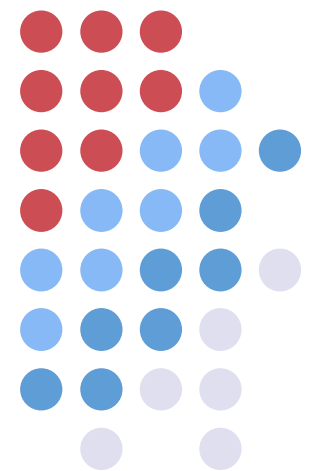
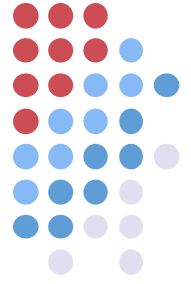


# CANOC

CIHR Team in HIV treatment  
outcomes: The Canadian  
Observational Cohort (CANOC)  
Collaboration





# Overview

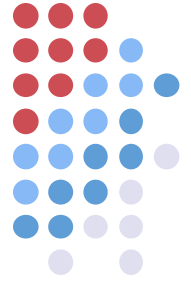
- This emerging team collaboration is an essential first step to evaluating the impact of antiretroviral care on the health and well being of persons infected with HIV/AIDS across various regions of Canada.



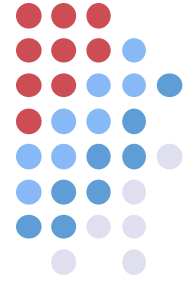
## Participating cohorts

- BC Centre for Excellence in HIV/AIDS
- Clinique Medicale L'Actuel
- Canadian Co-infection Cohort Study
- EARTH
- Maple Leaf Medical Clinic
- Montreal Chest Institute IDS
- Ontario HIV Treatment Network
- Toronto General Hospital
- University of Ottawa

# Investigators



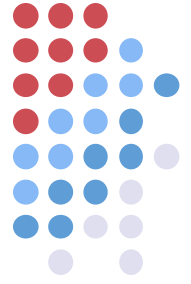
- Ms. Gloria Aykroyd (OHTN)
- Dr. Louise Balfour (OHTN, University of Ottawa)
- Dr. Ahmed Bayoumi (OHTN, University of Toronto)
- Dr. John Cairney (OHTN, University of Toronto)
- Dr. Liviana Calzavara (OHTN, University of Toronto)
- **Dr. Curtis Cooper** (OHTN, University of Ottawa)
- Dr. Kevin Gough (OHTN, University of Toronto)
- Dr. Silvia Guillemi (DTP, University of British Columbia)
- Dr. Richard Harrigan (DTP, University of British Columbia)
- Dr. Marianne Harris (DTP, Canadian HIV Trials Network)
- Dr. George Hatzakis (EARTH, University of Southern California, LA)
- **Dr. Robert Hogg** (DTP, Simon Fraser University)
- Dr. Don Kilby (OHTN)
- **Dr Marina Klein** (MCH and HIV/HCV, McGill University)
- Dr. Viviane Lima (DTP and the University of British Columbia)
- **Dr. Mona Loutfy** (OHTN, University of Toronto)
- **Dr. Nima Machouf** (Clinique medicale L'Actuel, Universite de Montreal)
- Dr. Ed Mills (DTP)
- Dr. Peggy Millson (OHTN, University of Toronto)
- **Dr. Julio Montaner** (DTP, University of British Columbia)
- Dr. David Moore (DTP, University of British Columbia)
- **Dr. Janet Raboud** (OHTN, University of Toronto)
- Dr. Anita Rachlis (OHTN, University of Toronto)
- Dr. Stanley Read (OHTN, University of Toronto)
- **Dr. Sean B. Rourke** (OHTN, University of Toronto, St. Michael's Hospital)
- Dr. Irving Salit (OHTN, University of Toronto)
- **Dr. Marek Smieja** (OHTN, McMaster University)
- Dr. Benoit Trottier (Clinique medicale L'Actuel, Universite de Montreal)
- **Dr. Chris Tsoukas** (EARTH, McGill University)
- Dr. Sharon Walmsley (OHTN, University of Toronto)
- Dr. Wendy Wobeser (OHTN, Queen's University)



# Objectives

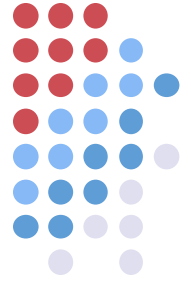
- To develop a nationally and internationally recognized and policy-relevant program of research in HIV therapeutics and population and public health and to build upon the expertise of Canadian researchers
- To establishing training and research opportunities for graduate students, post-doctoral fellows and clinicians across the country interested in HIV/AIDS cohort research
- To improve research dissemination to physicians and persons living with HIV and to improve the knowledge translation of research on HIV/AIDS therapeutics into provincial, national and international HIV/AIDS treatment guidelines

# Vision



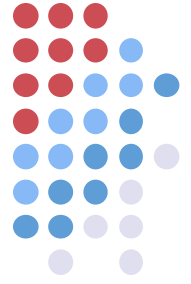
- To focus initially on a limited number of high-impact research questions that take advantage of the uniqueness of this cohort collaboration.
  - Up-to-date data on modern regimens in treatment naïve persons starting ART
  - Wealth of sociodemographic data
  - Potential for linkages to gather high quality data on vital statistics and major diagnoses

# Vision

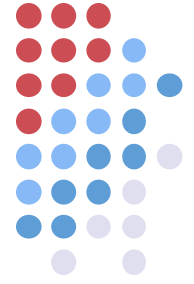


1. To perform studies that compare regional differences in health outcomes and access to care that can inform Canadian and global policies for HIV treatment
2. To perform high impact clinically relevant research that can inform HIV treatment decisions.

# Guiding Principles



- Multidisciplinary approach
- Build upon the expertise of Canadian researchers
- Longitudinal consideration of treatment effects as well as patient and other socio-demographic, geographic, and care-related factors

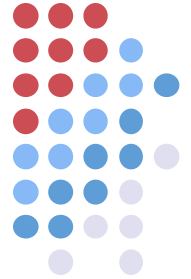


# Data Overview

- Current criteria for inclusion:
  - First HAART therapy date  $\geq$  Jan 1<sup>st</sup>, 2000
  - Must have a baseline CD4 and baseline viral load
  - Baselines must be from within the six months prior to therapy

# Data Overview

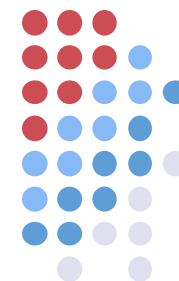
## ARV Start Dates



Naïve Start of ARV	B.C. (N = 1910)	Ontario (N = 1620)	Quebec (N = 1260)	Overall (N = 4790)
Year 2000-2002	810 (42.4%)	512 (31.6%)	372 (29.5%)	1694 (35.4%)
Year 2003-2005	922 (48.3%)	583 (36.0%)	417 (33.1%)	1922 (40.1%)
Year 2006-2008	178 ( 9.3%)	525 (32.4%)	471 (37.4%)	1174 (24.5%)

# Data Overview

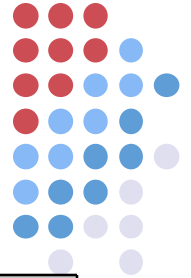
## First therapy



First Therapy	B.C. (N = 1910)	Ontario (N = 1620)	Quebec (N = 1260)	Overall (N = 4790)
<b>Nuc 2, NN</b>	837 (43.8%)	270 (46.2%)	224 (37.1%)	1312 (42.2%)
<b>Nuc 2, PI Boosted</b>	851 (44.6%)	109 (18.6%)	168 (27.8%)	1125 (34.2%)
<b>Nuc 2, PI Single</b>	174 (9.1%)	95 (16.2%)	97 (16.1%)	346 (12.8%)
<b>Nuc 3</b>	47 (2.5%)	21 (1.3%)	102 (8.1%)	170 (3.5%)
<b>Other</b>	1 (0.1%)	223 (13.8%)	95 (7.6%)	319 (7.6%)

# Data Overview

## Gender and Ethnicity

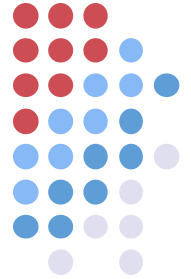


Gender	B.C. (N = 1910)	Ontario (N = 1620)	Quebec (N = 1260)	Overall (N = 4790)
Male	1505 (78.8%)	1324 (81.2%)	1022 (81.1%)	3851 (80.4%)
<b>Ethnicity</b>				
Known Ethnicity	1332 (69.7%)	699 (43.1%)	167 (13.3%)	2198 (45.9%)
<b>Among those known:</b>				
Black	32 (2.4%)	208 (29.8%)	20 (12.0%)	260 (11.8%)
Caucasian	534 (40.1%)	394 (56.4%)	139 (83.2%)	1067 (48.5%)
Asian	31 (2.3%)	36 (5.2%)	0 (0.0%)	67 (3.0%)
First Nation	123 (9.2%)	18 (2.6%)	4 (2.4%)	145 (6.6%)
Hispanic	25 (1.9%)	10 (1.4%)	4 (2.4%)	39 (1.8%)
More than 1 reported	527 (42.9%)	1 (0.2%)	0 (0.0%)	573 (26.1%)
Other	15 (1.1%)	32 (4.6%)	0 (0.0%)	47 (2.1%)
<b>Aboriginal Descent*</b>				
	149 (11.2%)	12 (2.6%)	4 (2.4%)	171 (7.8%)

\*Aboriginal Descent includes individuals of mixed race who have identified Aboriginal ancestry.

# Data Overview

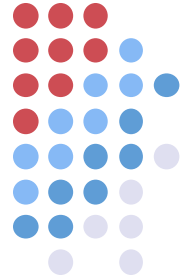
## Age at Enrollment



Baseline Age (Years)	B.C.	Ontario	Quebec	Overall
Median	40	40	40	40
Inter Quartile Range	34 - 47	34 - 46	34 - 46	34 - 46

# Data Overview

## Risk Factors and Co-Infection



	B.C. (N = 1910)	Ontario (N = 1620)	Quebec (N = 1260)	Overall (N = 4790)
<b>Baseline AIDS</b>	<b>290 (15.2%)</b>	<b>130 (7.8%)</b>	<b>154 (12.3%)</b>	<b>574 (12.0%)</b>
<b>Injection Drug Use: Ever</b>	<b>490 (25.7%)</b>	<b>121 (7.5%)</b>	<b>158 (12.5)<sup>(b)</sup></b>	<b>769 (16.1%)</b>
<b>Tested for Hep C Ab</b>	<b>1263 (66.1%)</b>	<b>1507 (93.0%)</b>	<b>923 (73.2%)<sup>(a)</sup></b>	<b>3152 (65.8%)</b>
<b>Positive for HCV Ab*</b>	<b>566 (44.8%)</b>	<b>185 (11.7%)</b>	<b>106 (27.3)<sup>(a)</sup></b>	<b>857 (26.5%)</b>

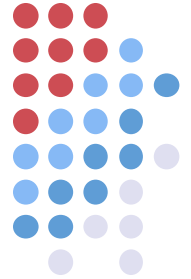
(a) IDTC May only have reported positive tests for Hep C antibodies and not those individuals tested for Hep C who were negative. The CCC cohort portion of this group is a co-infection cohort, Hep C co-infection in the CCC cohort is 100%.

(b) For the purpose of this calculation patients in the MUHC cohort with no history of Injection drug use (IDU = 0) and an unknown history of drug use (IDU = NULL) were both taken to be negative for injection drug use.

\* If the patient was tested for Hep C Ab

# Data Overview

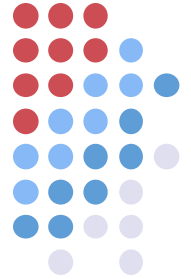
## Baseline CD4



Baseline CD4 Measurements	B.C.	Ontario	Quebec	Overall
(cells/mm <sup>3</sup> )	(N = 1910)	(N = 1615)	(N = 1253)	(N = 4778)
Median	170	210	220	192
Inter Quartile Range	70 - 250	116 - 306	130 - 299	100 - 280

# Data Overview

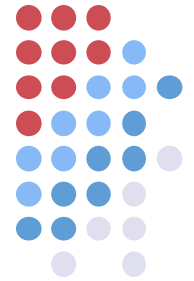
## Baseline Viral Load



Baseline Viral Load Measurements	B.C.	Ontario	Quebec	Overall
(c/mL)	(N = 1910)	(N = 1620)	(N = 1260)	(N = 4790)
<b>Median</b>	>100,000	67,841	53,370	80,500
<b>Inter Quartile Range</b>	39,200 – >100,000	16,534 - >100,000	12,479 – >100,000	21,300 - >100,000

# Data Overview

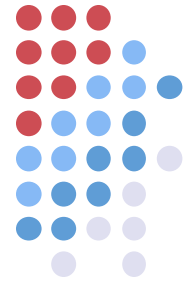
## Length of Follow-up



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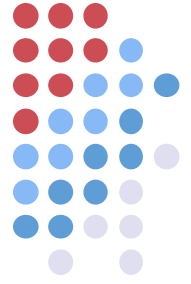
Follow-up time (Months)	B.C.	Ontario	Quebec	Overall
<b>Median</b>	38.8	33.0	30.7	35.0
<b>Inter Quartile Range</b>	20.9 - 59.8	14.0 - 60.2	11.3 - 58.3	16.2 - 59.4

# Census data by province compared to CANOC data



Province	Aboriginal Identity (%)			Median Income (\$)			Prevalence Low Income (%)			Unemployment (%)			High School Education (%)		
	CANOC	General	p-value	CANOC	General	p-value	CANOC	General	p-value	CANOC	General	p-value	CANOC	General	p-value
BC (1606)	2.2	4.8	<0.001	24,284	24,867	0.138	16.7	13.3	<0.001	5.9	6.0	0.192	82.5	80.1	<0.001
ON (1337)	0.5	2.0	<0.001	26,790	27,258	0.030	15.4	11.7	<0.001	7.0	6.4	<0.001	84.7	77.8	<0.001
QC (1268)	0.0	1.5	<0.001	21,220	24,430	<0.001	22.2	12.3	<0.001	8.2	7.0	<0.001	78.5	75.0	<0.001
CANADA	0.8	3.8	<0.001	23,982	25,615	<0.001	17.6	11.6	<0.001	6.7	6.6	0.266	81.9	76.2	<0.001

# Current Projects (1)



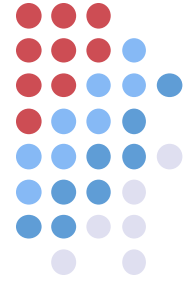
## Regional Differences in Rates of Viral Load Testing in Canada

**Lead Investigator:** Dr. Janet Raboud

**Background:** Frequency of viral load measurement is sometimes used as an indicator of quality of care of HIV infected individuals.

**Objective(s):** To examine whether regional and individual characteristics will be associated with differential use of viral load (VL) testing in Canada, where testing is available without charge to all HIV positive patients with provincial health insurance.

\* Accepted for publication in BMC ID



# Current Projects (2)

**Clinical outcomes associated with CD4 cell counts among virologically suppressed patients at one- and two-years after HAART initiation**

**Lead Investigators:** Mona Loutfy

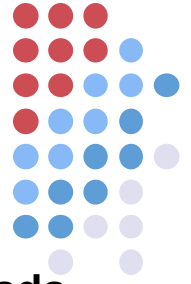
**Background:** It is unclear whether the traditionally used CD4 cell count threshold of 200 cells is the appropriate target by which to define immunologic non-response at all time-points in follow-up. Therefore, we would attempt to establish clinically important absolute CD4 cell count thresholds at one- and two-years after HAART initiation and see how these derived thresholds (if not 200 cells) compare with the traditional definition.

## **Objective(s)**

- 1:** To define absolute CD4 cell count thresholds at one year and two years after HAART initiation among virologically suppressed individuals, for which failure to achieve such thresholds impart increased risk for subsequent clinical events (AIDS or death).
- 2:** To examine the determinants of immunologic non-response among virologically suppressed patients one and two years after HAART initiation.

\* Final draft being circulated

# Current Projects (3)



**Time to virologic suppression among HIV-infected individuals on HAART in Canada**

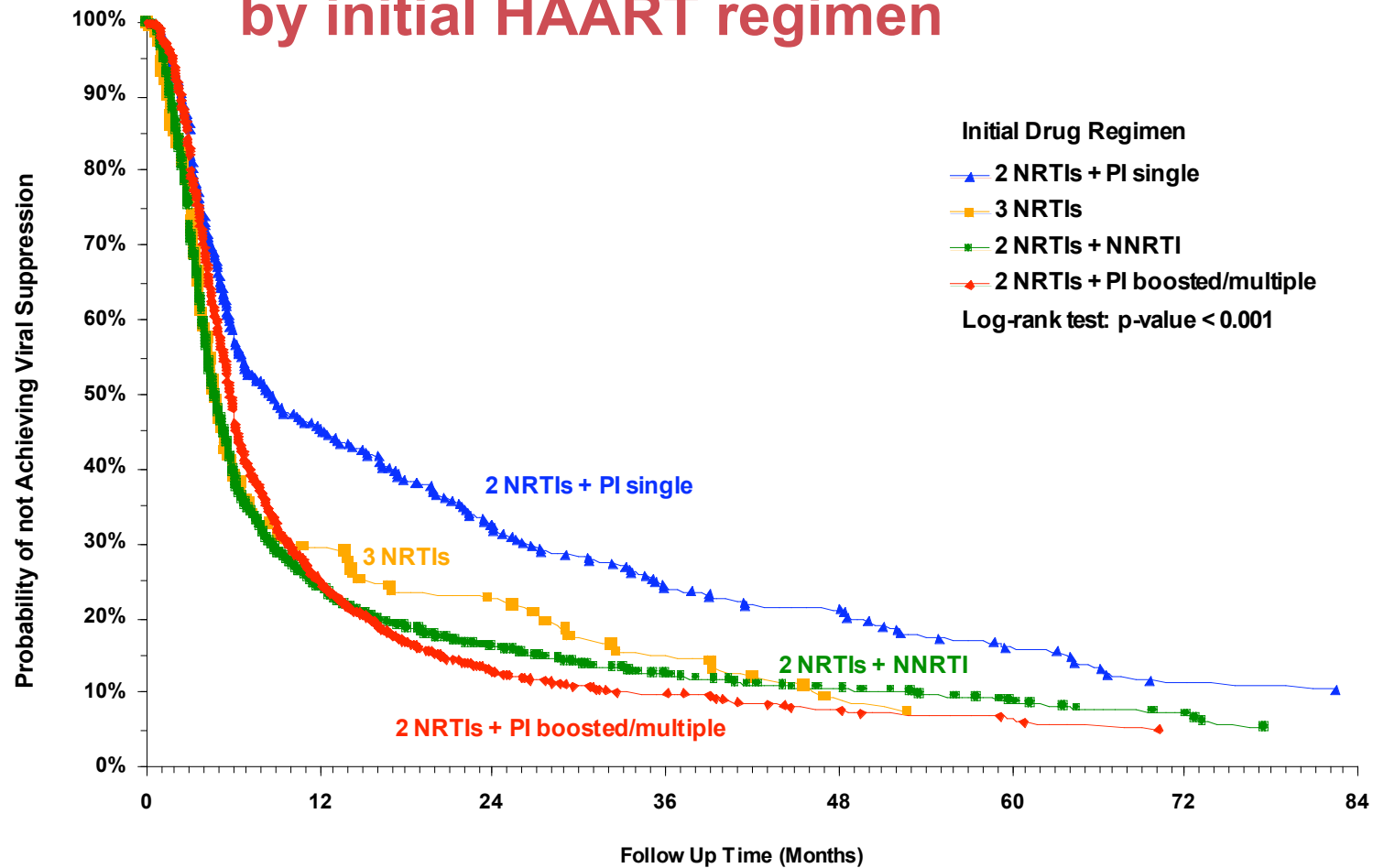
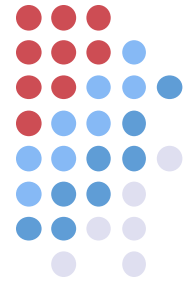
**Lead Investigator(s):** Drs. Curtis Cooper and Bob Hogg

**Background:** Complete HIV virologic suppression is a critically important objective following the initiation of HAART. Mortality, hospitalization, and risk for opportunistic infection are diminished when individuals on HAART achieve and maintain virologic suppression. Furthermore, the risk of these outcomes is reduced with complete suppression compared to partial suppression. Failure to achieve and maintain HIV viral load suppression results in the development of drug resistance, which increases morbidity and reduces future therapeutic options. Identifying factors that predict time to virologic suppression is thus vital to optimizing therapeutic success

**Objective(s):** To evaluate factors associated with virologic suppression in a Canadian cohort of individuals on HAART.

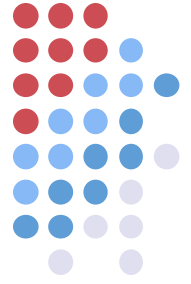
\* Draft being finalized

# Probability of not suppressing by initial HAART regimen



	Month	0	12	24	36	48	60	72	84
2 NRTIs + PI single	N=382		146	90	56	40	27	14	6
2 NRTIs + NNRTI	N=1774		343	189	119	83	41	17	4
2 NRTIs + PI boosted/multiple	N=1729		333	118	71	32	12	5	2
3 NRTIs	N=155		41	26	15	7	1	0	0

# Current Projects (4)

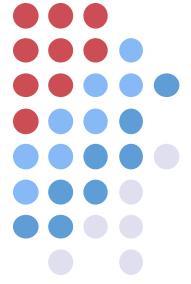


**Similar times to virologic suppression and switching for abacavir(ABC)/3TC and tenofovir(TDF)/FTC in antiretroviral-naive HIV-positive patients starting therapy.**

**Lead Investigator:** Dr. Mona R. Loutfy

**Background:** On the basis of the ACTG 5202 trial, DAD and SMART study results, ABC/3TC has been moved to an “alternative” dual fixed-dose NRTI option for treatment of naive HIV-positive patient in the DHSS guidelines; but it remains as a “preferred” option in international and European guidelines.

**Objective(s):** To compare 1. time to virologic suppression and 2. time to switch or stop of ABC/3TC or TDF/FTC in ART-naive HIV-positive patients who started cART containing either ABC/3TC or TDF/FTC.



# Current Projects (5)

**Should NRTI Still be Used in Salvage Regimens, with New Classes/ generations of Antiretrovirals in Three-class-experienced, Multi-drug Resistant Patients?**

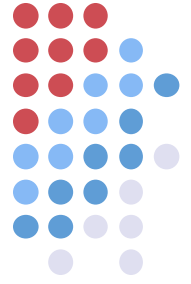
**Lead Investigator(s):** Dr. Nima Machouf

**Background:** Traditionally, an ARV regimen almost always includes a combination of 2 NRTIs, plus either an NNRTI or a PI. In multi-drug resistant (MDR) patients, those NRTI show possibly little antiviral activity, and can be associated with toxicity, drug interactions and cost several hundred dollars per month.

**Objective(s):** To evaluate the impact of using different numbers of NRTIs on the virologic efficacy of salvage regimens

\* Awaiting resistance data

# Current Projects (6)



**Persistent low-level viremia is associated with increased risk of virologic failure and mortality**

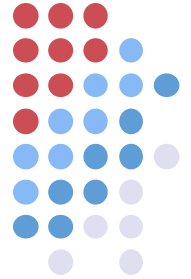
**Lead Investigator(s):** Dr. Mark Hull

**Background:** Detection of transient or persisting low-level viremia with plasma viral load  $>50$  copies/mL(c/mL) remains common amongst patients receiving antiretroviral therapy (ART).

**Objective(s):** The purpose of this study was to evaluate the effect of ongoing viremia on risk of virologic rebound and mortality.

\* Accepted to CROI 2010

# Current Projects (7)



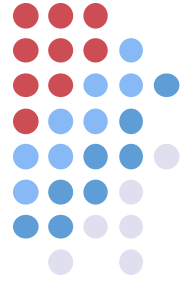
**Regional differences in demographics, antiretroviral use and response among HIV+ women in Canada**

**Lead Investigator(s):** Rebecca Harrison, Angela Cescon, Dr. Mona Loutfy

**Background:** Women represent one of one of Canada's fastest growing HIV-positive populations. Investigating regional trends in order to characterize and better understand this growing epidemic will allow for the creation of more effective and policy-relevant gender-specific programming where most needed.

**Objective(s):** To (1) evaluate the interprovincial differences in demographics and antiretroviral treatment (ART) use of HIV positive women, and (2) evaluate the interprovincial differences in viral response (suppression and rebound).

# Current Projects (8)



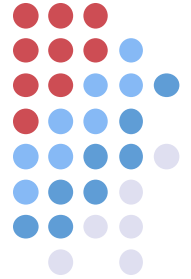
**Impact of different HIV viral load assays on viral load “blip” rates and their association with virologic failure**

**Lead Investigator(s):** Troy Grennan and Dr. Janet Raboud

**Background:** Virologic blips may occur when HIV replication bursts from stable reservoirs, ongoing cycles of replication, random statistical or biologic variation or laboratory error.

**Objective(s):** We studied the predictors of virologic ‘blips’ and compared duration of virologic suppression of patients with one or more blips, to patients without virologic blips among antiretroviral therapy (ART)-naive patients starting combination ART.

# Working Groups



## **Resistance Working Group**

- Dr. Nima Machouf, Dr. Richard Harrigan, Dr. Bob Hogg, Mark Fisher

## **Cardiovascular Working Group**

- Dr. Marek Smieja, Dr. Janet Raboud, Dr. Marina Klein

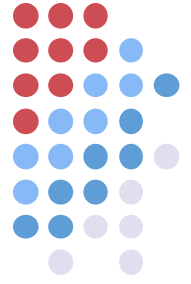
## **Women's Health Working Group**

- Dr. Mona Loutfy and others

## **Cancer Working Group**

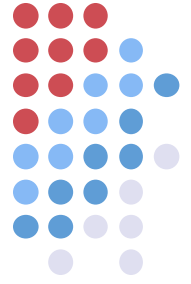
- To be determined in the next year of study

# Linkages?



- Vital Stats
- Canadian Cancer Agency
- Resistance Data

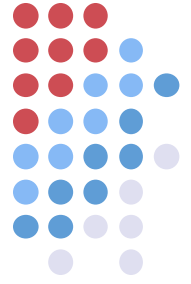
# Current Community Advisory Committee (CANOC-CAC)



## Membership

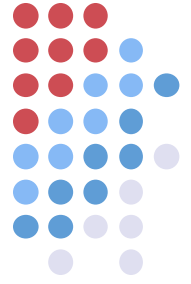
- **5 representatives**
  - Sean Hosein (chair): Ontario
  - Shari Margolese: Ontario
  - Zoran Stjepanovic: British Columbia
  - Bruno Lemay: Québec
  - Evelyne Ssendendo: Manitoba
- **Diverse backgrounds**
- **Representative of the HIV-affected communities**
- **Rotating membership with a two-year term**

# Community Advisory Committee (CANOC-CAC)



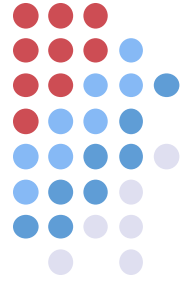
## Functions

- To advise on and help build community partnerships
- To contribute to research questions
- To assist with knowledge translation



# Scholarships/Awards

- First annual competition launched July 1, 2008
- Funding is for 1 year, at a funding level consistent with CIHR's funding scales, and according to CIHR policies
- \$100K available annually to support trainees



# Awardees (2009)

1. **Aranka Anema** (PhD Candidate, UBC)

**Project:** Assessing the impact of food insecurity and malnutrition on HIV treatment outcomes

2. **Tony Antoniou** (MSc level, post-PharmD, U of Toronto)

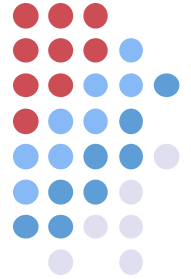
**Project:** Pharmacoepidemiologic research using the CANOC database

3. **Luke Swenson** (MSc Level, UBC)

**Project:** HIV immune escape and drug resistance mutations as probes for pathogenesis, abacavir hypersensitivity, and emergence of antiretroviral drug resistance

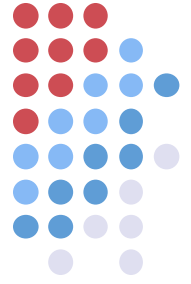
# Website

- Please visit [www.canoc.ca](http://www.canoc.ca)
- CTN Forum blog



# Discussion

- Questions/concerns



**Thank you**

