV-uninfected controls matched for age, sex, year of dialysis initiation, and the existence of a diabetic nephropathy. Patients were prospectively followed until December 2015. We used a competitive risk approach to assess the cumulative incidence of enrollment on WL and of KT, with death as a competing event (sub-distribution hazard ratio adjusted on comorbidities, asdHR). There were 255 PLHIV in the REIN (median age 47 years) of whom 180 (71%) were also found in the French Hospital Database on HIV (FHDH-ANRS CO4) including 126 (70%) known to be on antiretroviral therapy with HIV viral suppression (VS). Five years after dialysis initiation, 65%, and 76%, of treated PLHIV with VS, and of HIV-uninfected controls were enrolled on a WL (asdHR 0.68; 95% CI 0.50-0.91). Access to KT was also less frequent and delayed for treated PLHIV with VS (asdHR 0.75, 95% CI, 0.52-1.10). PLHIV continue to face difficulties to access KT.

Key words (5 max): End-Stage Renal Disease, kidney transplantation, renal replacement therapy, waiting list, HIV infection

List of abbreviations:

AIDS: Acquired Immune Deficiency Virus

ART: Antiretroviral Treatment

(a)sdHR: (adjusted) sub-distribution Hazard Ratio

CKD: Chronic Kidney Disease

ESRD: End-Stage Renal Disease

FHDH ANRS-CO4: French Hospital Database on HIV

HCV: Hepatitis C Virus

HIV: Human Immunodeficiency Virus

IQR: Interquartile Range

KT: Kidney Transplantation

PLHIV: People Living with HIV

REIN: Renal Epidemiology and Information Network

VL: HIV Viral Load

VS: HIV viral suppression

WL: Waiting List

1 INTRODUCTION

The prevalence of chronic kidney disease (CKD, defined by an estimated glomerular filtration rate <60 ml/min/1.73 m²) among people living with HIV (PLHIV) in Europe is about 4% (1). The incidence of end-stage renal disease (ESRD) is 6.7/10,000 person.years (2, 3). This is five times higher than what is estimated for the general population (4). Despite a stable incidence of ESRD in PLHIV for several years, its prevalence increases because patients live longer with effective antiretroviral therapy (ART) (5).

Kidney transplantation (KT) in selected PLHIV confers a significant survival benefit compared to those remaining on dialysis (6). While the survival of transplanted PLHIV appears to be comparable to that of recipients without HIV-infection of the same age in Europe and the US, the survival of their kidney transplant is lower, close to that of old (>65 years) HIV-uninfected recipients (7-19). At the time of this finding, this poor renal outcome was possibly, in part, due to a higher rate of acute rejection of PLHIV because of insufficient induction therapy (7, 8). Indeed, the importance of T-cell depleting induction in PLHIV has only recently been established (8, 20).

However, although KT should be the standard of care for eligible PLHIV (18, 21), nephrologists might still be reluctant to offer this therapeutic option, for fear of a higher risk of general or surgical site infection (9, 22, 23) due to profound immunosuppression. The possible interactions between antiretroviral and immunosuppressive drugs requiring complex drug monitoring (24, 25) might also be a disincentive. These considerations may explain the lower access to KT recently documented among HIV-infected waitlist candidates in the US (26).

Using the French national renal replacement therapy registry, and in a context of universal and free access to ART, we compared the access to the KT waiting list of PLHIV and

matched HIV-uninfected patients who initiated dialysis between 2006 and 2010 and who were followed until December 2015. Then, we compared the access to KT of the waitlist candidates.

2 MATERIAL AND METHODS

2.1 Study design

The Renal Epidemiology and Information Network (REIN) is the national registry of all patients who initiate renal replacement therapy in France (27). It includes all national private and public dialysis and transplant centers. Clinical, demographic and biological data are collected at renal replacement therapy initiation, followed by annual updates. Events such as death, enrollment on a waiting list, and kidney transplantation (from live and deceased donors) are systematically reported. From the REIN dataset we selected all adult (≥ 18 years) PLHIV who initiated dialysis in France between January 1, 2006 and December 31, 2010. Patients with a pre-emptive KT (*i.e.* who received a KT as their initial renal replacement therapy, without dialysis before KT), with a history of a previous KT, and those who needed a combined solid organ transplantation were not eligible. Patients with ongoing cancer were excluded. For each HIV-infected individual, two (whenever possible; if not, one) HIV-uninfected controls were randomly selected from the REIN among patients with the same age (± 3 years), sex, year of dialysis initiation, existence of a diabetic nephropathy, and when possible the continent of birth. A 1:2 (patient:control) ratio was chosen, as this was the highest number of controls we were able to select; we were able to find two HIV-uninfected counterparts with these criteria for almost all PLHIV, but rarely three. HIV infection status was recorded in the REIN but not HIV-specific data, *i.e.* antiretroviral treatment, HIV plasma viral load, and CD4⁺ cell count. For that purpose, we used data recorded in the French Hospital Database on HIV (FHDH ANRS-CO4), a national cohort covering about half of the PLHIV in care in France (28). The FHDH ANRS-CO4 uses a unique encrypted identifier that is generated by an algorithm based on the first name, the last name, and the date of birth.

Authorized personnel at the REIN used these data and the algorithm to generate the potential identifiers in the FHDH ANRS-CO4 of all selected PLHIV of the REIN. The FHDH ANRS-CO4 was then anonymously screened to look for the existing identifiers. The authors of this work never had access to identifying data. All patients were prospectively followed until December 31, 2015. Data collected for the REIN in 2015 were consolidated in 2016 and became available in 2017.

2.2 Institutional Review Board

Patients were informed that their clinical and biological data are systematically and anonymously included in the National REIN registry, unless they express personal opposition. Patients provided written consent to be included in the FHDH ANRS-CO4. The REIN, the FHDH ANRS-CO4 and the present work's protocols were all approved by the French Ethics Committee on the Treatment of Computerized Data in the Field of Medical Research, under the auspices of the French Ministry of Research.

2.3 Statistical analysis

Descriptive statistics are shown as median and interquartile ranges (IQR), or numbers and percentages. Comparisons were made by the Kruskal-Wallis test for continuous variables and the χ^2 test (or the Fisher exact test when numbers were small) for categorical variables.

A competing-risk approach was used to assess the cumulative incidence of enrollment on a waiting list after dialysis initiation, with pre-listing death considered as a competing risk for being listed. Subsequently, for patients enrolled on a WL (*i.e.*, KT candidates), the same competing-risk approach was used to assess the cumulative incidence of KT, with post-listing death as a competing risk for transplantation. Multivariable competing-risk regression models, yielding sub-distribution hazard ratios (sdHR), were used to estimate the effect of HIV infection on the access to the waiting list or on the access to KT after adjustment for variables

listed in Table 3. When studying the access to KT, we performed analyses both with and without adjustment on the inactivity while on the waiting list.

To investigate a possible change of care of PLHIV over time, an interaction term between the HIV infection status and the period of dialysis initiation was tested.

Analyses were performed on the total population of PLHIV identified in the REIN, and on the subset of PLHIV found in the FHDH-ANRS C04 known to be on ART with HIV viral suppression (VS) and their HIV-uninfected controls. Sensitivity analyses were performed after exclusion of patients with chronic hepatitis C virus (HCV) infection.

All statistical analyses were performed with SAS v9.4 software (SAS Institute Inc.).

2.4 Data availability

The data that support the findings of this study were obtained from the Agence de la Biomédecine (Saint Denis, France) (29) and from France Recherche Nord&Sud Sida-HIV Hépatites (ANRS, Paris, France) (30). Restrictions apply to the availability of these data, which were used under license for this study. Data are available with the permission of the Agence de la Biomédecine and the ANRS.

3 RESULTS

3.1 Patients characteristics

Two hundred and seventy people living with HIV (PLHIV) initiated dialysis in France between January 1, 2006 and December 31, 2010 (Figure 1). After exclusion of patients with cancer (n=15), 255 PLHIV (and 476 HIV-uninfected counterparts) were identified in the REIN registry of whom 180 (71%) were also found in the FHDH ANRS-CO4 cohort. All, but 4 (2%) with missing data, were treated with antiretroviral therapy (ART) (median duration 7.2 years), and 126 were known to have HIV viral suppression at dialysis initiation (31 missing data and 19 with HIV viral load >500 copies/ml) with median CD4⁺ 348/mm³ (IQR, 29-496).

These 126 PLHIV known to be on ART with VS and their HIV-uninfected controls (n=234) were followed after dialysis initiation for a median of 6.1 (IQR, 4.7-7.4) years, and 6.6 (IQR, 5.2-8.0) years, respectively. Their characteristics at dialysis initiation are listed in Table 1. The median age was 47 (IQR, 41-57) years and 64% were males. Compared to HIV-uninfected controls, PLHIV were more often treated in the Paris area (75% vs. 31%, $p<0.0001$), more often treated with hemodialysis (93% vs. 87%, $p=0.08$), less frequently affected by hypertension (63% vs. 81%, $p=0.003$), more frequently co-infected with HCV (21% vs. 3%, $p<0.0001$), and more frequently undernourished (27% vs. 15%, $p=0.009$).

3.2 Access to the waiting list

During follow-up, among the 126 PLHIV known to be on ART with VS, 85 were enrolled on a WL and 17 died before being listed (Figure 1). In comparison, among the 234 matched HIV-uninfected controls, 181 were enrolled on a WL and 20 patients died before they were listed. Figure 2 shows the cumulative probability of being enrolled on a KT waiting list (in Figure 2A for PLHIV, and in Figure 2B for HIV-uninfected controls) with death considered as a competing event. Preemptive enrollment on a waiting list, *i.e.* the percentage of patients already enrolled when starting dialysis out of the number of included patients, was lower for PLHIV than for HIV-uninfected controls (3% and 14.5% respectively, $p=0.005$). Five years after dialysis initiation, 65% of PLHIV had been enrolled on a waiting list and 12% had died, while 76% of HIV-uninfected controls had been enrolled and 8% had died. Overall, enrollment on a waiting list was less frequent and delayed for PLHIV compared to HIV-uninfected controls (crude sdHR; 0.72, 95% CI 0.56-0.93; adjusted sdHR 0.68, 95% CI 0.50-0.91; Figure 3 and Supplementary Table S1). The result was similar in the analysis including only patients without chronic HCV infection (asdHR 0.71, 95% CI, 0.52-0.96).

The discrepancy between PLHIV and HIV-uninfected controls was highlighted when all 255 PLHIV (including those with missing HIV-specific data) identified in REIN and their 476

controls (Supplementary Table 2) were included (sdHR 0.52, 95% CI 0.42-0.65 Figure 3). In addition in this larger population, PLHIV were twice more likely to die without being enrolled on a waiting list (adjusted sdHR 2.00, 95% CI 1.37-2.93; $p=0.0004$) than HIV-uninfected controls. There was a trend towards a reduction of the gap between PLHIV and HIV-uninfected controls for access to the waiting list over time. PLHIV initiating dialysis in 2006-2008 were half as likely to be listed as HIV-uninfected controls (adjusted sdHR 0.45, 95% CI 0.35-0.57; $p<0.0001$). For patients initiating dialysis in 2009-2010 this discrepancy persisted but was reduced (adjusted sdHR 0.66, 95% CI 0.46-0.93; $p=0.02$. The interaction test between the HIV status and period of dialysis initiation yielded a $p=0.07$).

3.3 Access to kidney transplantation

To analyze the access to KT, we restricted our analysis to KT transplantation candidates, *i.e.* to patients enrolled on a KT waiting list. This represented 85 PLHIV known to be on ART with VS and 181 HIV-uninfected controls. Their characteristics are listed in Table 2. The median age was 46 years for both groups. HIV-seropositive candidates had a longer duration of dialysis at enrollment and were more frequently treated in the Paris area than HIV-uninfected candidates. The incompatible transplant rate is the percentage of kidneys retrieved in France during the previous 5 years against which a given potential recipient harbors at least one significant anti-HLA donor-specific antibody. This is the French equivalent of the American calculated panel reactive antibody score (31), and it is the measure that is used in France of the immunological difficulty of access to KT for a given candidate. Indeed, as the French allocation system only authorizes compatible kidney transplantations, the higher the incompatible transplant rate, the lower the probability that a compatible kidney will be retrieved, and consequently, the longer the average waiting time on the list. The median incompatible transplant rate was higher for PLHIV, suggesting a greater difficulty to find a

compatible kidney transplant for these potential recipients: only 51% of wait-listed PLHIV had an incompatible transplant rate of 0%, compared to 71% of HIV-uninfected controls ($p=0.005$). Finally, PLHIV were also less frequently active on the waiting list (*i.e.*, they were more often declared as having a temporary contra-indication for a KT while on the waiting list): only 19% of them were always active while waiting compared to 53% of HIV-uninfected controls ($p<0.0001$).

Five years after enrollment, the probabilities of KT were 67%, and 84%, among PLHIV, and HIV-uninfected controls, respectively. (Figure 4). In multivariable analyses, access to KT seemed to be less frequent and delayed for PLHIV compared to HIV-uninfected controls (Adjusted sdHR 0.75, 95% CI 0.52-1.10; $p=0.14$; Figure 3 and Supplementary Table S3). When the analyses were performed on the subgroup of patients without chronic HCV infection, the access to KT remained compromised for PLHIV compared to HIV-uninfected individuals (sdHR 0.75, 95% CI, 0.51-1.10, $p=0.14$)

Because being undetectable on ART is a prerequisite to be enrolled on a waiting list for solid organ transplantation in Europe (32), we performed the same analysis including also PLHIV candidates with missing HIV-specific data ($n=149$) and their HIV-uninfected counterparts ($n=348$), whose characteristics are shown on Supplementary Table 4. In this larger population, access to KT was less frequent and delayed for PLHIV compared to HIV-uninfected controls (adjusted sdHR 0.70, 95%CI 0.53-0.92; $p=0.01$). Adjustment on transient inactivity on the waiting list slightly decreased the impact of HIV infection on the access to KT (adjusted sdHR=0.77, 95% CI [0.57 to 1.02, $p=0.07$).

4 DISCUSSION

Our study concludes that, in the era of widespread ART, consisting of well-tolerated regimens and in the context of free universal access to health care in France, the enrollment on a kidney

transplantation waiting list was lower for PLHIV compared to matched HIV-uninfected controls. Subsequently, for PLHIV who did pass the first bottleneck of waiting list enrollment, we showed that a second selection step further restrained their access to kidney transplantation.

One strength of this study is that thanks to the availability of a mandatory national registry of all patients who initiate dialysis in France, the included population is nationally comprehensive for mainland France, and there was no loss to follow up. This is the first report from a European country and the first report from a country where KT and HIV care are both free and accessible to all residents. Our work is also the first to compare PLHIV with HIV-uninfected controls matched for age, sex, year of dialysis initiation, and the existence of a diabetic nephropathy. PLHIV who initiated dialysis in 2006-2010 were young patients with a mean age of 47 years, strikingly younger than the national mean age of 66 years at dialysis initiation in 2008. Therefore, the comparison with HIV-seronegative controls selected for their similar distribution of age increased the power of statistical analyses to study the effect of HIV infection irrespective of age. This allowed us to evidence the specific role of the HIV infection in the access to KT more clearly than ever before. Sawinski *et al.* showed that only 20% of the PLHIV referred to their institution between 2000 and 2007 for KT evaluation were finally enrolled compared to 73% of the patients without HIV infection ($p < 10^{-5}$) (33) evidencing the difficulties PLHIV face in accessing the waiting list. Another study has compared PLHIV and HIV-uninfected patients' access to KT using a national registry of transplanted patients (26) That study focused on the second part of the selective process, *i.e.* access to KT transplantation of listed candidates. As REIN registry included all people with ESDR prospectively, we were able to address the access to KT from the beginning of the selective process (dialysis initiation) onwards. Importantly, we show that the access of KT candidates to KT described by Locke *et al.* does not account for all the hurdle for PLVIH to

be transplanted. As we demonstrate here, some of the difficulty lies prior to this step, in the enrollment on a WL.

We did not identify clear justifications for the difficulties faced by PLHIV to access the waiting list and KT. PLHIV and controls showed relatively similar comorbidities. One of the main differences was HCV coinfection, which was more frequent among PLHIV. Previous studies showed that active drug use, psychosocial difficulties, and medical insurance issues act as barriers to waiting list enrollment of PLHIV (33, 34), and HCV coinfection could be considered as a proxy for these characteristics. However, when the analyses were performed on the subgroup of patients without HCV, both the access to the waiting list and to KT remained severely compromised for PLHIV compared to HIV-uninfected individuals. Importantly, the availability of direct acting anti-HCV treatments for dialyzed patients was reported too late to have had any significant impact on our work (35). The other relevant difference between PLHIV and controls was undernutrition, which was more frequent among PLHIV. This could be considered as a marker for a more severe immune condition. However, the impaired access of PLHIV to the waiting list persisted in the analyses restricted to PLHIV known to be treated with ART with HIV viral suppression.

Interestingly, our study showed a trend of improvement of access by PLHIV to the WL over time, as patients who initiated dialysis in 2008-2010 were more likely to be enrolled than patients who started in 2006-2008. Of note, this trend overlapped with the introduction of raltegravir in France (December 20, 2007) and the first report of its successful use in KT PLHIV (36). It is possible that the availability of a new class of antiretrovirals devoid of drug-drug interaction with immunosuppressive drugs (36, 37), as shown in the recent ANRS 153 TREVE trial (38) has led to a more frequent referral of PLHIV to kidney transplant centers. It is also possible that other factors played a role, such as an increased awareness of the generally good prognosis of KT in PLHIV, and the publication of the Infection Diseases

Society of America on the management of CKD in PLHIV in 2005, in which KT is explicitly cited has a valid option (39).

Once on the waiting list, PLHIV had a lower likelihood to be transplanted. The same disparity was reported in the US over the same period with a predominant decrease of living donor KT for PLHIV (26). A very low prevalence of live donation was observed in our study, with 5 PLHIV and 21 HIV-uninfected controls who benefited from a KT from a live donation (5% and 7% of transplanted patients, respectively) preventing any further exploration. Of note, living donor KT is much less frequent in France (11%) (40) than in the US (33%) (41).

In our study, two transplantation-related parameters—the incompatible transplant rate and the inactivity on the waiting list—were markedly different between PLHIV and HIV-uninfected KT candidates as also noted by Locke *et al.* (26). The higher incompatible transplant rate observed in PLHIV candidates could indicate a higher anti-HLA immunization. Unfortunately, the two causes of immunization of candidates for a first kidney transplantation (history of blood transfusions and pregnancies) could not reliably be tracked in the REIN. PLHIV might have required more frequent blood transfusions because of a higher risk of anemia in case of AIDS or HCV co-infection (42). In our cohort, hemoglobin was slightly lower in PLHIV than in HIV-uninfected controls at dialysis initiation. The mode of HIV acquisition is not recorded in the REIN, but it is possible that the PLHIV cohort included a larger proportion of former intravenous drug users (active drug use is a contraindication to WL enrollment). These patients have a higher risk of developing anti-HLA antibodies through their exposition to allogeneic blood. Alternatively, false positive anti-HLA antibodies might have been detected more frequently in PLHIV than in HIV-uninfected controls given that polyclonal gammopathy is frequent among PLHIV (43). The difference in access to KT of PLHIV candidates remained significant despite adjustment for the incompatible transplant rate.

The second factor that differed between KT candidates was the higher proportion of episodes of inactivity on the WL among PLHIV than among controls. The negative impact of HIV infection on the probability of KT was attenuated after adjustment on inactivity on the waiting list. Inactivity is decided by the sole nephrologist in charge of the transplant candidate and is therefore highly subjective; it does not rely on a pre-specified algorithm. The justifications of the inactivity periods could unfortunately not be reliably exploited in the REIN, but one possibility is the higher occurrence of episodes with infectious complications among PLHIV. However, only patients with a durably medically controlled HIV infection are usually considered for KT and enrolled on a waiting list. The role of possible refusal bias of kidney offers for active PLHIV candidates on the waiting list compared to controls that has recently been reported (44) could not be excluded in France as well.

One limitation of our study was missing HIV-related data. Some PLHIV from the REIN could not be retrieved from the FHDH-ANRS CO4 database. There are several possible explanations. First, although FHDH-ANRS CO4 covers about half of the PLHIV in care in France, not all the French hospitals participate in the FHDH-ANRS CO4 cohort. Second, data matching between REIN and FHDH-ANRS CO4 relied on the unique encrypted identifier generated by an algorithm based on the first name, the last name, and birth date. Any misspelling could have prevented matching.

CONCLUSION

Despite free access to healthcare for all PLHIV and dialysis patients in France, their access to a waiting list and, subsequently, to kidney transplantation is reduced. We were not able to ascertain the underlying reasons, which might include specific psychosocial factors for PLHIV, a worse general health or cardiovascular condition due to the association of the HIV

infection and the ESRD, and possibly a persisting reluctance of healthcare providers in the fear of a more complicated follow-up, with an uncertain outcome. HIV patient practitioners and nephrologists need to be informed about the benefits of KT over dialysis for PLHIV, and about the availability of ART that is devoid of drug-drug interactions with immunosuppressive medications. Future observations are needed to ensure that the improving trend towards decreasing disparities continues.

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DISCLOSURE

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Table 1: Characteristics of PLHIV known to be on ART with HIV viral suppression and their HIV-uninfected controls at dialysis initiation (2006-2010) in France.

	PLHIV on ART with viral suppression ^a , n=126	HIV-uninfected controls ^a , n=234	p-value
Sociodemographic data			
Age*, years			0.88
<40	27 (21.4)	53 (22.6)	
40-49	45 (35.7)	87 (37.2)	
50+	54 (42.9)	94 (40.2)	
Men*	81 (64.3)	147 (62.8)	0.78
Region of birth: Sub-Saharan Africa*	26 (20.6)	37 (15.8)	0.25
Period of dialysis initiation*			0.74
2006-2008	71 (56.4)	137 (58.6)	
2009-2010	55 (43.6)	97 (41.4)	
Initial nephropathy			0.06

Diabetic nephropathy*	10 (7.9)	20 (8.6)	
Vascular nephropathy	12 (9.5)	35 (15.0)	
Chronic glomerulonephritis	38 (30.2)	63 (26.9)	
Polycystic Kidney Disease	3 (2.4)	22 (9.4)	
Other	47 (37.3)	64 (27.3)	
Unknown	16 (12.7)	30 (12.8)	
Initial dialysis modality			0.08
Hemodialysis	117 (92.9)	203 (86.7)	
Peritoneal dialysis	9 (7.1)	31 (13.2)	
Dialysis in Paris area	94 (74.6)	72 (30.8)	<0.0001
Associated medical conditions			
Diabetes mellitus	25 (19.8)	39 (16.7)	0.47
Hypertension	77 (62.6)	186 (80.9)	0.003
Chronic hepatitis C ^b	26 (21.1)	6 (2.6)	<0.0001
Undernutrition ^c	32 (26.9)	33 (14.8)	0.009
Cirrhosis of any origin	8 (6.5)	8 (3.5)	0.28

Congestive heart failure	17 (13.8)	25 (10.9)	0.49
Coronary heart disease ^d	6 (4.9)	25 (10.9)	0.07
Vascular disease ^e	13 (10.6)	28 (12.2)	0.73
Chronic respiratory failure	5 (4.1)	12 (5.2)	0.80
Number of severe conditions ^f			0.14
0	86 (70.5)	165 (72.4)	
1	28 (22.9)	37 (16.2)	
2+	8 (8.6)	26 (11.4)	
Biological parameters			
Hemoglobin (g/dL)	11.1 (10.2-12.1)	11.4 (10.3-12.3)	0.36

Data are median [IQR] or n (%)

BMI: Body Mass Index; alb.: albuminemia

* Characteristics used for matching: PLHIV and HIV-uninfected controls were matched on age (\pm 3 years), sex, region of birth, year of dialysis initiation, and the presence of a diabetic nephropathy.

a: Missing data: hypertension (n=7), diabetes mellitus (n=1), chronic hepatitis C (n=7), nutritional status (n=18), cirrhosis of any origin (n=8), chronic cardiac failure (n=9), coronary heart disease (n=8), vascular disease (n=8), chronic respiratory failure (n=9), number of severe conditions (n=10).

b: defined as at least one detectable HCV RNA by qPCR.

c: Defined as a BMI < 18.5 kg/m² or albuminemia < 27 g/l

d: defined as an history of cardiac infarction or angina.

e: defined as an history of stroke, transient ischemic attack, or peripheral artery disease

f: Add one for each of the following: cirrhosis of any origin, congestive heart failure, coronary heart disease, vascular disease, and chronic respiratory failure.

Table 2: Characteristics of transplant candidates living with HIV known to be on ART with HIV viral suppression and of HIV-uninfected transplant candidates (*i.e.* enrolled on a waiting list), who initiated dialysis between 2006 and 2010 in France.

	PLHIV on ART with viral suppression ^a , n=85	HIV-uninfected controls ^a , n=181	p-value
Sociodemographic data			
Age at dialysis initiation, years			0.97
<40	23 (27.1)	50 (27.6)	
40-49	33 (38.8)	72 (39.8)	
50+	29 (34.1)	59 (32.6)	
Men	48 (56.5)	109 (60.2)	0.59
Region of birth: Sub-Saharan Africa	22 (25.9)	32 (17.7)	0.14
Period of dialysis initiation			0.68
2006-2008	50 (58.8)	112 (61.9)	
2009-2010	35 (41.2)	69 (38.1)	
Initial nephropathy			0.01
Diabetic nephropathy	6 (7.1)	5 (2.8)	

High blood pressure	7 (8.2)	27 (14.9)	
Chronic glomerulonephritis	29 (34.1)	57 (31.5)	
Polycystic kidney disease	1 (1.2)	21 (11.6)	
Other	31 (36.5)	49 (27.1)	
Unknown	11 (12.9)	22 (12.1)	
Initial dialysis modality			0.08
Hemodialysis	79 (92.9)	154 (85.1)	
Peritoneal dialysis	6 (7.1)	27 (14.9)	
Dialysis in Paris area	66 (77.6)	63 (34.8)	<0.0001
Period of waiting list enrollment			0.13
2006-2010	59 (69.4)	142 (78.4)	
2011-2015	26 (30.6)	39 (21.6)	
Duration of dialysis at listing (years)			0.02
<1	40 (47.1)	118 (65.2)	
1 to <2	19 (22.4)	36 (19.9)	
2 to <3	11 (12.9)	12 (6.6)	

3+	15 (17.6)	15 (8.3)	
Associated medical conditions at dialysis initiation			
Diabetes mellitus	13 (15.3)	16 (8.9)	0.14
Hypertension	52 (62.7)	145 (81.9)	0.001
Chronic hepatitis C ^b	11 (13.2)	5 (2.8)	0.004
Undernutrition ^c	18 (21.9)	21 (12.3)	0.06
Cirrhosis of any origin	1 (1.2)	1 (0.6)	0.54
Congestive heart failure	9 (10.8)	12 (6.9)	0.33
Coronary heart disease ^d	1 (1.2)	13 (7.4)	0.04
Vascular disease ^e	9 (10.8)	12 (6.8)	0.33
Chronic respiratory failure	3 (3.6)	4 (2.3)	0.68
Number of severe conditions ^f			0.64
0	65 (78.3)	143 (81.7)	
1	14 (16.9)	22 (12.6)	
≥2	4 (4.8)	10 (5.7)	

Transplantation-related**parameters**

Blood Group: A	34 (40.0)	58 (32.0)	0.22
Incompatible transplant rate ^g			0.005
0%	40 (50.6)	123 (70.7)	
1%-85%	28 (35.4)	41 (23.6)	
>85%	11 (13.9)	10 (5.7)	
Status on waiting list : always active	16 (18.8)	97 (53.4)	<0.0001

Data are median [IQR] or n (%)

BMI: Body Mass Index.

a: Missing data: chronic hepatitis C (n=6), hypertension (n=6), diabetes mellitus (n=1), nutritional status (n=13), cirrhosis of any origin (n=7), chronic cardiac failure (n=8), coronary heart disease (n=7), vascular disease (n=7), chronic respiratory failure (n=7), number of severe conditions (n=8), incompatible transplant rate (n=13).

b: defined as at least one detectable HCV RNA by qPCR.

c: Defined as a BMI<18.5 kg/m² or albuminemia< 27 g/l

d: defined as any of history of cardiac infarction or of angina

e: defined as an history of stroke, transient ischemic attack, or peripheral artery disease

f: Sum of following: cirrhosis of any origin, congestive heart failure, coronary heart disease, vascular disease, and chronic respiratory failure,

g: the incompatible transplant rate is the percentage of kidneys retrieved in France in the previous 5 years against which a given potential recipient has at least one significant anti-HLA donor-specific antibody.

Table 3: variables used for adjustment of the multivariable competing-risk regression models.

Multivariable competing-risk regression models, yielding sub-distribution hazard ratios (sdHR), were used to estimate the effect of HIV infection on the access to the waiting list or on the access to kidney transplantation after adjustment for variables listed in this table.

Variable	Definition
Adjustment for the access to a waiting list	
Age	
Sex	
Continent of birth	Sub-Saharan Africa vs. other
Period of dialysis initiation	2006-2008 vs. 2009-2010
Initial dialysis modality	Peritoneal dialysis vs. hemodialysis
Dialysis localization	Paris region vs. other
Diabetes mellitus	As defined by the American Diabetes Association (46)
High blood pressure	Arterial blood pressure > 140/90 mmHg on two measurements
Chronic hepatitis C	Positive HCV viral load
Undernutrition	Body mass index < 18.5 kg/m ² or serum albumin < 27 g/L

Number of severe conditions among the following:

Cirrhosis	Clinically, biologically or histologically defined by the clinician
Chronic cardiac failure	Left ventricular ejection fraction < 50 % or defined by a cardiologist
Coronary heart disease	History of angina or of myocardial infarction
Vascular disease	Obliterative arterial disease of the lower limbs or history of stroke
Chronic respiratory failure	Arterial partial pressure of oxygen <70 mmHg

Adjustment for the access to kidney transplantation

All of the above except the period of dialysis initiation	
Period of enrollment	2006-2010 vs 2011-2015
Dialysis duration at enrollment on a waiting list	
Blood group	A vs. others
Incompatible transplant rate	0% vs. >0%
Inactivity on the waiting list	Categorical variable at least one period of inactivity vs. or none

All comorbidities were declared by the clinicians in charge of the patients of the REIN

FIGURE LEGENDS

Figure 1: Flowchart of included patients.

Flowchart representation of the access to the waiting list and to kidney transplantation of people living with HIV (A) and HIV-uninfected controls (B) over the follow-up period (2006-2015).

Figure 2: Cumulative incidence of enrollment on a waiting list.

Stacked probability curves of the competing events “enrollment on a waiting list” or “death” over time since the initiation of dialysis, for 126 people living with HIV on ART with viral suppression (A) or 234 HIV-uninfected controls (B)

Figure 3: Impact of HIV infection on the access to a waiting list and to a kidney transplantation among waitlist candidates.

Crude (diamond) and adjusted (square) represent subdistribution hazard ratios (sdHR)

LCL, UCL: lower, upper 95% confidence interval limits.

Figure 4: Cumulative incidence of kidney transplantation.

Stacked probability curves of the competing events “kidney transplantation” or “death” over time since the enrollment on a waiting list, for 85 people living with HIV on ART with viral suppression (A) or 181 HIV-uninfected controls (B)

Figure 1

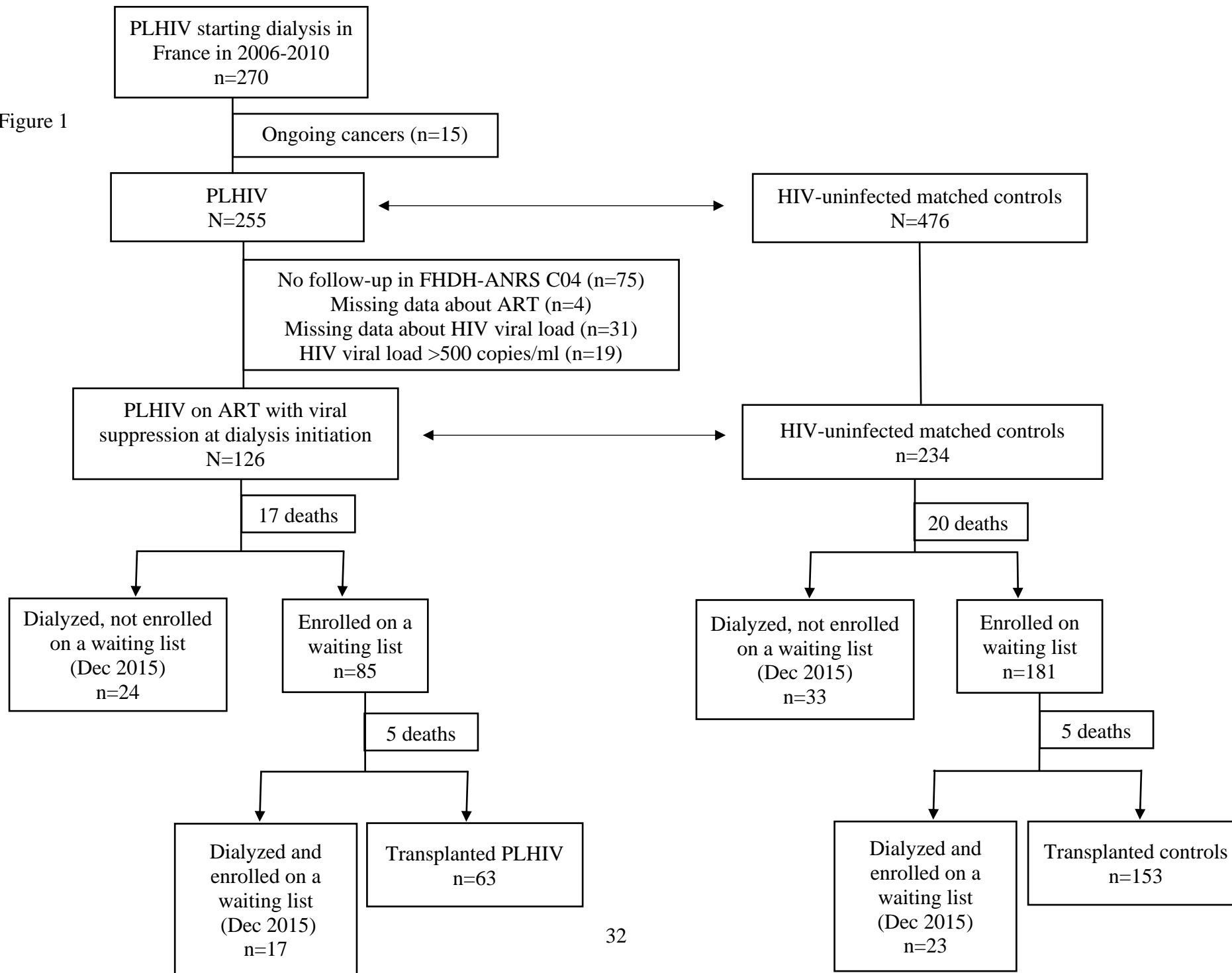
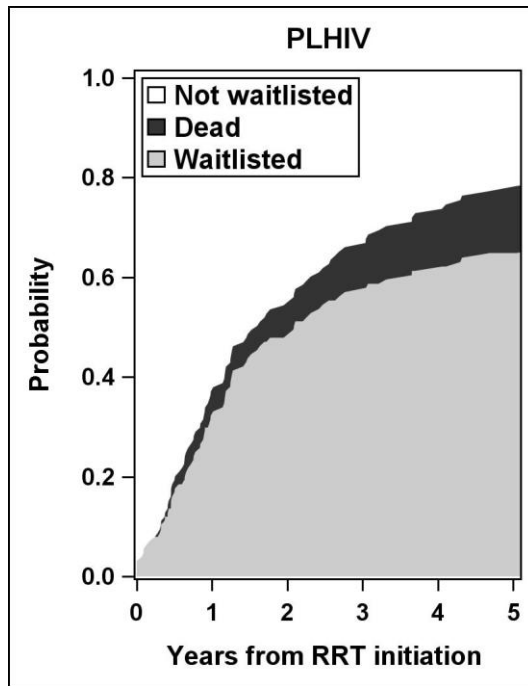


Figure 2 (A)



(B)

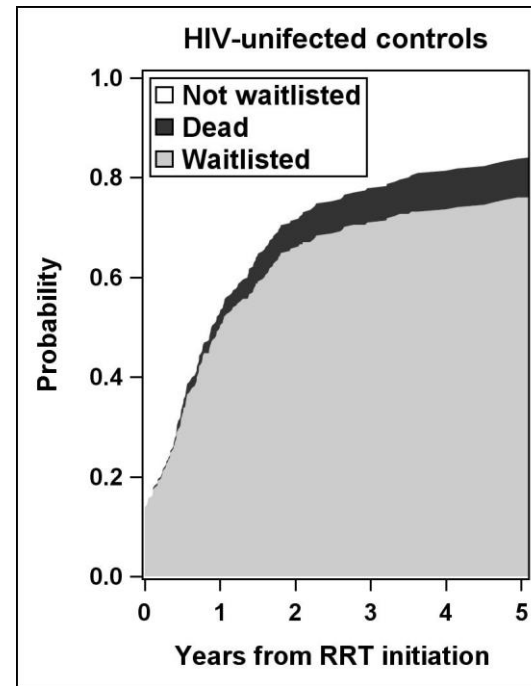


Figure 3

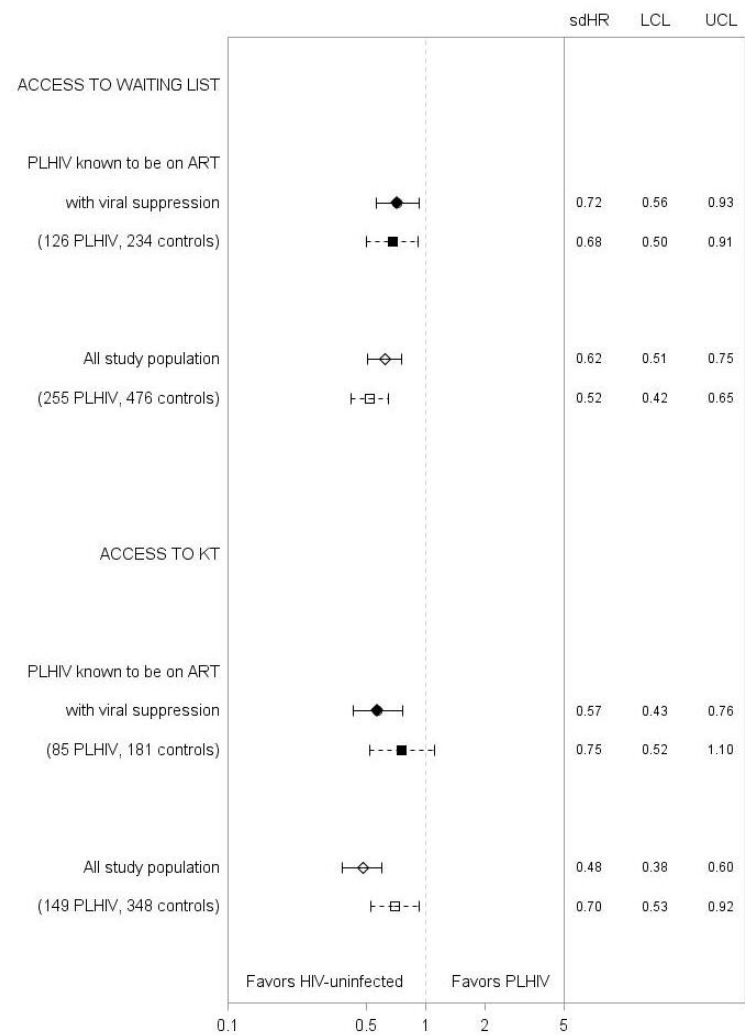
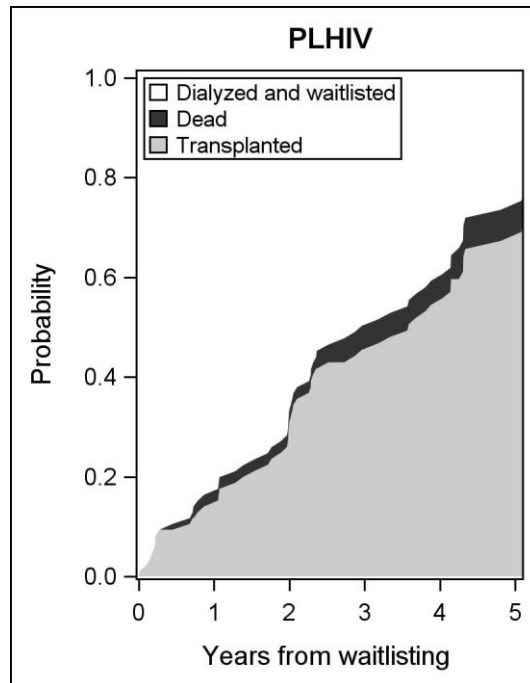
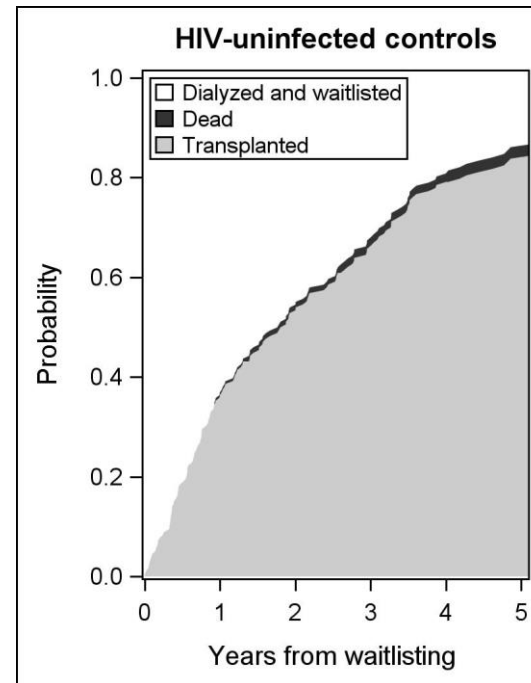


Figure 4 (A)



(B)



Supplementary Table S1: Factors associated with waiting list enrollment and prelisting mortality among 126 people living with HIV known to be on ART with viral suppression and 234 HIV-uninfected controls who initiated dialysis between 2006 and 2010 in France: multivariable competing risk regression analyses.

	Waiting list enrollment, asdHR* (95% CI)	p value	Prelisting mortality, asdHR* (95% CI)	p value
HIV infection (ref. HIV-uninfected)	0.68 (0.50-0.91)	0.01	0.96 (0.36-2.58)	0.94
Age (ref <40 years)		0.004		0.05
40-49	0.81 (0.58-1.14)		1.06 (0.28-4.05)	
50+	0.52 (0.35-0.78)		2.99 (0.77-11.59)	
Sex women (ref. men)	1.00 (0.78-1.30)	0.96	0.90 (0.41-1.97)	0.80
Region of birth (Sub-Saharan Africa vs. other)	1.17 (0.83-1.64)	0.37	0.17 (0.04-0.80)	0.02
Dialysis initiation in 2009-2010 (ref. 2006-2008)	1.02 (0.76-1.38)	0.87	0.32 (0.13-0.82)	0.02
Initial dialysis modality (PD vs. HD)	1.61 (0.98-2.64)	0.06	0.72 (0.24-2.16)	0.55
Region of care (Paris vs. other)	1.29 (0.98-1.70)	0.06	0.79 (0.32-1.98)	0.62
Hypertension (ref. no)	1.30 (0.98-1.73)	0.07	1.31 (0.50-3.44)	0.58
Diabetes mellitus (ref no)	0.57 (0.38-0.87)	0.01	1.03 (0.41-2.58)	0.94

Chronic hepatitis C (ref. no hepatitis C)	0.64 (0.39-1.04)	0.07	4.17 (1.66-10.48)	0.002
Undernutrition* (ref. no)	0.68 (0.47-0.98)	0.04	1.78 (0.72-4.42)	0.21
Number of severe conditions** (ref. none)		0.0005		0.002
1	0.59 (0.40-0.87)		2.14 (0.90-4.95)	
≥2	0.37 (0.21-0.67)		6.28 (2.29-17.23)	

asdHR: adjusted subdistribution hazard ratio. HD: hemodialysis. PD: peritoneal dialysis.

* defined as body mass index <18.5 kg/m² or albumin <27g/l).

** Add one for each of the following: cirrhosis of any origin, congestive heart failure, coronary heart disease, vascular disease, and chronic respiratory failure.

Supplementary Table 2: Characteristics of all PLHIV of REIN and of HIV-uninfected controls at dialysis initiation (2006-2010) in France.

	PLHIV in REIN ^a , n=255	HIV-uninfected controls ^a , n=476	p-value
Sociodemographic data			
Age*, years			0.80
<40	56 (22.0)	110 (23.1)	
40-49	93 (36.5)	180 (37.8)	
50+	106 (41.6)	186 (39.1)	
Men*	178 (69.8)	326 (68.5)	0.74
Region of birth: Sub-Saharan Africa*	52 (20.4)	79 (16.6)	0.23
Period of dialysis initiation*			0.75
2006-2008	149 (58.4)	284 (59.7)	
2009-2010	106 (41.6)	192 (40.3)	
Initial nephropathy			<0.0001

Diabetic nephropathy*	25 (9.8)	49 (10.3)	
Vascular nephropathy	23 (9.0)	95 (20.0)	
Chronic glomerulonephritis	78 (30.6)	106 (22.3)	
Polycystic Kidney Disease	5 (2.0)	49 (10.3)	
Other	98 (38.4)	112 (23.5)	
Unknown	26 (10.2)	65 (13.7)	
Initial dialysis modality			0.02
Hemodialysis	238 (93.3)	418 (87.8)	
Peritoneal dialysis	17 (6.7)	58 (12.2)	
Dialysis in Paris area	165 (64.7)	166 (34.9)	<0.0001
Associated medical conditions			
Diabetes mellitus	57 (22.5)	94 (19.8)	0.39
Hypertension	173 (70.0)	377 (80.0)	0.003
Chronic hepatitis C ^b	49 (19.8)	14 (3.0)	<0.0001
Undernutrition ^c	61 (25.1)	65 (14.2)	0.0006
Cirrhosis of any origin	13 (5.3)	15 (3.2)	0.22

Congestive heart failure	36 (14.6)	62 (13.2)	0.65
Coronary heart disease ^d	22 (8.9)	58 (12.3)	0.17
Vascular disease ^e	32 (13.0)	69 (14.7)	0.57
Chronic respiratory failure	14 (5.7)	26 (5.5)	1.00
Number of severe conditions ^f			0.33
0	165 (67.6)	322 (68.8)	
1	56 (23.0)	87 (18.6)	
2+	23 (9.4)	59 (12.6)	
Biological parameters			
Hemoglobin (g/dL)	11.0 (10.0-12.0)	11.3 (10.3-12.3)	0.04

Data are median [IQR] or n (%)

BMI: Body Mass Index; alb.: albuminemia

* Characteristics used for matching: PLHIV and HIV-uninfected controls were matched on age (\pm 3 years), sex, region of birth, year of dialysis initiation, and the presence of a diabetic nephropathy.

a: Missing data: hypertension (n=13), diabetes mellitus (n=3), chronic hepatitis C (n=13), nutritional status (n=32), cirrhosis of any origin (n=15), chronic cardiac failure (n=16), coronary heart disease (n=14), vascular disease (n=15), chronic respiratory failure (n=17), number of severe conditions (n=19).

b: defined as at least one detectable HCV RNA by qPCR.

c: Defined as a BMI < 18.5 kg/m² or albuminemia < 27 g/l

d: defined as an history of cardiac infarction or angina.

e: defined as an history of stroke, transient ischemic attack, or peripheral artery disease

f: Add one for each of the following: cirrhosis of any origin, congestive heart failure, coronary heart disease, vascular disease, and chronic respiratory failure.

Supplementary Table S3: Factors associated with kidney transplantation and post-listing mortality among 85 PLHIV known to be on ART with viral suppression and 181 HIV-uninfected controls who were enrolled on a waiting list between 2006 and 2015 in France: multivariable competing risk regression analyses.

	Kidney transplantation asdHR (95% CI)	p value	Post-listing mortality asdHR (95% CI)	p value
HIV infection (ref. HIV-uninfected)	0.75 (0.52-1.10)	0.14	1.49 (0.25-8.82)	0.66
Age (ref <40 years)		0.78		0.53
40-49	0.88 (0.59-1.31)		1.94 (0.31-12.02)	
50+	0.87 (0.57-1.33)		3.09 (0.43-21.98)	
Sex women (ref. men)	1.03 (0.75-1.41)	0.83	0.89 (0.27-2.95)	0.85
Region of birth (Sub-Saharan Africa vs. other)	1.04 (0.72-1.51)	0.82	1.24 (0.30-5.09)	0.77
Enrolment on waiting list in 2011-2015 (ref. 2006-2010)	0.84 (0.50-1.43)	0.53	1.26 (0.27-5.93)	0.77
Initial dialysis modality (PD vs. HD)	1.86 (1.30-2.66)	0.0007	NE	
Region of care (Paris area vs. other)	0.49 (0.35-0.69)	<0.0001	7.45 (0.57-98.08)	0.13
Hypertension (ref. no)	1.06 (0.73-1.53)	0.76	1.33 (0.33-5.39)	0.69
Diabetes mellitus (ref. no)	0.92 (0.50-1.67)	0.77	1.15 (0.09-14.96)	0.92

Chronic hepatitis C (ref. no hepatitis C)	0.60 (0.29-1.24)	0.17	2.28 (0.16-33.29)	0.55
Undernutrition * (ref. no)	1.11 (0.70-1.77)	0.66	0.75 (0.11-5.05)	0.76
Number of severe conditions ** (ref. none)		0.52		0.39
≥1	0.87 (0.58-1.32)		0.34 (0.03-4.04)	
Duration of dialysis before enrollment (per year)	1.22 (1.04-1.42)	0.01	0.83 (0.45-1.55)	0.56
Blood group (A vs. other)	1.92 (1.34-2.77)	0.0004	1.45 (0.38-5.57)	0.58
Incompatible transplant rate (ref. 0%)	0.55 (0.40-0.76)	0.0004	1.56 (0.55-4.43)	0.40

asdHR: adjusted subdistribution hazard ratio. HD: hemodialysis. PD: peritoneal dialysis.

NE : no estimate. No death on waitlist among 6 PLHIV on ART with viral suppression who initiated peritoneal dialysis.

* defined as body mass index <18.5 kg/m² or albumin <27g/l)

** Add one for each of the following: cirrhosis of any origin, congestive heart failure, coronary heart disease, vascular disease, and chronic respiratory failure.

Supplementary Table 4: Characteristics of all PLHIV and HIV-uninfected transplant candidates (*i.e.* enrolled on a waiting list) of REIN, who initiated dialysis between 2006 and 2010 in France.

	PLHIV ^a , n=149	HIV-uninfected controls ^a , n=348	p-value
Sociodemographic data			
Age at dialysis initiation, years			0.98
<40	43 (28.9)	101 (29.0)	
40-49	63 (42.3)	144 (41.4)	
50+	43 (28.9)	103 (29.6)	
Men	94 (63.1)	236 (67.8)	0.35
Region of birth: Sub-Saharan Africa	39 (26.2)	67 (19.2)	0.10
Period of dialysis initiation			0.23
2006-2008	83 (55.7)	214 (61.5)	
2009-2010	66 (44.3)	134 (38.5)	
Initial nephropathy			<0.0001
Diabetic nephropathy	9 (6.0)	15 (4.3)	

High blood pressure	13 (8.7)	64 (18.4)	
Chronic glomerulonephritis	51 (34.2)	91 (26.1)	
Polycystic kidney disease	3 (2.0)	42 (12.1)	
Other	56 (37.6)	87 (25.0)	
Unknown	17 (11.4)	49 (14.1)	
Initial dialysis modality			0.04
Hemodialysis	138 (92.6)	299 (85.9)	
Peritoneal dialysis	11 (7.4)	49 (14.1)	
Dialysis in Paris area	112 (75.2)	138 (39.7)	<0.0001
Period of waiting list enrollment			0.002
2006-2010	103 (69.1)	286 (82.2)	
2011-2015	46 (30.9)	62 (17.8)	
Duration of dialysis at listing (years)			<0.0001
<1	69 (46.3)	239 (68.7)	
1 to <2	39 (26.2)	65 (18.7)	
2 to <3	16 (10.7)	20 (5.7)	

3+	25 (16.8)	24 (6.9)	
Associated medical conditions at dialysis initiation			
Diabetes mellitus	23 (15.5)	39 (11.2)	0.19
Hypertension	102 (70.8)	276 (80.2)	0.03
Chronic hepatitis C ^b	22 (15.3)	11 (3.2)	<0.0001
Undernutrition ^c	30 (20.7)	39 (11.7)	0.01
Cirrhosis of any origin	2 (1.4)	4 (1.2)	1.00
Congestive heart failure	15 (10.5)	27 (7.9)	0.38
Coronary heart disease ^d	5 (3.5)	21 (6.1)	0.28
Vascular disease ^e	14 (9.8)	23 (6.7)	0.26
Chronic respiratory failure	3 (2.1)	8 (2.3)	1.00
Number of severe conditions ^f			0.72
0	111 (77.6)	275 (80.4)	
1	26 (18.2)	52 (15.2)	
≥2	6 (4.2)	15 (4.4)	

Transplantation-related**parameters**

Blood Group: A	48 (32.4)	123 (35.3)	0.60
Incompatible transplant rate ^g			<0.0001
0%	55 (39.0)	246 (72.6)	
1%-85%	70 (49.7)	74 (21.8)	
>85%	16 (11.3)	19 (5.6)	
Status on waiting list : always active	32 (21.5)	174 (50.0)	<0.0001

Data are median [IQR] or n (%)

BMI: Body Mass Index.

a: Missing data: chronic hepatitis C (n=9), hypertension (n=9), diabetes mellitus (n=2), nutritional status (n=20), cirrhosis of any origin (n=10), chronic cardiac failure (n=12), coronary heart disease (n=11), vascular disease (n=11), chronic respiratory failure (n=11), number of severe conditions (n=12), blood group (n=1), incompatible transplant rate (n=17).

b: defined as at least one detectable HCV RNA by qPCR.

c: Defined as a BMI<18.5 kg/m² or albuminemia< 27 g/l

d: defined as any of history of cardiac infarction or of angina

e: defined as an history of stroke, transient ischemic attack, or peripheral artery disease

f: Sum of following: cirrhosis of any origin, congestive heart failure, coronary heart disease, vascular disease, and chronic respiratory failure,

g: the incompatible transplant rate is the percentage of kidneys retrieved in France in the previous 5 years against which a given potential recipient has at least one significant anti-HLA donor-specific antibody.