sophie_patterson@sfu.ca

Mortality among ART recipients: a comparison between patients in the United Kingdom and Canada.

S Patterson[1,2], H Samji[1], K Chan[1], A Cescon[1], S Jose[3], S Shurgold[1], JSG Montaner[1,2,4], CANOC & UK CHIC PIs*, C Sabin[3], RS Hogg[1,2], CANOC-UK CHIC Collaboration.

[1]British Columbia Centre for Excellence in HIV/AIDS, Vancouver; [2]Simon Fraser University, Burnaby; [3]Department of Infection and Population Health, University College London; [4]Faculty of Medicine, University of British Columbia.

Background

- Canada and the United Kingdom (UK) represent two high-income countries with notable differences healthcare provision and treatment guidelines for people living with HIV.

Methods

- **The Canadian Observational Cohort CANOC Collaboration** is a pan-provincial collaborative cohort of HIV+ individuals initiating ART naively in Canada. Over 10,000 participants contribute data from British Columbia, Ontario and Quebec.

- **The UK Collaborative HIV Cohort (CHIC) Study** is a collaborative cohort of 45,000 individuals from 19 participating centres within England and Scotland.

•A subset of data from the CANOC Collaboration and UK CHIC Study were merged in September 2013.

Inclusion criteria:
•Participants were presumed ART-naïve at treatment initiation, aged ≥18 years, and had initiated ART between 2000 - 2010 with ≥1 year of follow-up.
•Individuals had complete information on sex, baseline CD4 cell count and viral load, with ≥1 follow-up measure.
•Limited to individuals presumed infected via sexual transmission to improve cohort comparability.

Outcomes:
•The primary outcome of interest: all-cause mortality.
•Explanatory variables: age at ART initiation, sexual transmission risk category (MSM, heterosexual male, heterosexual female), diagnosis of AIDS-defining illness (ADI) prior to ART initiation (yes vs. no), baseline CD4 cell count (cells/μL), baseline viral load (copies/ml), composition of initial ART regimen, and era of ART initiation (2000-2003, 2004-2007, 2008-2010).

Statistical methods:
•Competing risks Cox regression evaluated the difference in mortality risk between cohort collaborations, accounting for loss to follow-up (LTFU) as a competing risk, and adjusting for key socio-demographic and clinical characteristics at baseline.
•LTFU was defined as no contact for at least 18 months.

Results

18,156 individuals were included in the analytic sample; 3,218 CANOC and 14,938 UK CHIC participants.

Table 1: Comparison of socio-demographic and clinical characteristics for the CANOC collaboration and UK CHIC Study (n=18,156)

Variable	Category	Total	CANOC n (%) or median (IQR)	UK CHIC n (%) or median (IQR)	P-value
Sex	Male Female	13458 4698	3055 (94.9) 163 (5.1)	10403 (69.6) 4535 (30.4)	<0.001
Age	-	18156	40 (34,46)	36 (31,43)	<0.001
ADI prior to ART initiation	No Yes	15127 3029	2390 (74.3) 828 (25.7)	12737 (85.3) 2201 (14.7)	<0.001
MSM risk	No Yes	7395 10761	470 (14.6) 2748 (85.4)	6925 (46.4) 8013 (53.6)	<0.001
Baseline CD4 (cells/μL)	<200 200-349 350+	8034 6772 3350	1402 (43.6) 1236 (38.4) 580 (18.0)	6632 (44.4) 5536 (37.1) 2770 (18.5)	0.351
Baseline VL (copies/ml)	<10,000 10,000-99,999 100,000+	3721 6997 7438	391 (12.2) 1356 (42.1) 1471 (45.7)	3330 (22.3) 5641 (37.8) 5967 (39.9)	<0.001
Initial 3rd drug	Nevirapine Efavirenz Lopinavir Atazanavir Other	2369 9062 2339 1520 2866	316 (9.8) 1095 (34.0) 538 (16.7) 756 (23.5) 513 (15.9)	2053 (13.7) 7967 (53.3) 1801 (12.1) 764 (5.1) 2353 (15.8)	<0.001
Backbone regimen	Tenofovir / Emtricitabine Zidovudine / Lamivudine Tenofovir / Lamivudine Abacavir / Lamivudine Stavudine/ Lamivudine Other	7386 4845 841 2286 603 2195	1215 (37.8) 742 (23.1) 262 (8.1) 513 (15.9) 283 (8.8) 203 (6.3)	6171 (41.3) 4103 (27.5) 579 (3.9) 1773 (11.9) 320 (2.1) 1992 (13.3)	<0.001
Era ART initiated	2000-2003 2004-2007 2008-2010	6614 7706 3836	1156 (35.9) 1346 (41.8) 716 (22.2)	5458 (36.5) 6360 (42.6) 3120 (20.9)	0.228

Results (continued)

•In the unadjusted analysis, the mortality rate of CANOC participants was greater than UK CHIC Study participants; 9.6 per 1000 PY (95% CI 8.1-11.2) vs. 6.8 per 1000 PY (95% CI 6.2-7.4) respectively (**Figure 1**).

•No difference in mortality risk was observed between the collaborations in the competing risks analysis, accounting for LTFU as a competing risk (adjusted hazard ratio 1.06 [95% CI 0.87-1.29]) (**Table 2**).

•The prevalence of LTFU of cohort participants was lower among the CANOC Collaboration as compared to the UK CHIC Study (10% vs. 12%, p<0.001) (**Figure 1**).

Figure 1: Comparison of crude mortality rate and loss to follow-up within the CANOC Collaboration and UK CHIC Study by era of ART initiation.

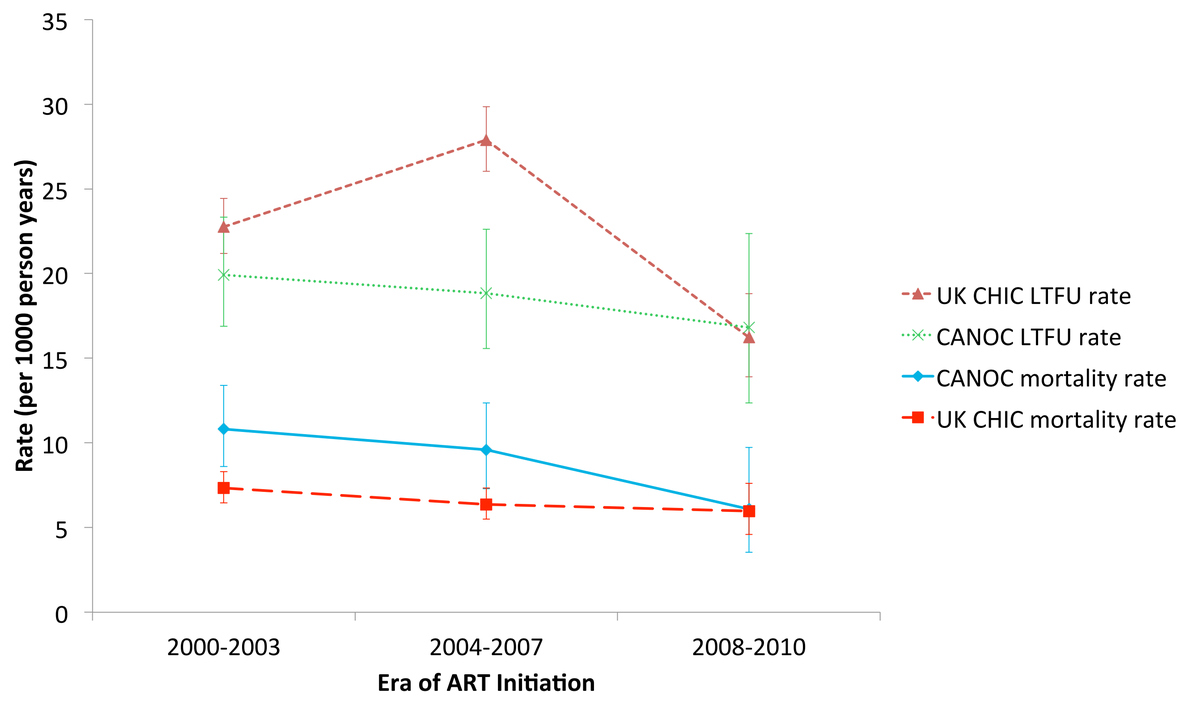

Table 2: Competing risk survival analysis of death during follow-up (n=18,156)

Variable	Unadjusted Hazard Ratio (95% CI)	P-value	Adjusted Hazard Ratio (95% CI)	P-value
Collaboration		<0.001		0.560
UK CHIC	1.00		1.00	
CANOC	1.44 (1.2-1.72)		1.06 (0.87-1.29)	
Era				
2000-2003	1.00		1.00	
2004-2007	0.79 (0.66-0.93)	0.005	0.94 (0.77-1.15)	0.540
2008-2010	0.61 (0.47-0.79)	<0.001	0.87 (0.61-1.24)	0.440
Age (per decade)	1.67 (1.56-1.79)	<0.001	1.63 (1.52-1.75)	<0.001
ADI prior to ART initiation	2.15 (1.82-2.53)	<0.001	1.65 (1.39-1.96)	<0.001
Baseline CD4 (cells/μL)				
<200	1.77 (1.39-2.25)	<0.001	1.42 (1.09-1.86)	0.009
200-349	0.95 (0.73-1.24)	0.710	0.95 (0.72-1.26)	0.720
350+	1.00		1.00	
Baseline VL (copies/ml)				
<10,000	1.00		1.00	
10,000-99,999	1.21 (0.95-1.55)	0.120	0.09 (0.84-1.41)	0.530
100,000+	1.68 (1.34-2.12)	<0.001	1.21 (0.93-1.57)	0.150
Initial 3rd Drug				
Nevirapine	1.01 (0.81-1.27)	0.920	1.14 (0.91-1.44)	0.250
Efavirenz	1.00		1.00	
Lopinavir	1.16 (0.92-1.48)	0.210	1.09 (0.85-1.39)	0.490
Atazanavir	1.13 (0.82-1.55)	0.450	1.13 (0.81-1.59)	0.470
Other	1.33 (1.09-1.64)	0.006	1.29 (1.03-1.61)	0.025
Backbone regimen				
Tenofovir / Emtricitabine	0.81 (0.65-1.01)	0.058	0.85 (0.63-1.13)	0.260
Zidovudine / Lamivudine	1.00		1.00	
Abacavir / Lamivudine	1.01 (0.77-1.33)	0.920	0.99 (0.74-1.33)	0.950
Other	1.45 (1.21-1.75)	<0.001	1.24 (1.03-1.51)	0.026

Conclusions

- CANOC participants demonstrated suboptimal baseline clinical characteristics as compared with UK CHIC Study participants, including higher HIV-RNA viral load and a greater prevalence of ADIs.
- The composition of initial ART regimen also varied significantly between the collaborations.
- All-cause mortality did not differ significantly between participants from the CANOC Collaboration and UK CHIC Study in the adjusted analysis.
- Additional studies within the CANOC-UK CHIC Collaboration evaluate virological outcomes and late initiation of ART.

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).*

***Funding**: 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.*

Acknowledgements: We would like to thank all individuals who contributed their information to the CANOC & UK CHIC Collaborations.

Canadian Observational Cohort (CANOC) collaboration

Principal Investigators: *Ann Burchell (Ontario HIV Treatment Network), Curtis Cooper (University of Ottawa, OCS Co-Investigator), Robert Hogg (British Columbia Centre for Excellence in HIV/AIDS, Simon Fraser University), Marina Klein (Montreal Chest Institute Immunodeficiency Service Cohort, McGill University), Mona Loutfy (University of Toronto, Maple Leaf Medical Clinic, OCS Co-Investigator), Nima Machouf (Clinique Medicale l'Actuel, Université de Montréal), Julio Montaner (British Columbia Centre for Excellence in HIV/AIDS, University of British Columbia), Janet Raboud (University of Toronto, University Health Network, OCS Co-investigator), Chris Tsoukas (McGill University),*

Co-Investigators: *Gloria Aykroyd (Ontario HIV Treatment Network, OHTN), Louise Balfour (University of Ottawa, OHTN Cohort Study, OCS Co-Investigator), Ahmed Bayoumi (University of Toronto, OCS Co-Investigator), John Cairney (University of Toronto, OCS Co-Investigator), Liviana Calzavara (University of Toronto, OCS Co-Investigator), Angela Cescon (British Columbia Centre for Excellence in HIV/AIDS), Kevin Gough (University of Toronto, OCS Co-Investigator), Silvia Guillemi (British Columbia Centre for Excellence in HIV/AIDS, University of British Columbia), P. Richard Harrigan (British Columbia Centre for Excellence in HIV/AIDS, University of British Columbia), Marianne Harris (British Columbia Centre for Excellence in HIV/AIDS), George Hatzakis (McGill University), Sean Hosein (CATIE), Mark Hull (British Columbia Centre for Excellence in HIV/AIDS), Don Kilby (University of Ottawa, Ontario HIV Treatment Network), Richard Lalonde (The Montreal Chest Institute Immunodeficiency Service Cohort and McGill University), Viviane Lima (British Columbia Centre for Excellence in HIV/AIDS, University of British Columbia), Ed Mills (British Columbia Centre for Excellence in HIV/AIDS, University of Ottawa), Peggy Millson (University of Toronto, OCS Co-Investigator), David Moore (British Columbia Centre for Excellence in HIV/AIDS, University of British Columbia), Alexis Palmer (British Columbia Centre for Excellence in HIV/AIDS), Anita Rachlis (University of Toronto, OCS Co-Investigator), Stanley Read (University of Toronto, OCS Co-Investigator), Sean Rourke (Ontario HIV Treatment Network, University of Toronto), Hasina Samji (British Columbia Centre for Excellence in HIV/AIDS), Marek Smieja (McMaster University, OCS Co-Investigator), Irving Salit (University of Toronto, OCS Co-Investigator), Darien Taylor (Canadian AIDS Treatment Information Exchange, OCS Co-Investigator), Benoit Trottier (Clinique Medicale l'Actuel, Université de Montréal), Sharon Walmsley (University of Toronto, OCS Co-Investigator), and Wendy Wobeser (Queens University, OCS Co-Investigator).*

Analysts and Staff: *Mark Fisher (OHTN), Sandra Gardner (University of Toronto), Nada Gataric (British Columbia Centre for Excellence in HIV/AIDS), Guillaume Colley (British Columbia Centre for Excellence in HIV/AIDS), Susan Shurgold (British Columbia Centre for Excellence in HIV/AIDS), Sergio Rueda (OHTN), and Benita Yip (British Columbia Centre for Excellence in HIV/AIDS).*

Funding: *CANOC is funded through an Emerging Team Grant from the Canadian Institutes of Health Research (CIHR) and is supported by the CIHR Canadian HIV Trials Network (CTN 242).*