Baseline renal function is an independent predictor of death and progression to severe chronic kidney disease

Fowzia Ibrahim, Lisa Hamzah, Caroline Sabin, Dorothea Nitsch, Rachael Jones and Frank Post for the UK CHIC / CKD Study

Background

Stage	Description	GRF (mL/min/1.73m^2)
1	Kidney damage with normal or ↓GFR	≥90
2	Kidney damage with mild ↓GFR	60-89
3	Moderate ↓GFR	30-59
4	Severe ↓GFR	15-29
5	Kidney failure	<15 or dialysis

- In the absence of information on proteinuria or renal morphology, chronic kidney disease (CKD) can be defined as kidney damage or glomerular filtration rate (GFR) <60mL/min/1.73m^2 for >3 months[1]
- The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula was developed to more accurately estimate GFR[2]

[1]NKF KDOQI Clinical Practice Guidelines for Chronic Kidney Disease
[2]Ann Intern Med. 1999;130:461-470

Kidney Disease in HIV

- Based on the presence of ↓GFR and/or proteinuria, CKD affects 15-20% HIV infected individuals[1]
- End stage renal failure (ESRF) prevalence has increased in the HAART era, 0.31% in the UK[2]
- A number of factors are associated with developing CKD[3,4]
  - HIV-related:
    - CD4 <200, AIDS
    - Exposure to Indinavir, Tenofovir, and Atazanavir
  - Non-HIV related:
    - Age, diabetes, hypertension

[1]Curr Opin Infect Dis 2009, 22:43-48
[2]AIDS 2009, 23: 2517
[3]AIDS 2004, 18: 2171
[4]AIDS 2007, 21: 1119

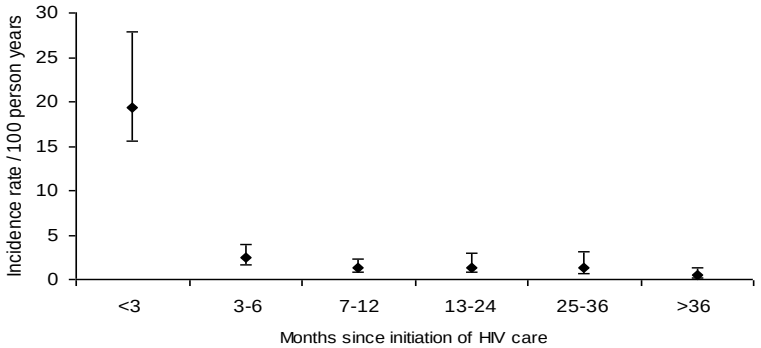
Aims

- To assess the effects of baseline renal function on mortality and progression to severe CKD (stage 4/5)

- To compare MDRD and CKD-EPI formulae in an HIV infected population

Methods -1

- UK Collaborative HIV Cohort (CHIC) Study
  - Ongoing observational cohort initiated in 2001
  - Dataset includes outpatient routinely collected HIV parameters on 32,607 patients from 11 UK centres
- Inclusion criteria
  - Adults (>16 yrs) with at least one creatinine level ≥ 3 months after HIV diagnosis
- Baseline renal function was defined as the first available eGFR > 3 months after HIV diagnosis[1]



[1]CID 2008:47

Methods -2

- GFR was estimated using MDRD and CKD-EPI and stratified by stage of CKD
  - 1 (≥90), 2 (60-89), 3 (30-59), 4 (15-29), and 5 (<15 mL/min)
  - Stage 2 was further divided into 75-89 and 60-74 mL/min
- Stage 4/5 CKD was defined as an eGFR <30 mL/min for >3 months
- Statistical methods used include
  - Kappa statistics
  - Kaplan-Meier graphs
  - Cox regression
  - Competing-risk regression

Patient characteristics at baseline

Total N (%)		**19,111 (100)**
Male N (%)		**15,094 (79)**
Ethnicity N (%)	**Black**	**4,640 (24)**
	White/Other	**14,471 (76)**
Hepatitis B surface antigen positive	**N (%)**	**1,097 (6)**
Hepatitis C antibody positive	**N (%)**	**1,333 (7)**
CD4 cell count (cells/mm^3)	**Median (IQR)**	**352 (212, 520)**
Viral load (copies/ml)	**Median (IQR)**	**1995 (50, 32154)**
eGFR-MDRD ml/min/1.73m^2	**Median (IQR)**	**95 (83, 108)**
eGFR-CKD-EPI ml/min/1.73m^2	**Median (IQR)**	**100 (87, 112)**
On cART	**N (%)**	**12,034 (62)**

Median time from HIV diagnosis to baseline eGFR was 4 [3, 9] months

1,837 (9.6%) died

79 (0.41%) progressed to stage 4/5 CKD

Baseline eGFR using MDRD and CKD-EPI

GFR mL/min/1.73m^2	MDRD n (%)	CKD-EPI n (%)
≥90	11,628 (60.8)	13,584 (71.1)
89-75	5,227 (27.4)	3,948 (20.7)
74-60	1,808 (9.5)	1,199 (6.3)
59-30	341 (1.8)	290 (1.5)
29-15	48 (0.3)	45 (0.2)
<15	44 (0.2)	45 (0.2)

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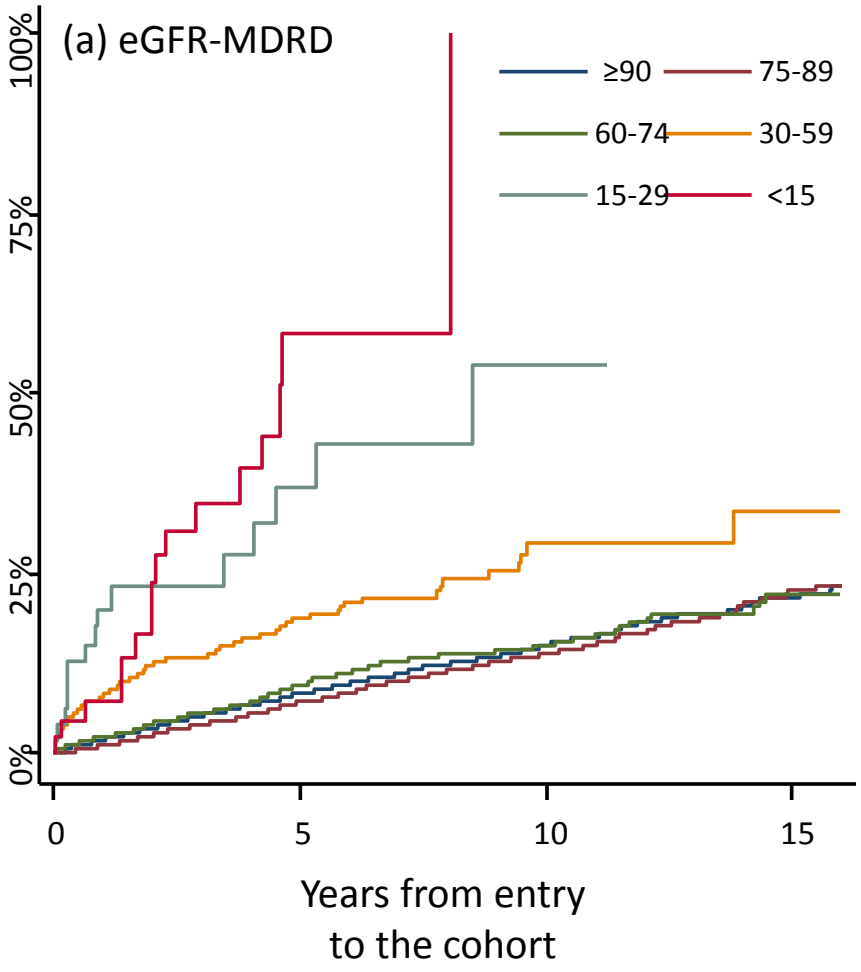
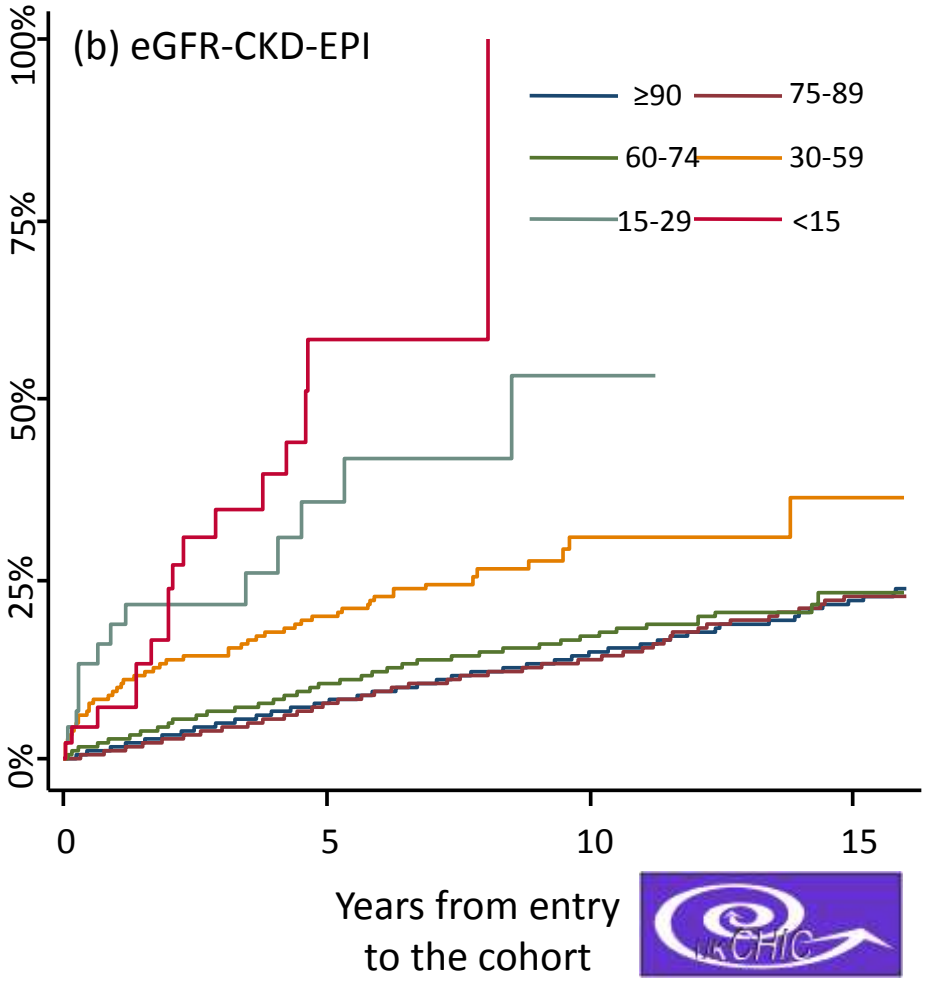
Good agreement was observed between eGFR MDRD and CKD-EPI (kappa 72%; 95% CI: 70%, 73%)

Time to death stratified by baseline eGRF





Adjusted mortality hazard ratios (95% CI) stratified by baseline eGRF

	MDRD		CKD-EPI	
eGFR	Adjusted[1] HR (95%CI)	P	Adjusted[1] HR (95%CI)	P
≥90	1		1	
60-89	0.93 (0.84, 1.02)	0.13	1.02 (0.92, 1.13)	0.75
30-59	1.98 (1.53, 2.56)	<0.001	2.24 (1.72, 2.94)	<0.001
15-29	5.31 (3.13, 9.01)	<0.001	5.25 (3.04, 9.08)	<0.001
<15	6.69 (4.07, 11.00)	<0.001	6.90 (4.20, 11.33)	<0.001

[1] Estimates were adjusted for gender, ethnicity, age at entry to cohort, and AIDS, CD4 cell count and cART at baseline

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Factors associated with progression to stage 4/5 CKD

	MDRD		CKD-EPI	
eGFR	Adjusted SHR (95%CI)	P	Adjusted SHR (95%CI)	P
≥90	1		1	
89-75	3.50 (0.98, 12.6)	0.054	2.17 (0.61 ,7.7)	0.23
74-60	11.86 (3.2, 44.5)	<0.001	14.00 (4.6, 43.1)	<0.001
59-30	140.9 (42.4, 463.1)	<0.001	115.9 (42.1, 319.6)	<0.001
Ethnicity				
Black	3.38 (1.58, 7.25)	0.002	2.52 (1.20, 5.28)	0.01
CD4 cell count (cells/mm^3) (per 50 cell increase)	0.95 (0.87, 1.04)	0.27	0.95 (0.86, 1.03)	0.26

Estimates were adjusted for all the variables in table
SHR= Sub-hazard ratios, CI=Confidence intervals

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Summary

- The presence of CKD at baseline had a dramatic effect on mortality
- Having a baseline eGFR <90 increase the risk of progression to severe CKD and this became statistically significant with a eGFR <75
- CKD-EPI is more restrictive when describing the severity of CKD, however, mortality and progression to severe CKD was similar for patients stratified by eGFR using both methods

Discussion

- Limitations of study
  - Using baseline a eGRF at 3 months excludes patients with acute renal failure, some of whom may have had CKD and died within 3 months of HIV diagnosis
  - Analysis of clinical outcomes with renal disease is limited by the observational nature of the data, selection bias and loss to follow-up

- Data suggests monitoring of patients with reduced eGFR (<90 mL/min) may be warranted to reduce the risk of progression to severe CKD

Acknowledgements

UK CHIC/CKD study group

Brighton:	Steve Holt, Martin Fisher
C&W:	Amelia Hughes, Jeremy Levy, Rachael Jones
Edinburgh:	Clifford Leen, Sheila Morris
LSHTM:	Dorothea Nitsch
King's:	Frank Post, Fowzia Ibrahim, Lisa Hamzah, Lucy Campbell, Bruce Hendry
St Mary's:	Nicky Mackie
Royal Free/Mortimer Market:	Loveleen Bansi, Teresa Hill, Caroline Sabin, Sanjay Bhagani, John Connolly, Margaret Johnson, Simon Edwards, Ian Williams

UK CHIC Steering Committee

Jonathan Ainsworth, Jane Anderson, Abdel Babiker, David Dunn, Philippa Easterbrook, Martin Fisher, Brian Gazzard (Chair), Richard Gilson, Mark Gompels, Teresa Hill, Margaret Johnson, Clifford Leen, Chloe Orkin, Andrew Phillips, Deenan Pillay, Kholoud Porter, Caroline Sabin, Tariq Sadiq, Achim Schwenk, Nicky Mackie, Alan Winston, Valerie Delpech.

Central Co-ordination

Medical Research Council Clinical Trials Unit (MRC CTU), London (David Dunn, Kholoud Porter, Stephen Sheehan); Royal Free NHS Trust and RFUCMS, London (Loveleen Bansi, Teresa Hill, Andrew Phillips, Caroline Sabin).

Participating Centres

Barts and The London NHS Trust, London (Chloe Orkin, Kevin Jones, Rachel Thomas); Brighton and Sussex University Hospitals NHS Trust (Martin Fisher, Nicky Perry, Anthony Pullin, Duncan Churchill,Wendy Harris); Chelsea and Westminster NHS Trust, London (Brian Gazzard, Steve Bulbeck, Sundhiya Mandalia, Jemima Clarke); Health Protection Agency – Centre for Infections London (HPA) (Valerie Delpech); Homerton University Hospital NHS Trust, London (Jane Anderson, Selina Gann); King's College Hospital, London (Frank Post, Hardik Korat, Chris Taylor, Mary Poulton, Lucy Campbell, Fowzia Ibrahim); Medical Research Council Clinical Trials Unit (MRC CTU), London (Abdel Babiker, David Dunn, Kholoud Porter, Stephen Sheehan); Mortimer Market Centre, Royal Free and University College Medical School (RFUCMS), London (Richard Gilson, Julie Dodds, Shuk-Li Man, Ian Williams); North Middlesex University Hospital NHS Trust, London (Achim Schwenk); Royal Free NHS Trust and RFUCMS, London (Margaret Johnson, Mike Youle, Fiona Lampe, Colette Smith, Helen Grabowska, Clinton Chaloner, Dewi Ismajani Puradiredja, Loveleen Bansi, Teresa Hill, Andrew Phillips, Caroline Sabin); St. Mary's Hospital, London (John Walsh, Jonathan Weber, Christian Kemble, Mark Carder); The Lothian University Hospitals NHS Trust, Edinburgh (Clifford Leen, Alan Wilson).

UK CHIC is funded by the UK Medical Research Council


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Agreement between MDRD and CKD-EPI formulae

	eGFR-MDRD						
eGFR-CKD-EPI	**≥90**	**89-75**	**74-60**	**59-30**	**29-15**	**<15**	**Total**
≥90	**11,628**	**1,956**	**0**	**0**	**0**	**0**	**13,584**
89-75	**15**	**3,255**	**678**	**0**	**0**	**0**	**3,948**
74-60	**0**	**16**	**1,118**	**65**	**0**	**0**	**1,199**
59-30	**0**	**0**	**12**	**276**	**2**	**0**	**290**
29-15	**0**	**0**	**0**	**0**	**45**	**0**	**45**
<15	**0**	**0**	**0**	**0**	**1**	**44**	**45**
Total	**11,643**	**5,227**	**1,808**	**341**	**48**	**44**	**19,111**

- Good agreement was observed between eGFR MDRD and eGFR CKD-EPI (kappa 72%; 95% CI: 70%, 73%)