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# Renal impairment is associated with coronary heart disease (CHD) in HIV patients

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# Background

## Increased risk of CHD in HIV+ people

- Traditional CHD risk factors<sup>1-4</sup>
- HIV replication and cART<sup>5,6</sup>
- Immune activation<sup>7,8</sup>
- Prothrombotic / fibrinolytic state<sup>7,8</sup>
- Endothelial dysfunction<sup>9</sup>
- Carotid artery intima-media thickness<sup>10,11</sup>
- Coronary artery calcification<sup>12-13</sup>

<sup>1</sup>Currier JS et al. *Circulation* 2008. <sup>2</sup>Klein D et al. *J Acquire Immune Defic Syndr* 2002. <sup>3</sup>Triant VA et al. *Clin Endocrinol Metab* 2007. <sup>4</sup>Currier JS et al. *J Acquire Immune Defic Syndr* 2002. <sup>5</sup>Aberg JA et al. *J Acquire Immune Defic Syndr* 2009. <sup>6</sup>Calza L et al. *AIDS* 2010. <sup>7</sup>Neuhaus J et al. *J Infect Dis* 2010. <sup>8</sup>Kaplan RC et al. *J Infect Dis* 2011. <sup>9</sup>Solages A et al. *Clin Infect Dis* 2006. <sup>10</sup>Grunfield C et al. *AIDS* 2009. <sup>11</sup>Hsue PY et al. *AIDS* 2009. <sup>12</sup>Kingsley LA et al. *AIDS* 2008. <sup>13</sup>Lo J et al. *AIDS* 2010.

# Background

## Chronic kidney disease (CKD)

- Proteinuria
- eGFR <60 ml/min/1.73m<sup>2</sup>
  - Present in ~15% of HIV+ patients<sup>14</sup>

## CKD is associated with CHD in HIV

- CKD is an independent risk factor for MI<sup>15,16</sup>
- Higher carotid intima-media thickness scores<sup>17,18</sup>

<sup>14</sup>Post F *et al.* *Curr Opin Infect Dis* 2009. <sup>15</sup>Choi AL *et al.* *Circulation* 2010. <sup>16</sup>George E *et al.* *AIDS* 2010.

<sup>17</sup>Serrano-Villar S *et al.* *J Acquire Immune Defic Syndr* 2012. <sup>18</sup>Jotwani V *et al.* *Am J Nephrol* 2011.

# Aims

## Large multi-ethnic cohort in South London

- Define incidence of CHD
- Describe association between eGFR and CHD

# Methods

## Observational cohort study HIV+ adults attending between 2004 - 2009

- King's College
- Guy's and St Thomas'
- St George's

## CHD case ascertainment

- Linkage of HIV and Cardiac databases
- Review of all patients with elevated troponin levels
- Physician recall

## CHD events - INSIGHT criteria<sup>19</sup>

- MI
- Angioplasty
- Bypass graft

## Multivariable Poisson regression analysis

<sup>19</sup>Lifson AR *et al.* *HIV Clin Trials* 2010.

# Results: patient characteristics

		All N = 7828	CHD** n = 29 (0.4%)	No CHD** n = 7799	p-value
<b>Follow-up (yr)</b>	median (IQR)	3.8 (1.2, 7.1)			
<b>CHD events</b>			34		
Myocardial infarct			30		
Angioplasty / Bypass graft			4		
<b>Age (yr)*</b>	mean (SD)	35.7 (9.3)	47.1 (12.3)	35.7 (9.2)	<0.0001
<b>Males</b>	n (%)	5033 (64)	28 (97)	5005 (64)	<0.0001
<b>Ethnicity</b>	n (%)				0.001
White/other		3594 (47)	22 (79)	3572 (47)	
Black		4010 (53)	6 (21)	4004 (53)	
<b>Time since HIV <math>\Delta</math> (yr)</b>	median (IQR)	6.1 (3.4, 88)	9.9 (7.8, 13.9)	6.1 (3.4, 8.7)	0.0001
<b>Ever received cART</b>	n (%)	5800 (74)	28 (97)	5772 (74)	0.06
Ever received ABC		1673 (21)	11 (38)	1662 (21)	0.03
Ever received TDF		2674 (37)	20 (71)	2654 (37)	0.0001
<b>eGFR*</b>	median (IQR)	110 (95, 123)	95 (74, 113)	110 (96, 123)	0.009

\* At cohort entry    \*\* At last follow-up

# Results: CHD incident rate in 5005 HIV+ men

	Incident Rate per 1000 PYFU (95% CI)
<b>Ethnicity/Gender</b>	
White Men	1.7 (1.2, 2.5)
Black Men	0.8 (0.4, 1.8)
<b>During Drug Exposure</b>	
Abacavir	1.1 (0.4, 2.9)
Tenofovir	1.7 (0.2, 3.6)
<b>eGFR (ml/min/1.73m<sup>2</sup>)</b>	
<75	3.6 (1.3, 9.5)
75-89	0.8 (0.4, 1.8)
≥90	0.8 (0.3, 1.7)



# Results: Factors associated with CHD in HIV+ men

	Univariate IRR (95% CI)	p-value	Multivariate IRR (95% CI)	p-value
<b>Baseline Parameters</b>				
<b>Age per 10yr increase</b>	<b>2.48 (1.84, 3.33)</b>	<b>&lt;0.001</b>	<b>2.54 (1.54, 4.19)</b>	<b>&lt;0.0001</b>
Black ethnicity (vs. white/other)	0.38 (0.13, 1.15)	0.09		
Heterosexual (vs. MSM)	0.49 (0.18, 1.35)	0.17		
HBV-sAg+	0.77 (0.99, 5.88)	0.80		
HCV-IgG+	2.34 (0.78, 7.05)	0.13		
<b>Time Updated Parameters</b>				
On cART	0.81 (0.33, 1.99)	0.65		
CD4 cell count (per 50 cells)	1.02 (0.93, 1.12)	0.68		
<b>HIV RNA &lt;400 (vs. ≥400)</b>	<b>8.37 (1.10, 63.6)</b>	<b>0.04</b>	2.73 (0.32, 23.2)	0.36
<b>eGFR (per 10 mL/min increase)</b>	<b>0.81 (0.73, 0.91)</b>	<b>&lt;0.001</b>	0.97 (0.72, 1.31)	0.85
<b>Total/HDL Cholesterol</b>	<b>1.24 (1.02, 1.52)</b>	<b>0.03</b>	1.22 (0.92, 1.63)	0.17
ABC use	0.94 (0.30, 2.99)	0.92		
<b>TDF use</b>	<b>2.94 (1.16, 7.46)</b>	<b>0.02</b>	1.35 (0.39, 4.73)	0.64

# Results: Associations of eGFR <75 with CHD in HIV+ men

	<b>eGFR &lt;90</b>	<b>p-value</b>	<b>eGFR &lt;75</b>	<b>p-value</b>
<b>Unadjusted</b>	<b>4.12 (1.53, 11.6)</b>	<b>0.005</b>	<b>8.61 (3.13, 23.6)</b>	<b>&lt;0.001</b>
<b>Adjusted for</b>				
<b>TDF and VL&lt;40</b>	<b>3.74 (1.39, 10.0)</b>	<b>0.009</b>	<b>8.37 (3.10, 22.6)</b>	<b>&lt;0.001</b>
<b>TC/HDL-C</b>	<b>3.56 (1.21, 10.5)</b>	<b>0.02</b>	<b>7.51 (2.53, 22.3)</b>	<b>&lt;0.001</b>
<b>Age</b>	<b>1.88 (0.51, 7.00)</b>	<b>0.35</b>	<b>4.30 (1.33, 14.5)</b>	<b>0.02</b>

# Discussion

## Low rate of CHD events in HIV+ men

- High prevalence of traditional CHD risk factors

## Associations with CHD

- ABC not associated with increased risk
- Sub-normal eGFR (<75) identifies at-risk patients
  - Targeted risk-reduction

# Discussion

## Limitations

- Retrospective study design
- CHD ascertainment at local centre of care only
- Lack of denominator data prevented adjusted
  - Hypertension, diabetes, smoking, proteinuria
- Underpowered
  - 34 events in 29 patients

## Strengths

- Large, unselected study population
- All events met INSIGHT criteria

# Conclusions

Low overall incidence of CHD

No association between Abacavir and CHD

Further evidence of an association between impaired renal function and CHD

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