

CD4:CD8 RATIO NORMALIZATION AMONG WOMEN



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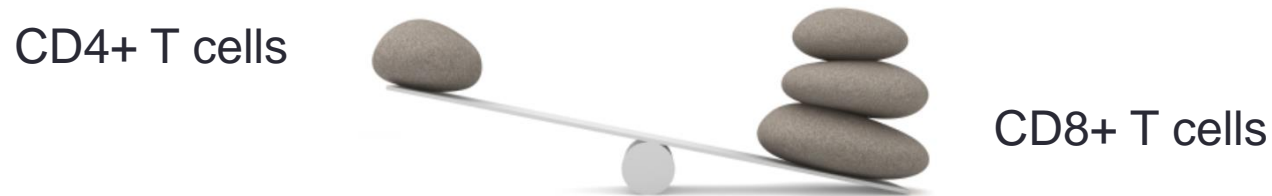
Disclosures

- I have no conflicts of interest

Overview

- Review the epidemiology and consequences of an inverted CD4:CD8 ratio
- Describe the Canadian Observational Cohort (CANOC)
 - Study design
 - Results
 - Conclusions

Implications of immune profile changes in HIV infection



- Low CD4:CD8 ratio associated with non-AIDS morbidities
 - Cardiovascular disease
 - Renal and liver disease
 - Malignancy
- Low ratio often persists despite effective ART

Low rates of CD4:CD8 ratio normalization

- CANOC - *Leung et al 2013* (2000-2010 enrollment)
 - 4206 ART-naïve participants starting cART
 - Median baseline CD4+ count 190 cells/ul
 - 7.2% achieved ratio normalization

- Italian cohort - *Mussini et al 2015* (1997-2013 enrollment)
 - 3236 ART-naïve participants who achieved virological suppression
 - Median baseline CD4+ count 223 cells/ul
 - 14% achieved ratio normalization

Predictors of ratio normalization

- CANOC - *Leung et al 2013*
 - Participants with baseline CD4 count >350, baseline CD8 <500, and suppressed VL significantly more likely to achieve ratio normalization
 - MSM associated with lower likelihood to normalize (HR 0.65)
- Thai cohort - *Han et al 2018* (1996-2017 enrollment)
 - 800 ART-naïve participants who achieved virological suppression
 - Factors associated with normalization were female sex (HR 2.47) and baseline CD4 count >350 (HR 3.65)

Impact of current treatment practices

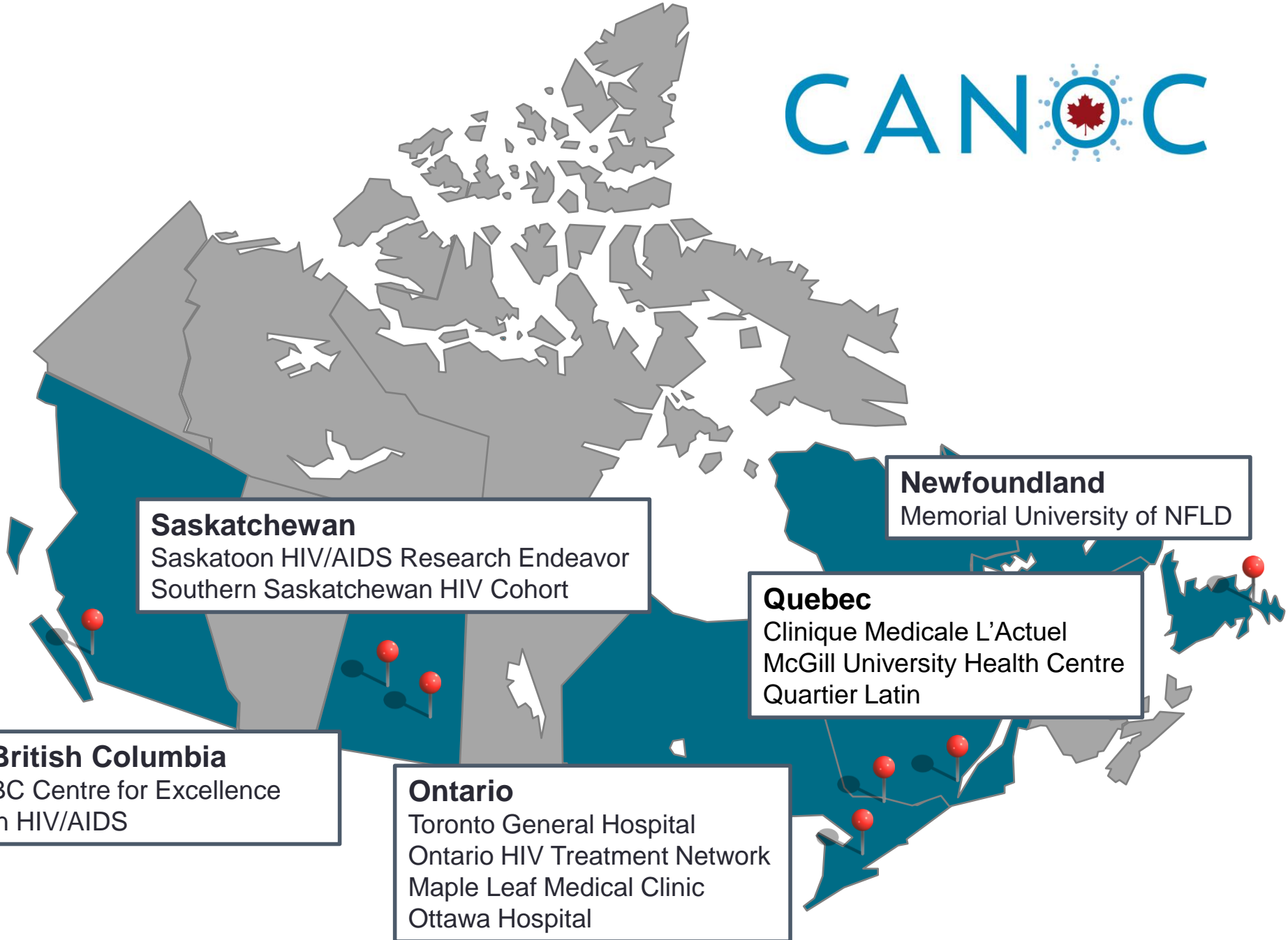
- Current treatment guidelines emphasize early initiation of cART (START trial 2015)
- Improved treatment adherence with more tolerable drugs and single tablet regimens

1. Are treatment naïve patients starting cART in the modern era more likely to achieve CD4:CD8 normalization relative to historical values?

2. Are women more likely to normalize their ratio?

Study Design

- Canadian Observational Cohort (CANOC)
 - Interprovincial collaborative cohort of HIV-infected individuals from 9 treatment centers across Canada
- Retrospective analysis of CD4:CD8 ratio normalization among participants based on gender and other baseline characteristics



Saskatchewan

Saskatoon HIV/AIDS Research Endeavor
Southern Saskatchewan HIV Cohort

Newfoundland

Memorial University of NFLD

Quebec

Clinique Medicale L'Actuel
McGill University Health Centre
Quartier Latin

British Columbia

BC Centre for Excellence
in HIV/AIDS

Ontario

Toronto General Hospital
Ontario HIV Treatment Network
Maple Leaf Medical Clinic
Ottawa Hospital

Inclusion Criteria

- Treatment naïve participants initiating cART between 2011-2016
- Participants starting on 2 NRTIs with either:
 - INSTI, NNRTI or PI
- Pre-treatment CD4:CD8 ratio <1.0
- ≥ 2 follow-up ratios within 6 months of treatment initiation

Participant Demographics

- 2650 participants
 - 344 (13%) women
 - 2306 (87%) men
- Followed for a median 2.8 years
- Median age 39

Participant Demographics

	Women (n = 344)	Men (n = 2306)
Race*		
Caucasian	28.7%	59.1%
Black	31.6%	9.6%
Other	39.7%	31.2%
HCV co-infection*	34.2%	14.4%
HBV co-infection	7.6%	11.4%
IVDU*	37.9%	10.6%
Baseline CD4 count*	306	350
Baseline CD4:CD8 ratio*	0.39	0.35

*Statistically significant differences in baseline characteristics at $p < 0.05$

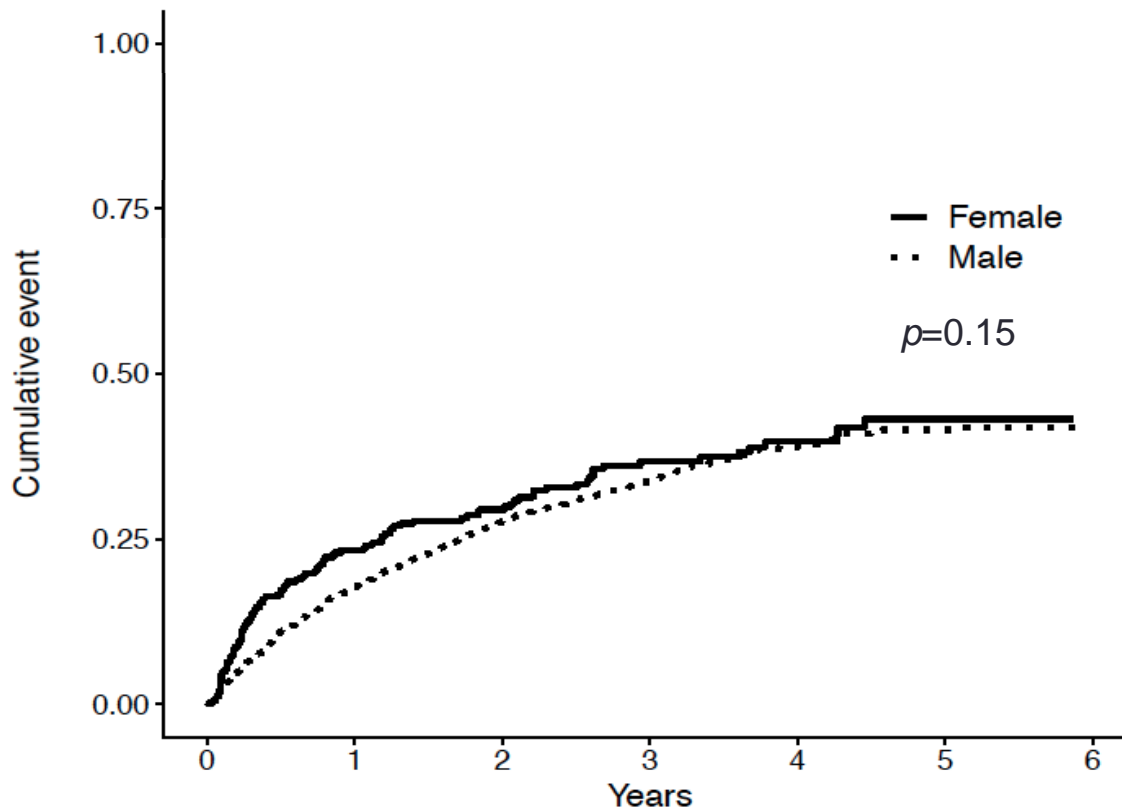
Initial ART Regimens

	Women (n = 344)	Men (n = 2306)
INSTI + 2NRTIs	80 (23%)	759 (32.9%)
NNRTI + 2NRTIs	93 (27%)	832 (36.1%)
PI + 2NRTIs	171 (49.7%)	715 (31%)

Results

- 33% of women and 30% of men normalized their ratio during follow up
- After adjusting for baseline characteristics:
 - Province, initial ART regimen, pre-treatment CD4 count, baseline viral load, risk factor, hepatitis B and C co-infection
 - Women achieved normalization with a HR=1.32 (95%CI 0.97, 1.81)

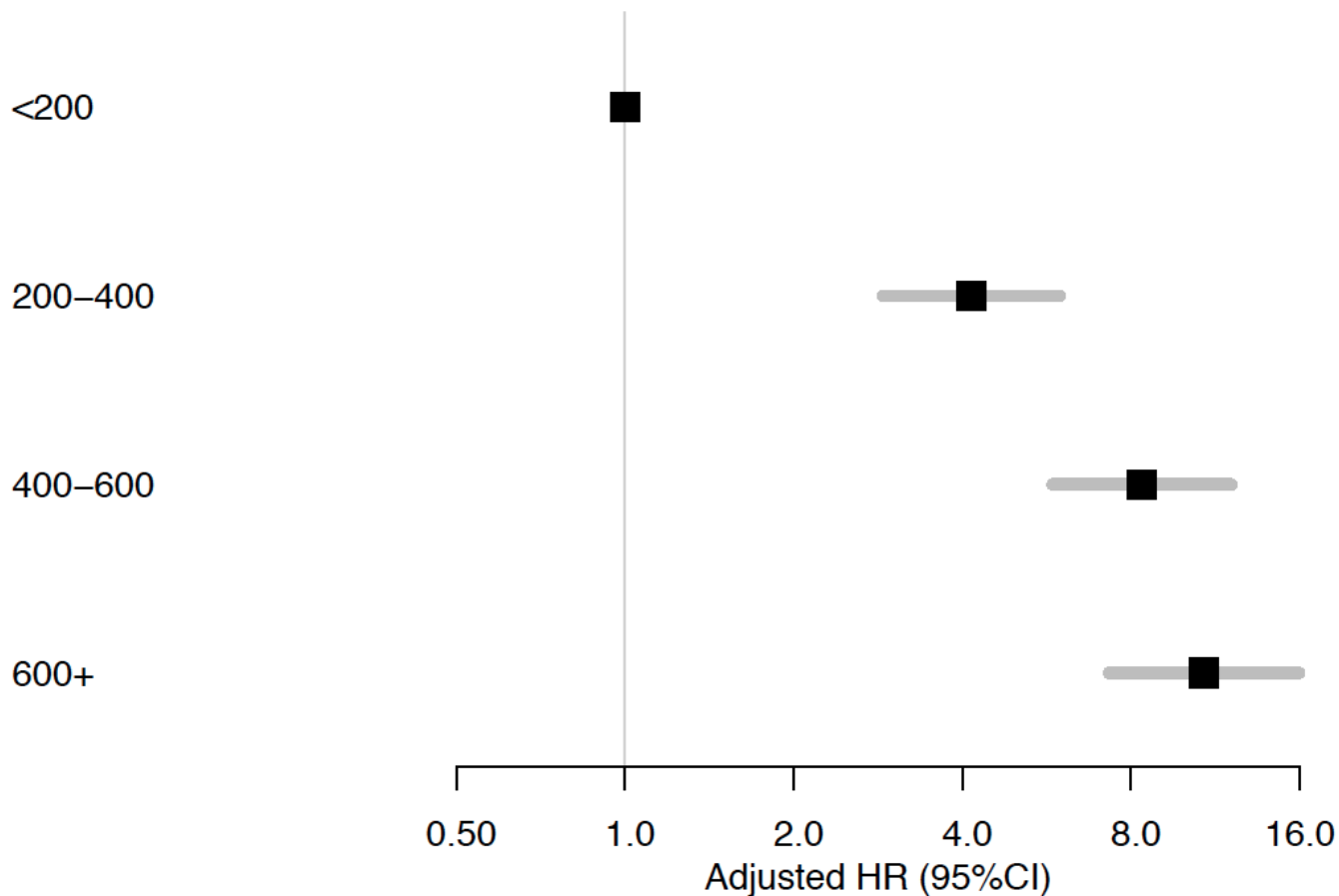
Cumulative Distribution of Time to Ratio Normalization



Year	Probability of Normalization
1	0.19 (0.17, 0.2)
2	0.28 (0.26, 0.3)
3	0.34 (0.32, 0.36)
4	0.39 (0.37, 0.41)
5	0.42 (0.39, 0.44)

Baseline CD4 count is predictive of CD4:CD8 ratio normalization

Baseline CD4 Count



Conclusions

- Higher rates of CD4:CD8 ratio normalization relative to historical values
- Early treatment initiation at higher CD4 counts is important across genders to achieve ratio normalization
- No gender differences in CD4:CD8 ratio normalization

Limitations

- No documentation of treatment interruption
- Insufficient data on individual antiretroviral drugs
- Did not account for switching between ART regimens

Future Directions

- Do increased rates of CD4:CD8 ratio normalization translate into improved health outcomes?
 - Non-AIDS morbidity
 - Mortality
- Are newer ART regimens associated with improved ratio normalization?
 - i.e. INSTI, two-drug regimens

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