



End-stage kidney disease and kidney transplantation in HIV positive patients



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BACKGROUND

End-stage kidney disease (ESKD) is a major complication of HIV infection which particularly affects patients of black ethnicity [1]. Antiretroviral drug therapy (ART) has dramatically improved the outcome of HIV positive patients with ESKD [2, 3]. Kidney transplantation has become a viable treatment modality for HIV/ESKD. Although the overall survival has been favourable, it remains unclear whether kidney transplantation (KT) affords a survival benefit over dialysis in those who are suitable for KT.

AIMS

The aims of this study were:

- To describe the trends in prevalence and incidence of ESKD in HIV positive patients
- To examine the factors associated with ESKD
- To describe the use of and barriers to KT and to compare survival of ESKD patients managed with KT and dialysis.

METHODS

The UK CHIC Study is an on-going observational cohort study collecting data from many of the largest HIV treatment centres in the UK. The current collaboration includes data from 8 centres that provided routinely available data on renal function.

Identification of ESKD patients

- Review of all HIV positive patients with an estimated glomerular filtration rate (eGFR) <15 mL/min/1.73m² at any point in time for having received permanent renal replacement therapy (pRRT) during the study period (01/2000-12/2011)
- Review of renal databases for HIV positive patients with ESKD

Suitability for kidney transplantation was assessed for patients who received pRRT from 2005 onwards and required patients to have

- HIV RNA <50 copies/mL for at least 6 months
- No medical comorbidities that precluded KT

Statistical analyses

- Univariable and multivariable Poisson regression analyses were used to identify factors associated with ESKD
- Survival was calculated from the time of initiation of pRRT using Kaplan-Meier methods and compared by log-rank test
- Follow up time was divided into time spent on dialysis "pre-KT", and for those who underwent KT, follow up from the date of first KT to the last clinic visit ("post-KT", censored at 31/12/2012).

RESULTS

- Between January 2000 and December 2011, 28,630 patients received HIV care at the participating clinics, with a median follow up of 6.4 (2.5, 11.1) years
- The median age was 38 years (0.4%), 69% were male, and 64% of black ethnicity
- 117 received pRRT during the study period, of whom 115 could be included in the analyses
- HIVAN was the commonest ESKD diagnosis (n=54, 46%)
- Patient characteristics at cohort entry according to ESKD status over follow-up are shown in Table 1

RESULTS (cont.)

Table 1 Characteristics of patients at cohort entry according to ESKD status over follow-up

	ESKD	No ESKD	P
N	115	28515	
Age, median (IQR)	years 38 (32, 44)	35 (29, 41)	0.001
Gender, n (%)	Male 80 (39.6)	22436 (78.7)	0.02
Ethnicity, n (%)	Black 73 (64.5)	7234 (25.4)	<0.0001
Mode of acquisition, n (%)	MSM 29 (25.2)	17031 (59.7)	<0.0001
CD4 count, median (IQR)	cells/mm ³ 207 (79, 329)	360 (210, 530)	<0.0001
Viral load, median (IQR)	log ₁₀ copies/ml 3.6 (1.7, 4.7)	3.6 (1.7, 4.7)	0.41
eGFR, median (IQR)	ml/min/1.73m ² 22 (11, 55)	103 (89, 115)	<0.0001
ART, n (%)	No 68 (59.1)	20131 (70.6)	0.007
Hepatitis B co-infection, n (%)	Yes 3 (2.7)	528 (1.9)	0.62
Hepatitis C co-infection, n (%)	Yes 4 (3.6)	647 (2.3)	0.56

Prevalence and Incidence of ESKD

- There was a steady increase in ESKD prevalence among patients of black ethnicity (from 0.44% (0.25%, 0.78%) in 2000/1 to 1.09% (0.85%, 1.41%) in 2010/11, p=0.008) (Figure 1A).
- There was a 4-5 fold higher ESKD incidence rate (1.14 [95% CI 0.81, 1.47] vs. 0.24 [0.16, 0.32] per 1000 person years for black vs. white/other patients) (Figure 1B).

Figure 1A Prevalence (%) of ESKD with 95CI in those of black and other ethnicities, stratified by year of follow-up

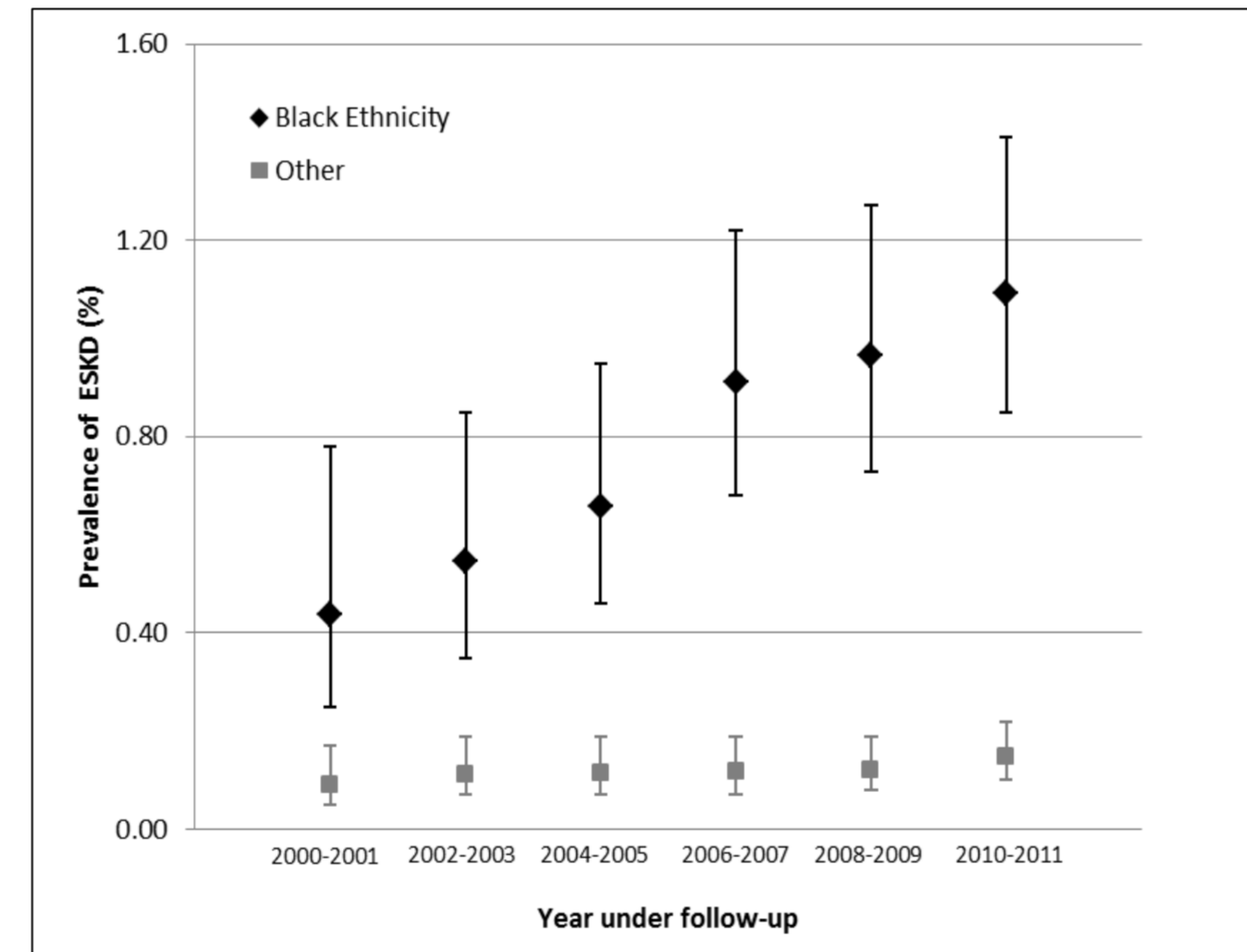
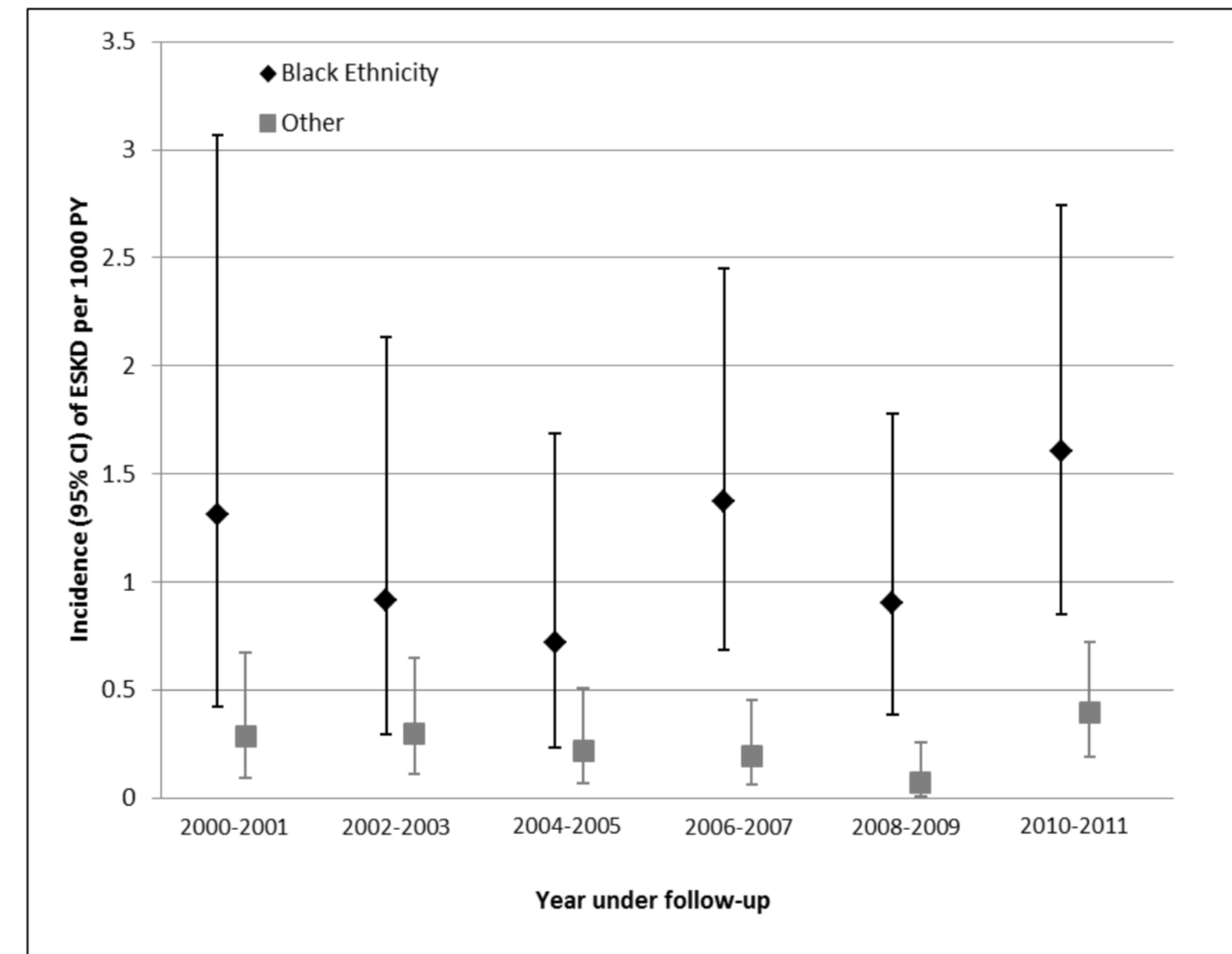


Figure 1B Incidence of ESKD in those of black and other ethnicities, stratified by year of follow-up



Factors associated with ESKD

- In the multivariable model, older age, black ethnicity, lower CD4 cell count and HIV RNA level, and hepatitis B and hepatitis C co-infection were independently associated with ESKD. (Table 2)

Table 2 Results from univariable & multivariable Poisson regression analyses identifying factors associated with ESKD

	Univariable Models		Multivariable Model	
	IRR (95% CI)	P	IRR (95% CI)	P
Age (per 10 years older)	1.28 (1.02, 1.59)	0.030	1.45 (1.14, 1.83)	0.002
Gender (Female)	1.78 (1.09, 2.89)	0.021	excluded	
Ethnicity (Black)	4.88(3.11, 7.67)	<0.0001	4.57 (2.79, 7.48)	<0.001
Mode of acquisition:				
Heterosexual	5.44 (3.25, 9.10)	<0.0001	excluded	
Other	4.07 (1.92, 8.65)	0.0003		
CD4 count (per 50 cells/mm³ higher)	0.91 (0.87, 0.95)	<0.0001	0.93 (0.88, 0.99)	0.017
HIV RNA (per log₁₀ copies/ml higher)	0.20 (0.13, 0.31)	<0.0001	0.40 (0.22, 0.74)	0.004
Started cART (Yes)	1.63 (0.81, 3.26)	0.17		
HBV:				
Yes	3.59 (1.68, 7.65)	0.001	2.66 (1.24, 5.71)	0.012
Not Tested	1.46 (0.91, 2.35)	0.12	1.40 (0.73, 2.68)	0.31
HCV:				
Yes	1.97 (0.93, 4.17)	0.077	2.89 (1.33, 6.25)	0.007
Not Tested	1.18 (0.72, 1.93)	0.51	0.96 (0.48, 1.91)	0.91

IRR=Incidence Rate Ratio; CI=Confidence Interval; P=p-value

RESULTS (cont.)

Kidney Transplantation as a Treatment Modality for ESKD

- From 2005 onwards, kidney transplantation (KT) was increasingly used to treat ESKD (Figure 2A).
- Of the 107 ESKD patients who were followed up after 01/2005, 69 (64%) were considered suitable for KT, 30 (28%) were unsuitable for KT, and the status could not be confirmed for 8 patients.
- By December 2012, 34 (49%) had received a kidney allograft. (Figure 2B)
- Reasons for unsuitability were persistent HIV replication (n=16), prior diagnosis of progressive multifocal leuco-encephalopathy (PML, n=2) and presence of medical co-morbidities (liver, cardiovascular or urological disease, recent history of cancer, or general frailty [n=10]); 2 patients declined to be considered for KT.

Figure 2a No. of patients under follow-up with ESKD, suitable for kidney transplantation, & having received a kidney transplant, stratified by calendar year

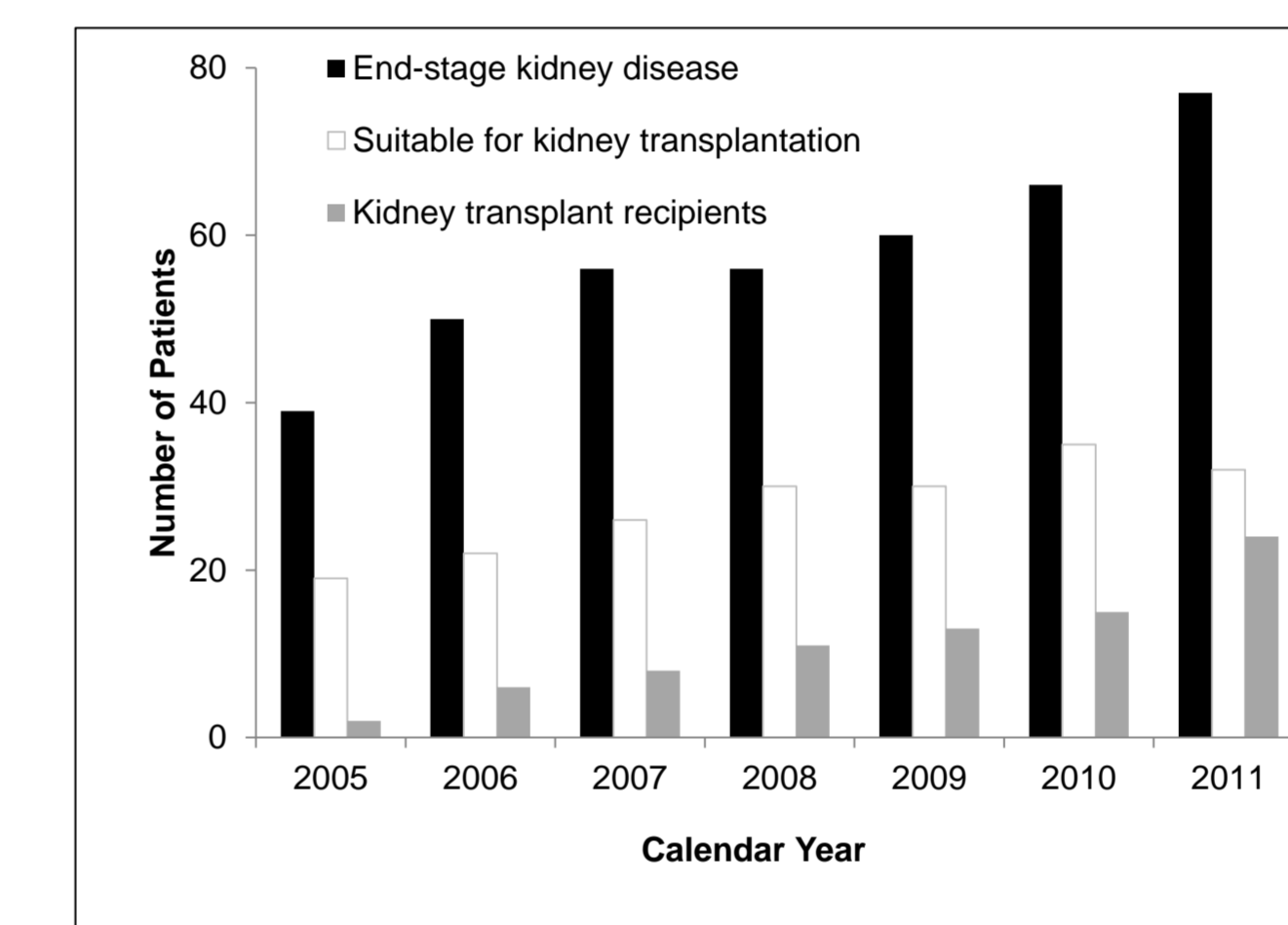
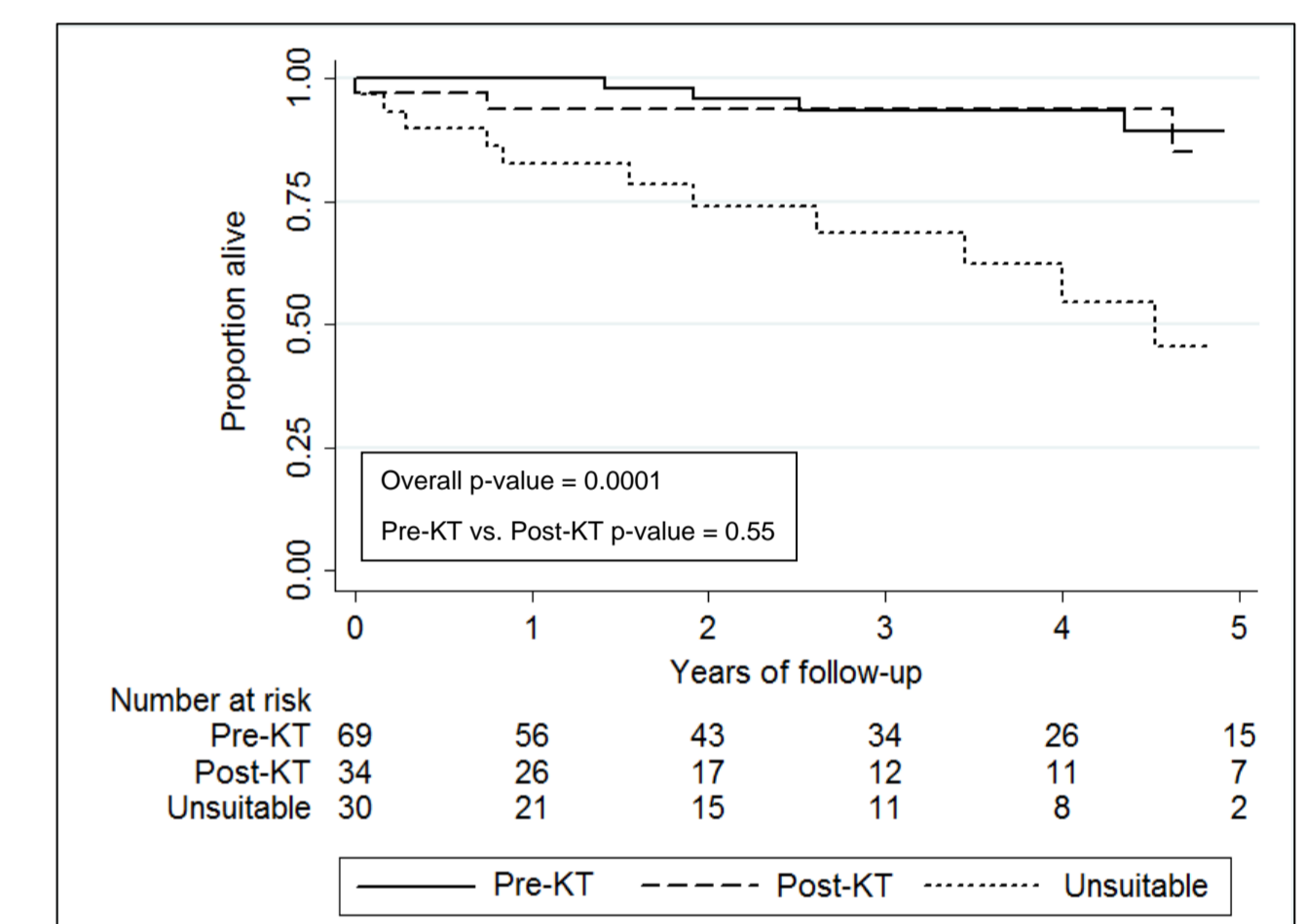


Figure 2b Kaplan-Meier plots showing survival of patients with ESKD, stratified by a) pre-KT, b) post-KT, and c) unsuitable for KT.



DISCUSSION

Summary:

- The incidence of ESKD has remained unchanged despite widespread use of cART.
- Excellent survival was observed among patients with ESKD who were eligible for transplantation irrespective of whether they had been maintained on dialysis or successfully transplanted.
- As the majority of patients have advanced kidney disease at the time of HIV diagnosis, ESKD prevention strategies should include efforts to diagnose HIV infection earlier, especially in those of black ethnicity.

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