P156

Correspondence:
sophie.jose@ucl.ac.uk

Treatment switches following periods of low-level viraemia

Sophie Jose[1], Erasmus Smit[2], Fabiola Martin[3], David Dunn[4], Nicola Mackie[5], Duncan Churchill[6] and Caroline Sabin[1] for the UK Collaborative HIV Cohort (CHIC) Study

[1]UCL, Royal Free Campus, London, UK; [2]Heart of England NHS Foundation Trust, Birmingham, UK; [3]York Teaching Hospital and University of York, York, UK; [4]Medical Research Council Clinical Trials Unit at UCL, London, UK; [5]Imperial College Healthcare NHS Trust, London, UK; [6]Brighton and Sussex University Hospitals NHS Trust, Brighton, UK.

BACKGROUND

- Prolonged low-level viraemia could increase the risk of virological failure or accumulation of resistance and has been linked to increased mortality[1,2]
- There is currently little evidence to guide the optimal management of patients with low-level viraemia, particularly regarding when or if changes to ART regimens should be made at low (but detectable) viral loads and without the aid of a resistance test
- Introduction of more sensitive assays since 2008, with high test variability at low viral loads leading to more frequently recorded viraemia[3], raises the concern that patients may be unnecessarily switched to salvage regimens following low but detectable viraemia

AIMS

We wanted to describe treatment switching in clinical practice at different viral load thresholds over time

Our objectives were:

- To describe frequency and duration of periods of low-level viraemia in the range 51-1000 copies/ml
- To estimate rates of treatment switch following viral load measurements in viral load strata <50, 51-100, 101-200, 201-500, 501-1000 and >1000 copies/ml.
- To investigate predictors of treatment switch over at viral load >50 copies/ml, with particular interest in viral load changes over time

METHODS

Patients:

- Data were from the UK Collaborative HIV Cohort (CHIC) Study, an on-going observational cohort that collates routinely collected data on HIV-positive individuals accessing care at many of the largest HIV centres in the UK
- Patients eligible for inclusion had initiated ART between 2000-2011 and achieved an undetectable viral load. Pregnant women were excluded as were those without at least 1 baseline and follow up viral load measurement.

Statistical Analysis:

- Treatment switch was defined as an intensification of the regimen or a change to the '3rd drug' in the regimen
- Each viral load was treated as a separate observation and was said to result in a treatment switch if a switch occurred within the following six month interval and prior to the next viral load measurement. Confirmatory viral loads (within 30 days) were excluded
- The rate of treatment switch following viral loads <50, 51-100, 101-200, 201-500, 501-1000 and >1000 copies/ml were calculated
- Poisson regression with generalised estimating equations was used to investigate predictors of a treatment switch at viral loads >50 copies/ml from the following covariates:

Viral load, calendar year, previous viral failure, previous viraemia, previous viral load blip, duration of current viraemia episode, cART regimen, time on cART, CD4 count, previous AIDS-defining event, HBV co-infection, HCV co-infection, age, sex, ethnicity, mode of HIV acquisition.

- An interaction effect between calendar year and viral load was tested in the Poisson regression model to determine whether rates of treatment switch at lower viral load measures had changed in over time.

RESULTS

- A total 14814 individuals were included in the analysis. Patient characteristics at cART initiation are shown in table 1.

Table 1: Patient characteristics at cART initiation

		N =14814
Age, median (IQR)	(years)	37 (32, 44)
Sex, n (%)	Male	11449 (77.3)
	Female	3365 (22.7)
Ethnicity, n (%)	White	8227 (55.5)
	Black	4914 (33.2)
	Other/unknown	1673 (11.3)
Mode of HIV acquisition, n (%)	Men having sex with men	8059 (54.4)
	Heterosexual	5588 (37.7)
	Other/unknown	1167 (7.9)
Hepatitis B co-infection, n (%)	Yes	385 (2.6)
	No	7427 (50.1)
	No test	7002 (47.3)
Hepatitis C co-infection, n (%)	Yes	562 (3.8)
	No	7892 (53.3)
	No test	6360 (52.9)
CD4 count, median (IQR)	(cells/mm^3)	210 (115, 300)
Viral load, median (IQR)	(log_{10}copies/ml)	4.8 (4.2, 5.3)
cART regimen class, n (%)	NNRTI	10335 (69.8)
	PI	3456 (23.3)
	Other	1023 (6.9)

- Median (IQR) time to viral suppression was 3.7 (2.4, 5.7) months
- 4991 (33.7%) individuals experienced at least 1 episode of viraemia
- Most (78.4%) episodes of viraemia were transient (viral load 'blips')
- Median (IQR) duration of viraemia episodes was 3.9 (2.2, 6.5) months
- The majority (89.4%) of viraemia episodes ended with re-suppression without a treatment switch, whilst only 6.7% involved a switch. The remaining 3.9% episodes had not resolved by follow-up end

RESULTS (continued)

Table 2: Rate of treatment switch according to viral load

Viral load (copies/ml)	N	N (%) VL followed by treatment switch	Incidence (95% CI) per 100 pyrs
<50	151599	7492 (4.9%)	17.2 (16.8, 17.6)
51-100	6391	464 (7.3%)	30.7 (28.0, 33.7)
101-200	2826	265 (9.4%)	44.9 (39.5, 50.5)
201-500	2599	301 (11.6%)	53.1 (47.3, 59.5)
501-1000	921	141 (15.3%)	82.2 (69.2, 97.0)
>1000	3933	934 (23.8%)	130.5 (122.2, 139.1)

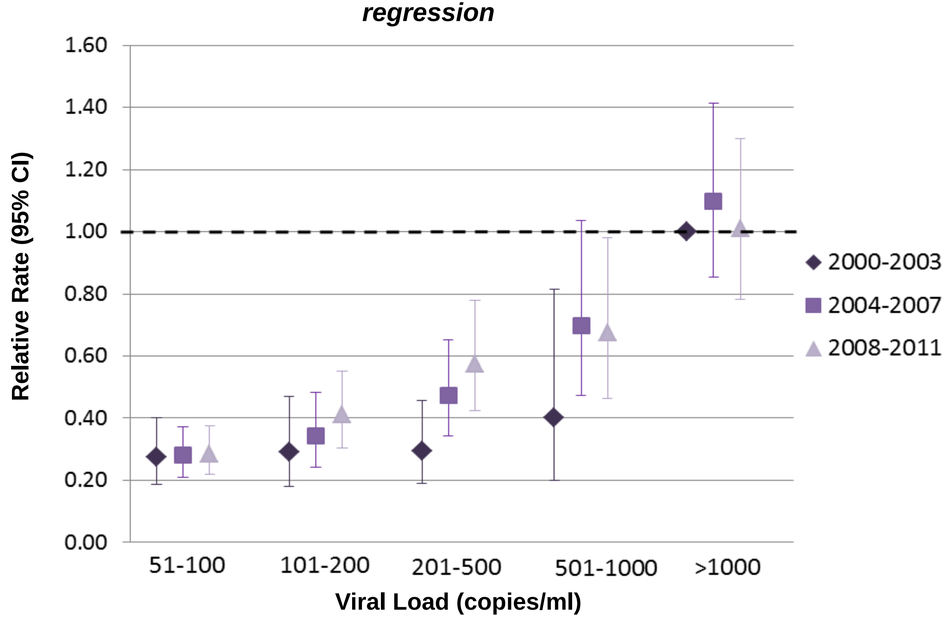
- Treatment switch was increasingly likely at higher viral loads (Table 2).
- Predictors of a treatment switch at viral loads >50 copies/ml are shown in Table 3.
- There was some evidence of an increasing propensity to switch treatment at viral loads between 201-500 copies/ml in more recent calendar years in Poisson regression (Figure 1).

Table 3: Factors associated with treatment switch at viral loads >50 copies/ml in Poisson regression analysis

		Univariable RR (95%CI)	Multivariable RR (95%CI)
Viral load (copies/ml)	>1000	1.00	1.00
	501-1000	0.61 (0.50, 0.76)	0.61 (0.49, 0.77)
	201-500	0.41 (0.35, 0.48)	0.46 (0.39, 0.55)
	101-200	0.32 (0.27, 0.38)	0.35 (0.29, 0.42)
	51-100	0.23 (0.20, 0.26)	0.27 (0.23, 0.31)
Calendar year	2000-2003	1.00	1.00
	2004-2007	0.91 (0.77, 1.09)	1.19 (1.00, 1.42)
	2008-2011	0.86 (0.72, 1.01)	1.21 (1.01, 1.46)
cART regimen	NNRTI-based	1.00	1.00
	PI-based	1.05 (0.92, 1.21)	0.99 (0.85, 1.14)
	Other	1.96 (1.70, 2.26)	1.93 (1.66, 2.64)
Length of time on cART	(per 6 months)	0.96 (095, 0.98)	0.96 (0.94, 0.98)
CD4 count	(per 50 cells/mm^3)	0.94 (0.93, 0.96)	0.98 (0.97, 1.00)
Number of viral load in viraemia episode (since start/switch)	1	1.00	1.00
	2	1.74 (1.52, 2.00)	1.24 (0.92, 1.67)
	3-5	2.08 (1.80, 2.40)	1.83 (1.36, 2.46)
	6-10	1.70 (1.34, 2.16)	1.78 (1.23, 2.58)
	>10	1.38 (0.94, 2.04)	1.40 (0.86, 2.28)
Duration of current viraemia episode (months)	0	1.00	1.00
	0-2 months	2.52 (2.11, 3.00)	1.65 (1.18, 2.32)
	2-6 months	1.84 (1.60, 2.11)	1.22 (0.89, 1.66)
	>6 months	1.57 (1.35, 1.83)	0.84 (0.61, 1.17)

[1]Model also includes previous viral failure, previous viral blip, time suppressed prior to viraemia, centre, previous AIDS-defining event, sex, age and mode of acquisition.

Figure 1: Relative rate of treatment switch according to viral load and calendar year in Poisson regression



DISCUSSION

- The majority of low-level viraemia experienced in this cohort was transient (viral load 'blips') and only 6.7% of viraemia episodes involved a switch
- Treatment switch was increasingly likely at higher viral loads, but there was some evidence of an increasing tendency to switch treatment at lower viral loads over time, particularly between 201-500 copies/ml
- A limitation of this study is that reasons for treatment switch are unknown. We are unable to establish, where no treatment switch was made, whether a recommendation for switch was made by the clinician but not taken up due to patient choice
- Future work will consider the implications of switching therapy during low-level viraemia on long term outcomes such as viral failure and development of resistance

REFERENCES

1. Taiwo B, Gallien S, Aga E, et al. **Antiretroviral drug resistance in HIV-1-infected patients experiencing persistent low-level viremia during first-line therapy.** *The Journal of infectious diseases.* 2011;204(4):515-520.
2. Wright ST, Hoy J, Mulhall B, et al. **Determinants of Viraemia Copy-Years in People with HIV/AIDS Following Initiation of Antiretroviral Therapy**. *J Acquir Immune Defic Syndr.* 2014.
3. Lima V, Harrigan R, Montaner JS. **Increased Reporting of Detectable Plasma HIV-1 RNA Levels at the Critical Threshold of 50 copies per mililitre with the Taqman Assay in Comparison to the Amplicor Assay**. *J Acquir Immune Defic Syndr* 2009;51(1)

United Kingdom Collaborative HIV Cohort (UK CHIC)

UK CHIC Steering Committee: *Jonathan Ainsworth, Jane Anderson, Abdel Babiker, Valerie Delpech, David Dunn, Philippa Easterbrook, Martin Fisher, Brian Gazzard (Chair), Richard Gilson, Mark Gompels, Teresa Hill, Margaret Johnson, Clifford Leen, Fabiola Martin, Chloe Orkin, Andrew Phillips, Deenan Pillay, Kholoud Porter, Caroline Sabin, Achim Schwenk, John Walsh.*

Central co-ordination: ***Research Department of Infection & Population Health, UCL, London*** *(T Hill, S Huntington, S Jose, A Phillips, C Sabin, A Thornton);* ***Medical Research Council Clinical Trials Unit (MRC CTU), London*** *(D Dunn, A Glabay).*

Participating centres: ***Barts and The London NHS Trust, London*** *(C Orkin, J Lynch, J Hand, C de Souza);* ***Brighton and Sussex University Hospitals NHS Trust*** *(M Fisher, N Perry, S Tilbury, D Churchill);* ***Chelsea and Westminster NHS Trust, London*** *(B Gazzard, M Nelson, M Waxman, D Asboe, S Mandalia);* ***Health Protection Agency Centre for Infections London*** *(V Delpech);* ***Homerton University Hospital NHS Trust, London*** *(J Anderson, S Munshi, D Awosika);* ***King's College Hospital, London*** *(F Post, H Korat, C Taylor, Z Gleisner, F Ibrahim, L Campbell);* ***UCL Medical School and The Mortimer Market Centre, London*** *(R Gilson, N Brima, I Williams);* ***North Bristol NHS Trust*** *(M Gompels, S Allen);* ***North Middlesex University Hospital NHS Trust, London*** *(A Schwenk, J Ainsworth, C Wood, S Miller);* ***Royal Free NHS Trust and Department of Infection & Population Health, UCL, London*** *(M Johnson, M Youle, F Lampe, C Smith, H Grabowska, C Chaloner, D Puradiredja);* ***Imperial College Healthcare NHS Trust, London*** *(J Walsh, N Mackie, A Winston, J Weber, F Ramzan);* ***The Lothian University Hospitals NHS Trust, Edinburgh*** *(C Leen, A Wilson);* ***University of Leicester NHS Trust*** *(A Palfreeman, A Moore, L Fox);* ***South Tees Hospitals NHS Foundation Trust*** *(D Chadwick, K Baillie);* ***Woolwich NHS Trust*** *(S Kegg, P Main);* ***Coventry NHS Trust*** *(S Allan);* ***St. George's NHS Trust*** *(P Hay, M Dhillon);* ***York*** *(F Martin, S Douglas).*

UK CHIC is funded by the UK Medical Research Council (Grant numbers G0000199, G0600337 and G0900274). The views expressed in this poster are those of the researchers and not necessarily those of the Medical Research Council.