HAART as Prevention:
Integrating Research and Clinical Care

Thomas Kerr

Urban Health Research Initiative,
British Columbia Centre for Excellence in HIV/AIDS
Faculty of Medicine, University of British Columbia

British Columbia
Centre *for* Excellence
in HIV/AIDS

URBAN
HEALTH
RESEARCH
INITIATIVE

UHRI

Vancouver's raging HIV epidemic most rampant in developed world

Nearly half the 6,000 to 10,000 addicts in Downtown Eastside are infected, AIDS expert says.

MARGARET MUNRO

The HIV epidemic raging at the heart of Vancouver is now considered to be the most rampant in the developed world.

Close to half the 6,000 to 10,000 addicts who frequent the seedy hotels and back alleys in the Downtown Eastside are believed to be infected with the AIDS-causing virus, which passes from drug user to drug user on the tips of used syringes.

Thousands more in Surrey and New Westminster, where the virus is known to be spreading, are also threatened, as are native Indian communities around the province and young street people.

"Basically, I don't think it gets any worse," said veteran AIDS researcher Dr. Martin Schechter, whose team is documenting how a potent mixture of drugs, despair and poverty is fueling the epidemic.

According to studies at the B.C. Centre for Excellence in HIV/AIDS, the infection rate among injection drug users in Vancouver has been running at close to 20 per cent per year. "What that means is that out of every 1,000 people who are negative at the beginning of the year, 200 will become infected by the

GRIM WARNING: Dr. David Patrick, who is charting the HIV epidemic in Vancouver, stands before Carnegie Centre at Main and Hastings where sign on door says it all. Nearly 50 per cent of area's injection drug users are believed infected.

end of the year," said Schechter, who is co-director of the centre.

"This is the highest incidence rate we know of in the developed world."

Bangkok, Edinburgh, and New York likely experienced similar infection rates when the virus swept through their injection drug using communities, but he said Vancouver's rate is higher now.

"It's not a very good way to get well known," said Schechter, referring to the way the Vancouver epidemic is attracting attention from around the world.

People with new infections, if untreated, will go on to develop AIDS in five to 10 years.

Needle exchange is not enough: lessons from the Vancouver injecting drug use study

Steffanie A. Strathdee*‡, David M. Patrick†§, Sue L. Currie*,
Peter G.A. Cornelisse*, Michael L. Rekart†§, Julio S.G. Montaner*§¶,
Martin T. Schechter*‡ and Michael V. O'Shaughnessy*¶#

Objective: To describe prevalence and incidence of HIV-1, hepatitis C virus (HCV) and risk behaviours in a prospective cohort of injecting drug users (IDU).

Setting: Vancouver, which introduced a needle exchange programme (NEP) in 1988, and currently exchanges over 2 million needles per year.

Design: IDU who had injected illicit drugs within the previous month were recruited through street outreach. At baseline and semi-annually, subjects underwent serology for HIV-1 and HCV, and questionnaires on demographics, behaviours and NEP attendance were completed. Logistic regression analysis was used to identify determinants of HIV prevalence.
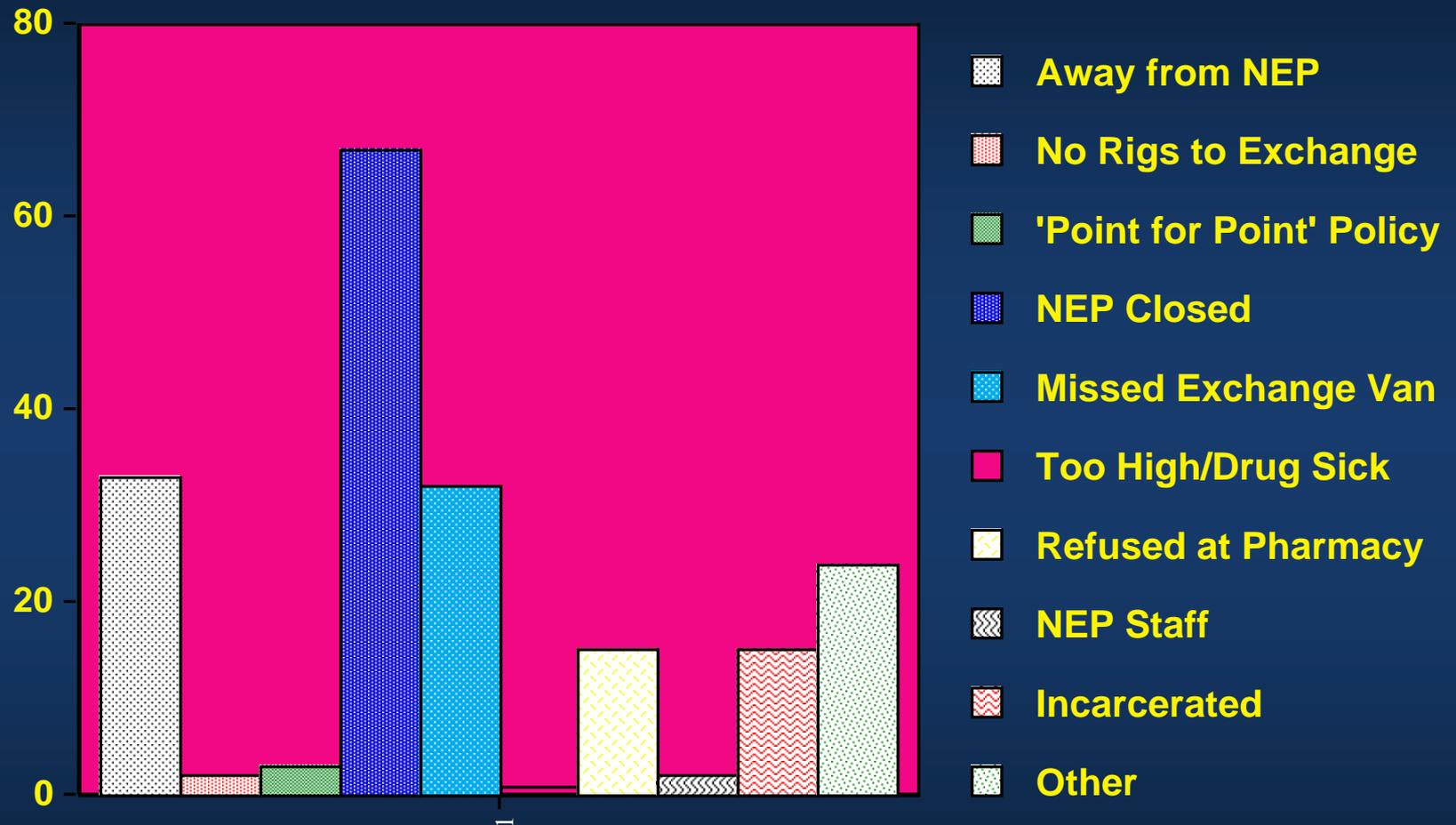
Results: Of 1006 IDU, 65% were men, and either white (65%) or Native (27%). Prevalence rates of HIV-1 and HCV were 23 and 88%, respectively. The majority (92%) had attended Vancouver's NEP, which was the most important syringe source for 78%. Identical proportions of known HIV-positive and HIV-negative IDU
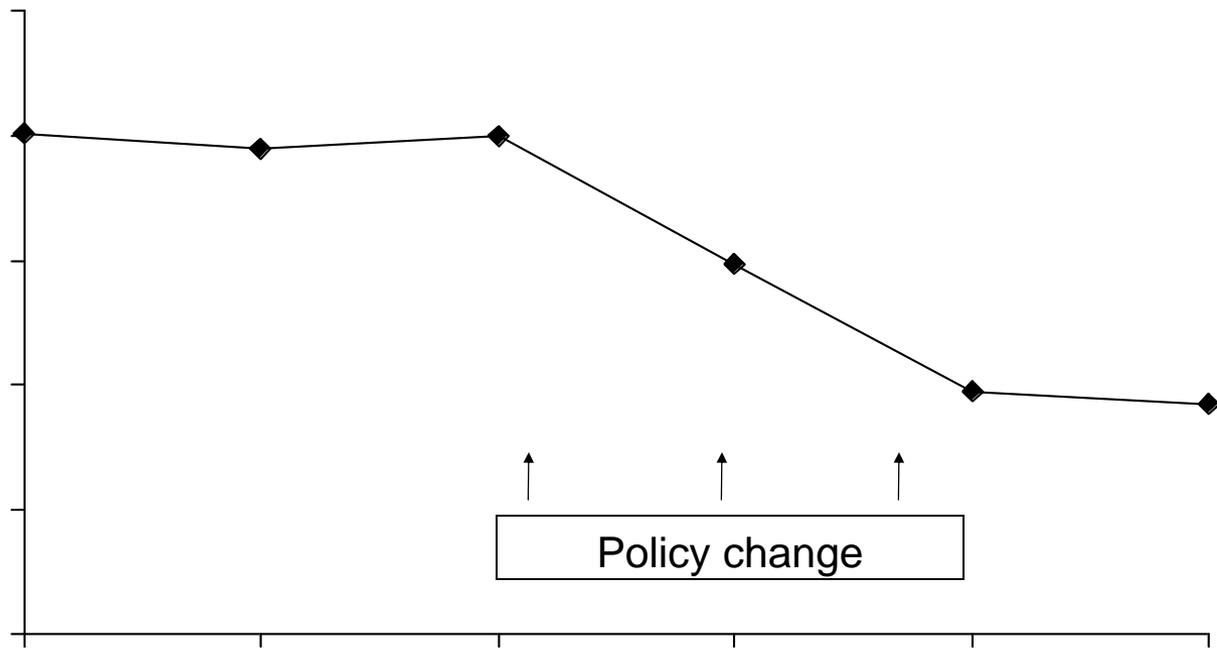
Table 1. Logistic regression analysis of factors associated with high-risk needle sharing during the past 6 months.

Variable	Adjusted odds ratio	95% CI
Hard to get clean needles (Yes versus no)	3.43	(2.11–5.58)
Bingeing (Yes versus no)	1.80	(1.13–2.86)
Cocaine use frequency (> 1 daily versus < 1)	2.01	(1.23–3.29)
Gender (Male versus female)	1.93	(1.17–3.19)
NEP as exclusive syringe source (Yes versus no)	0.46	(0.28–0.77)

CI, Confidence interval; NEP, needle exchange programme.
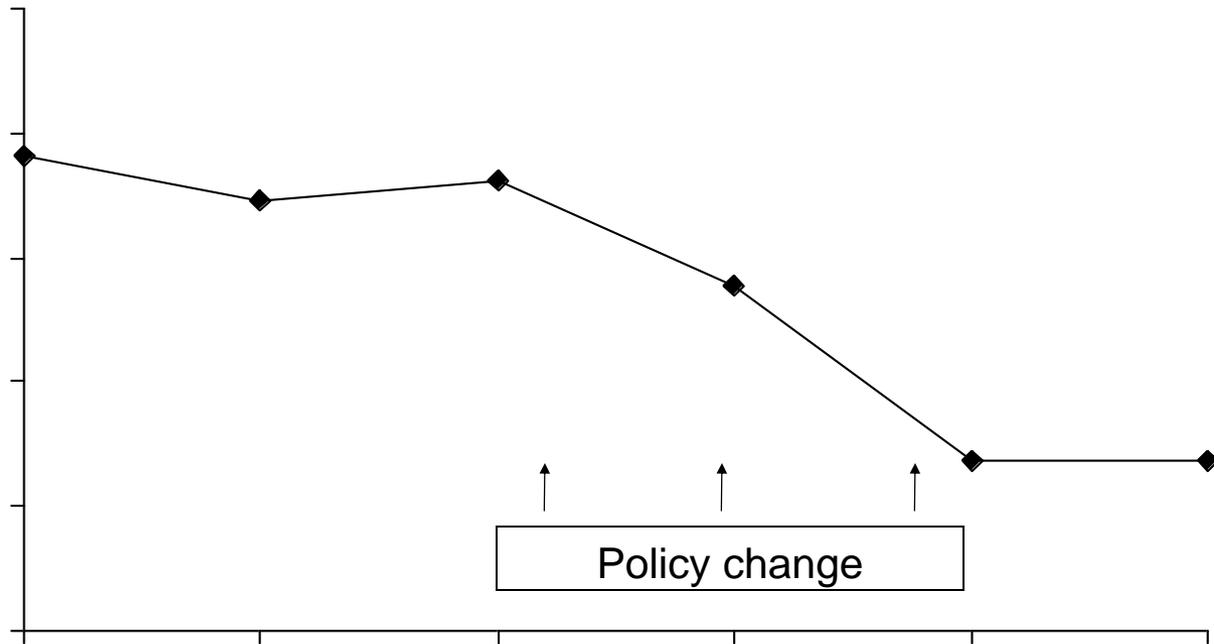
Reasons for difficulty accessing syringes

Legend:
- Away from NEP
- No Rigs to Exchange
- 'Point for Point' Policy
- NEP Closed
- Missed Exchange Van
- Too High/Drug Sick
- Refused at Pharmacy
- NEP Staff
- Incarcerated
- Other

Policy change

Policy change

Table 1a. Multivariate GEE* of factors associated with syringe borrowing.

Characteristic	Adjusted Odds Ratio (95% CI‡)	p-value
Age	0.97 (0.96 - 0.98)	<0.001
Gender (male vs. female)	1.14 (0.92 - 1.42)	0.241
Aboriginal ethnicity (yes vs. no)	0.64 (0.50 – 0.81)	<0.001
Daily heroin injection (yes vs. no)	1.31 (1.13 - 1.52)	<0.001
Daily cocaine injection (yes vs. no)	1.34 (1.16 - 1.54)	<0.001
HIV positive serostatus (yes vs. no)	0.70 (0.56 - 0.87)	0.002
Period of interest (after 2001)	0.57 (0.49 - 0.65)	<0.001

Table 1b. Multivariate GEE* of factors associated with syringe lending.

Characteristic	Adjusted Odds Ratio (95% CI‡)	p-value
Age	0.97 (0.96 - 0.98)	<0.001
Gender (male vs. female)	1.63 (1.32 - 2.03)	<0.001
Aboriginal ethnicity (yes vs. no)	0.62 (0.49 – 0.79)	<0.001
Daily heroin injection (yes vs. no)	1.53 (1.32 - 1.79)	<0.001
Daily cocaine injection (yes vs. no)	1.20 (1.03 - 1.41)	0.021
HIV positive serostatus (yes vs. no)	0.49 (0.39 – 0.62)	<0.001
Period of interest (after 2001)	0.52 (0.45 - 0.60)	<0.001

* GEE = Generalized Estimating Equation
‡ CI = Confidence Interval

Table 2. Multivariate Cox proportional hazard analyses of time to HIV infection.

Characteristic	Adjusted Hazard Ratio (95% CI‡)	p - value
Age	0.99 (0.97 - 1.00)	0.129
Gender (male vs. female)	1.12 (0.77 - 1.62)	0.561
Aboriginal ethnicity (yes vs. no)	1.71 (1.19 - 2.46)	0.004
Daily heroin injection (yes vs. no)	1.10 (0.76 - 1.58)	0.626
Daily cocaine injection (yes vs. no)	3.19 (2.22 - 4.57)	<0.001
Unprotected sex[†] (yes vs. no)	0.84 (0.57 - 1.20)	0.307
Period of interest (after 2001)	0.13 (0.06 - 0.31)	<0.001

* GEE = Generalized Estimating Equation
‡ CI = Confidence Interval
† Denotes unprotected vaginal or anal intercourse

The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic

Julio S G Montaner, Robert Hogg, Evan Wood, Thomas Kerr, Mark Tyndall, Adrian R Levy, P Richard Harrigan

"The upshot of this widespread failure to recognize that AIDS is an exceptional crisis and threat is that the response to the pandemic is not made commensurate to the challenges—and so the epidemic escalates even while it erodes our capacities to check it."

Dr Peter Piot, UNAIDS Executive Director[1]

(THE LANCET) RED

"The fundamental challenge we face is to sustain a full-scale AIDS response over at least another generation."
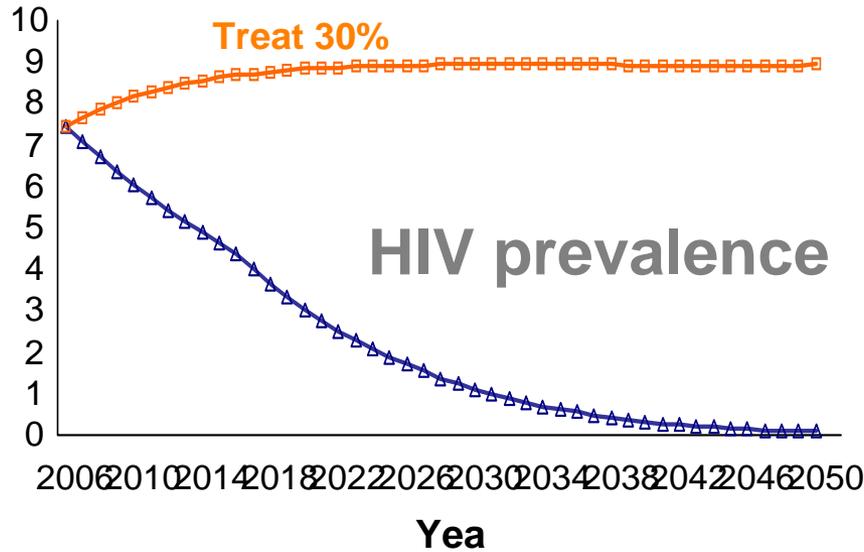
International AIDS Society
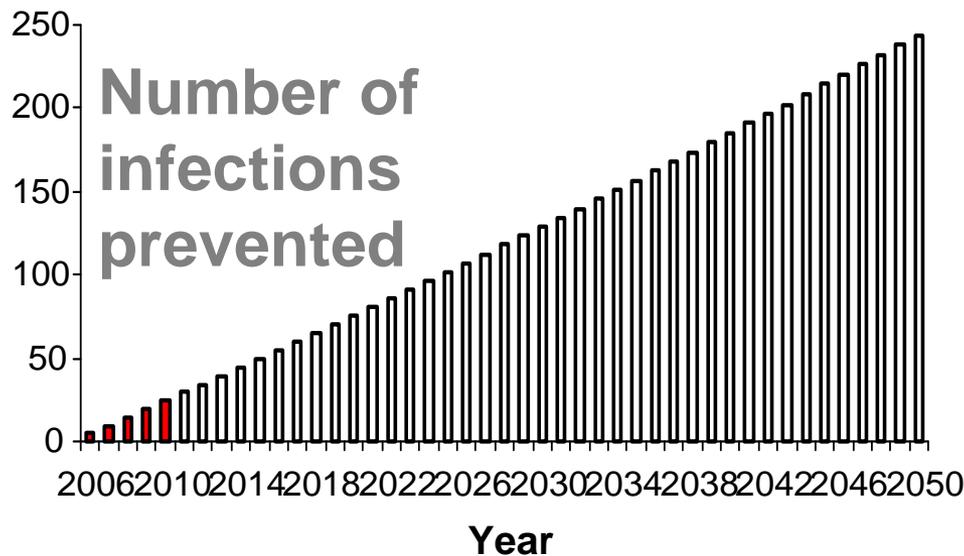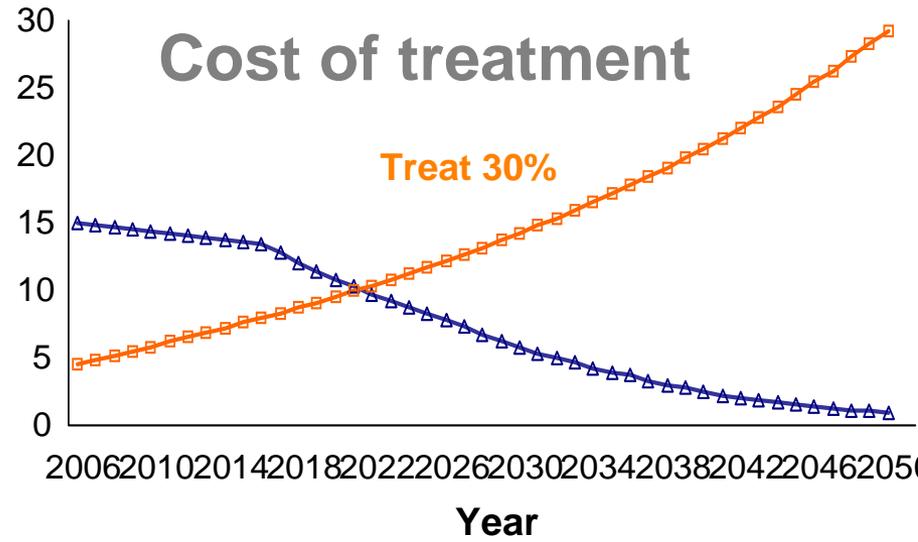Stronger Together

AIDS 2006
XVI International AIDS Conference
Time to *Deliver*

The Power of HAART: Demographic Model

Montaner et al, Lancet 2006

Expansion of HAART for HIV Prevention: The Challenges
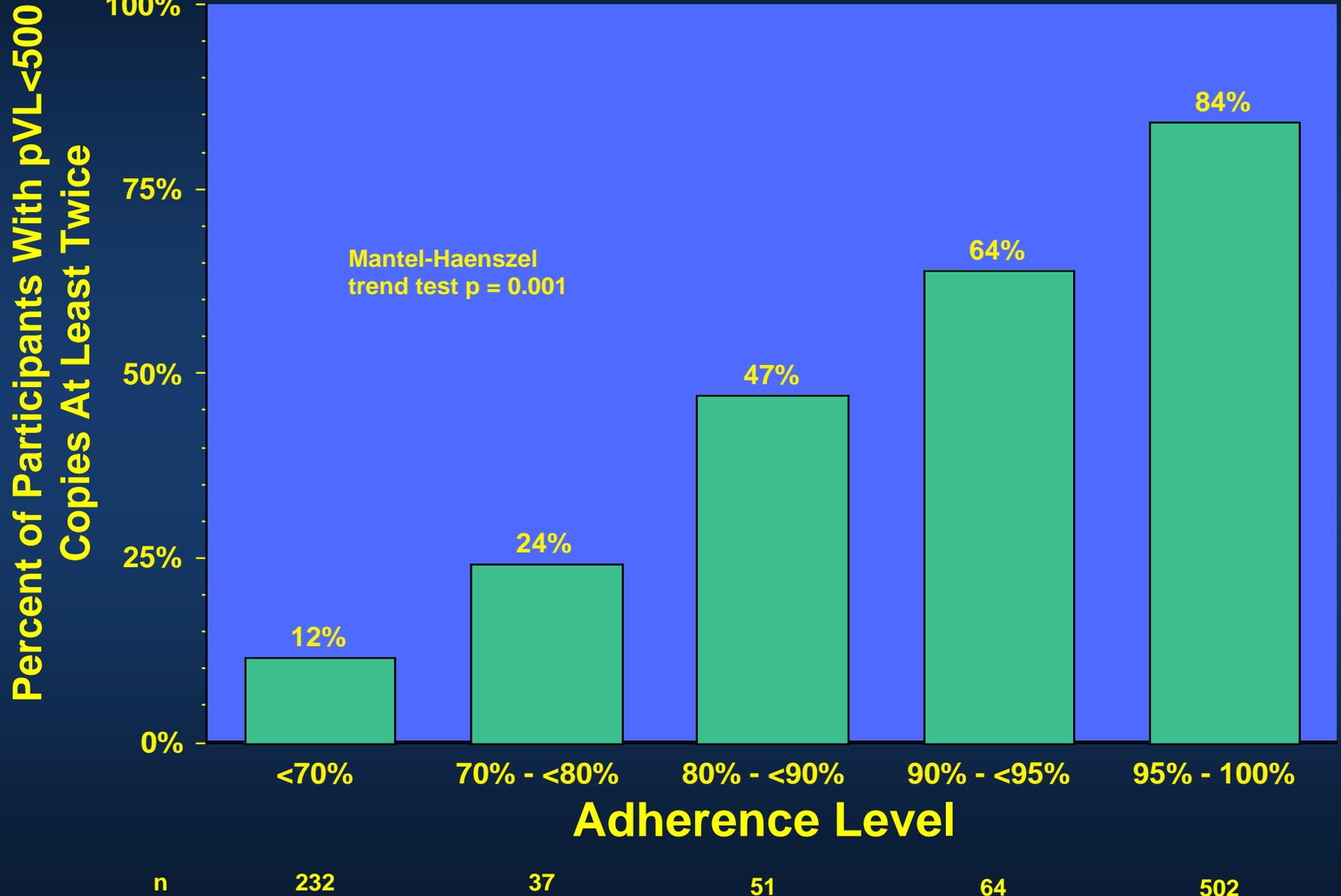
Untested hypothesis in "real world "setting
- ✓ Safety/toxicity
- ✓ Human rights
- ✓ Development challenges
- ✓ Adherence/Resistance
- ✓ Hidden epidemics
- ✓ Logistics
- ✓ Erosion of prevention effort
- ✓ Cost

British Columbia
HIV/AIDS Drug Treatment Program

o In BC antiretrovirals have been centrally distributed free of charge to eligible HIV+ individuals since 1986

o In October 1992, the HIV/AIDS Drug Treatment Program became the responsibility of the BC Centre for Excellence

o Currently over 3000 persons on therapy

Viral Load Stratified by Adherence level in the first 12 months of therapy

Percent of Participants With pVL<500 Copies At Least Twice

Mantel-Haenszel trend test p = 0.001

12%	24%	47%	64%	84%

Adherence Level

	<70%	70% - <80%	80% - <90%	90% - <95%	95% - 100%
n	232	37	51	64	502

Low-Beer et al. JAIDS 23, 4; 360-1

VIDUS

The Vancouver Injection Drug Users Study:

- Builds on VIDUS (1996-2005) – a prospective cohort of 1500 injection drug users (IDU)
- 2006: VIDUS became a prospective cohort of 1000 HIV negative IDU
- 33% women, 37% ethnic minorities (29% Aboriginal)
- Newly funded in 2009 by the US National Institutes of Health (RO1-DAO11591-04A1)

British Columbia
Centre *for* Excellence
in HIV/AIDS

ACCESS

AIDS Care Cohort Evaluating the impact of Exposure to Survival Services (ACCESS):

- New cohort launched in Jan 2008
- Will involve over 1000 HIV+ IDU
- Among approximately 600 IDU, 38% are women, 48% are ethnic minorities (42% Aboriginal)
- Newly funded by US National Institutes of Health (R01DA011591-07)

British Columbia
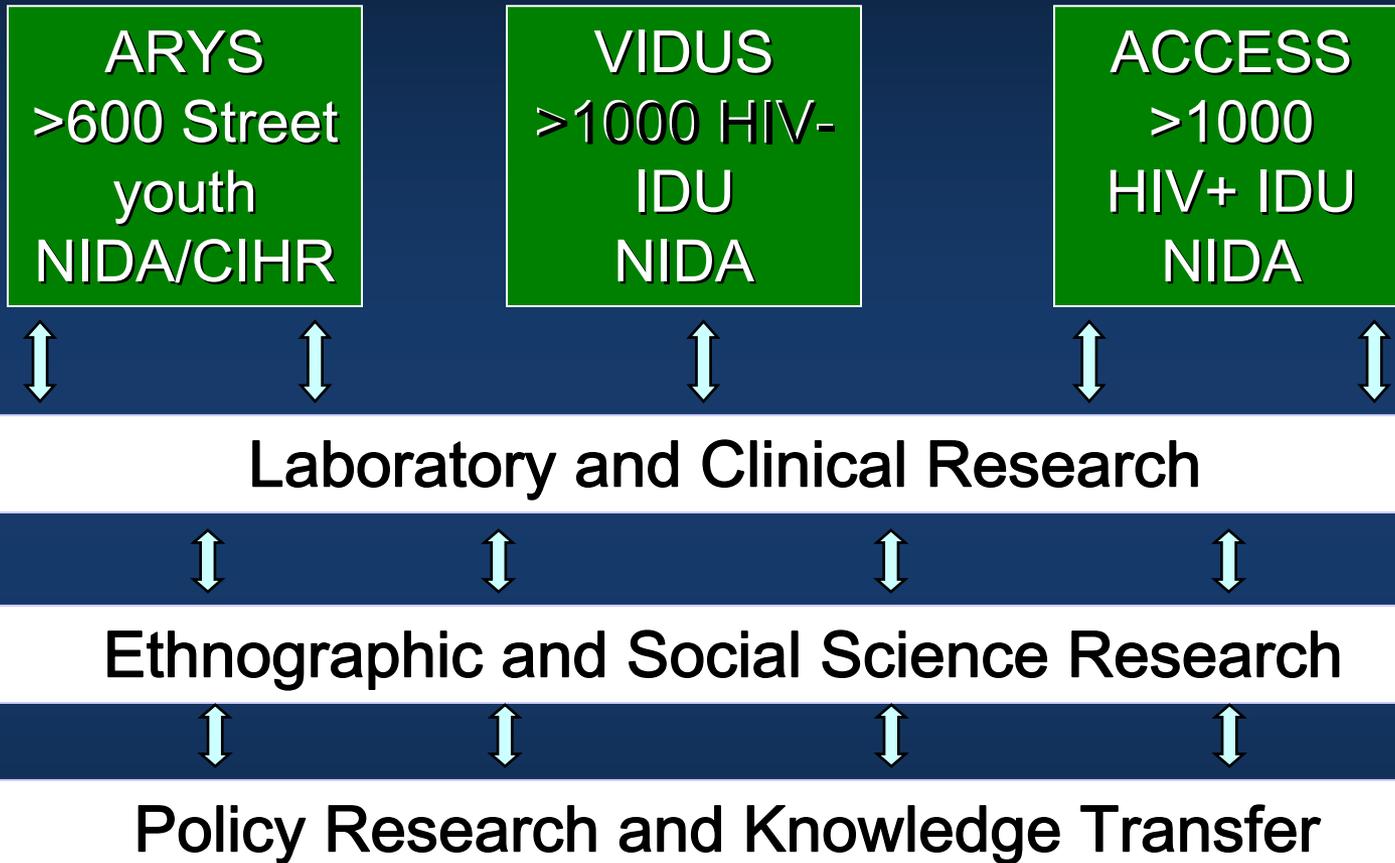Centre *for* Excellence
in HIV/AIDS

VIDUS & ACCESS

Study Methods:

- Baseline and semi-annual visits
- Interviewer-administered questionnaires
- Nurses questionnaire
- HIV & Hep C testing for "negatives"
- Viral load, CD4, Resistance monitoring for HIV positives
- Survey and biological data linked to administrative databases via personal health numbers
- Linkages with specialty HIV care

British Columbia
Centre *for* Excellence
in HIV/AIDS

STOP HIV & AIDS =
Interdisciplinary Clinical Research Program

ARYS >600 Street youth NIDA/CIHR	VIDUS >1000 HIV-IDU NIDA	ACCESS >1000 HIV+ IDU NIDA

Laboratory and Clinical Research

Ethnographic and Social Science Research

Policy Research and Knowledge Transfer

Prevalence and Correlates of Untreated Human Immunodeficiency Virus Type 1 Infection among Persons Who Have Died in the Era of Modern Antiretroviral Therapy

Evan Wood,[1,2] Julio S. G. Montaner,[1,4] Mark W. Tyndall,[1,2] Martin T. Schechter,[1,2] Michael V. O'Shaughnessy,[1,3] and Robert S. Hogg[1,2]

[1]British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital, and Departments of [2]Health Care and Epidemiology, [3]Pathology and Laboratory Medicine, and [4]Medicine, University of British Columbia, Vancouver, British Columbia, Canada
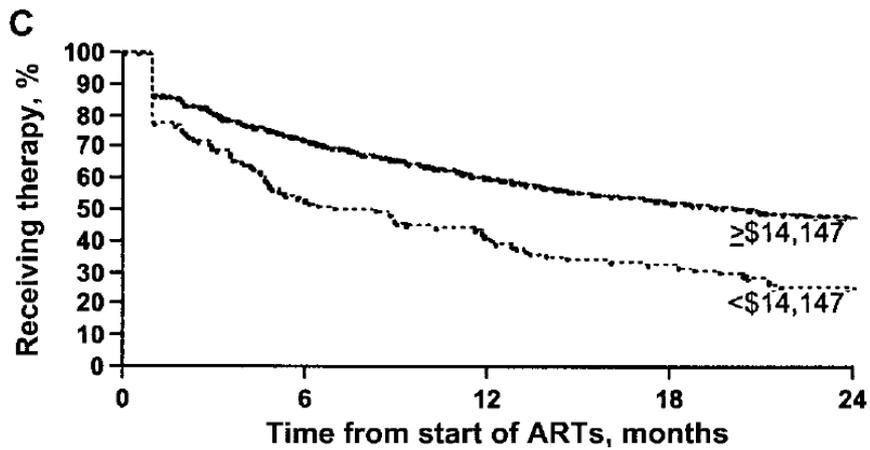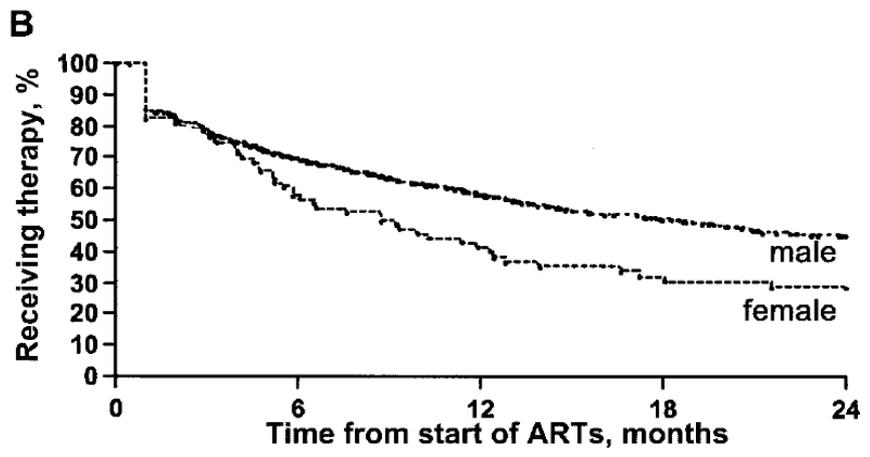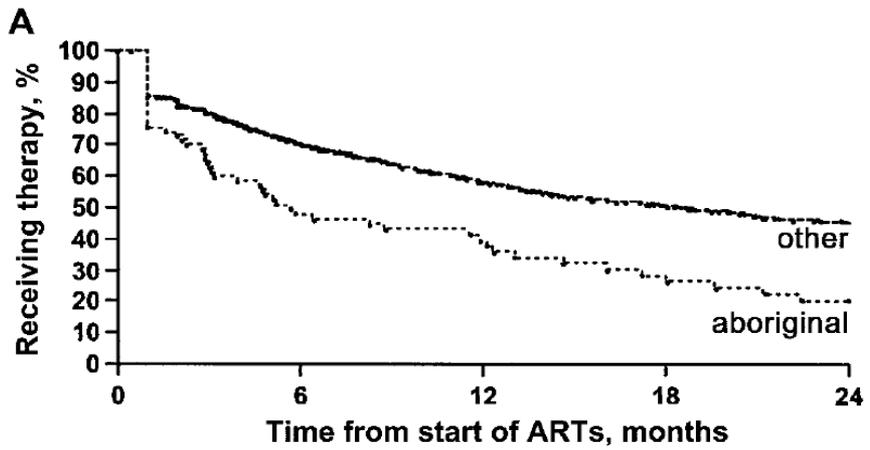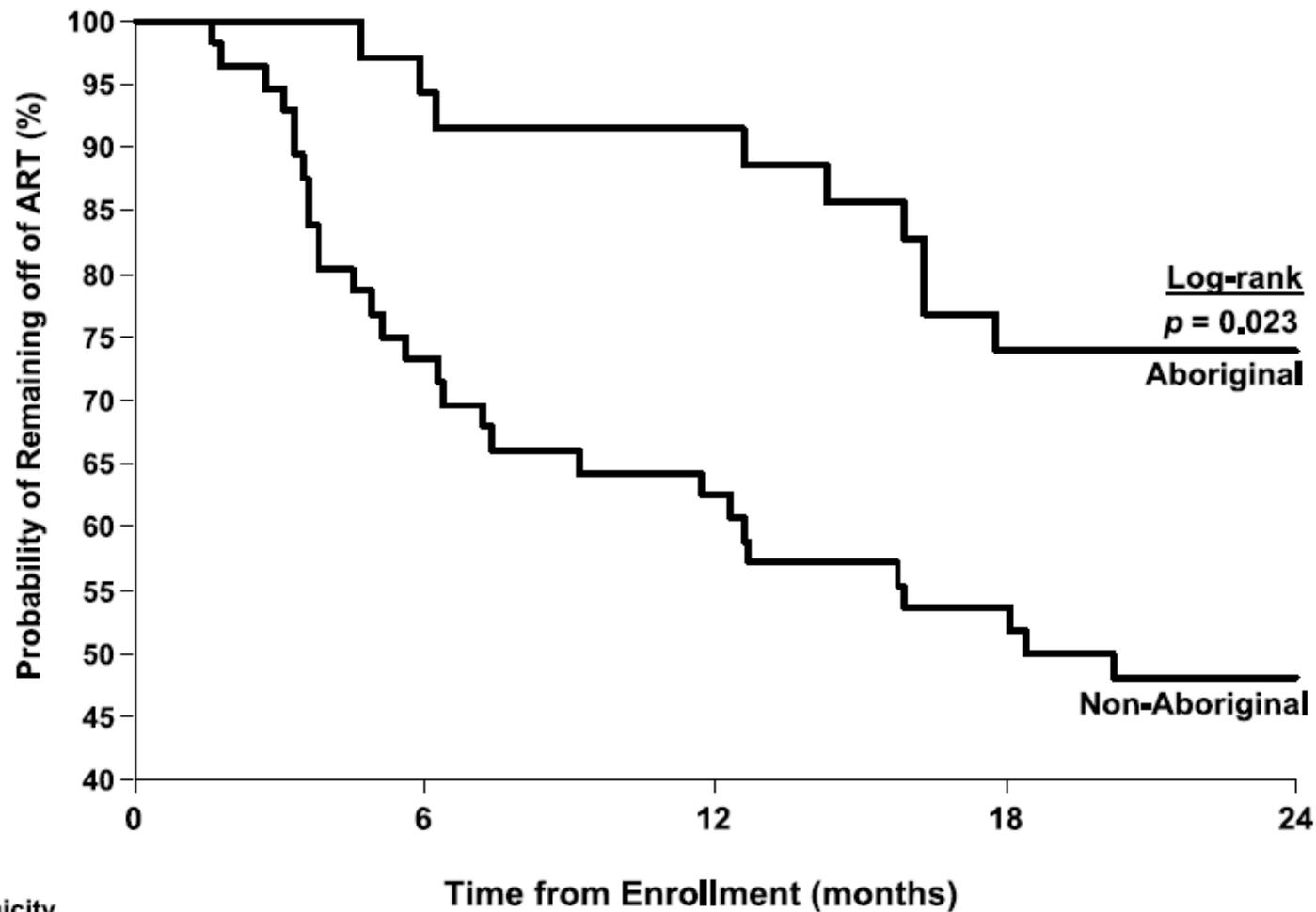
Figure 1 Cumulative probability of ART initiation among IDU stratified by Aboriginal ethnicity.

Table 1 Cox proportional hazards analyses of the time to first ART use

Variable	Type of analysis; relative hazard (and 95% CI)[a]	
	Unadjusted	Adjusted[b]
Aboriginal (yes vs. no)	0.51 (0.29-0.92)	0.37 (0.15-0.93)
Cocaine injection ($\geq$daily vs. <daily)	0.82 (0.48-1.40)	
Heroin injection ($\geq$daily vs. <daily)	0.82 (0.47-1.45)	
Age (per year older)	1.01 (0.98-1.05)	
Gender (female vs. male)	0.90 (0.53-1.53)	
Methadone use (yes vs. no)	2.33 (1.08-5.03)	1.94 (0.89-4.23)

Note: CI, confidence interval; ART, antiretroviral.
[a] Relative hazard values for which the CI does not cross 1.0 are significant at the $\alpha = 0.05$ level.
[b] The final model was adjusted for the duration between the baseline and the first follow-up visit for each individual.

Figure. Kaplan-Meier Cumulative Rate of First CD4 Cell Count Monitoring Among Injection Drug Users Stratified by Sex and Race
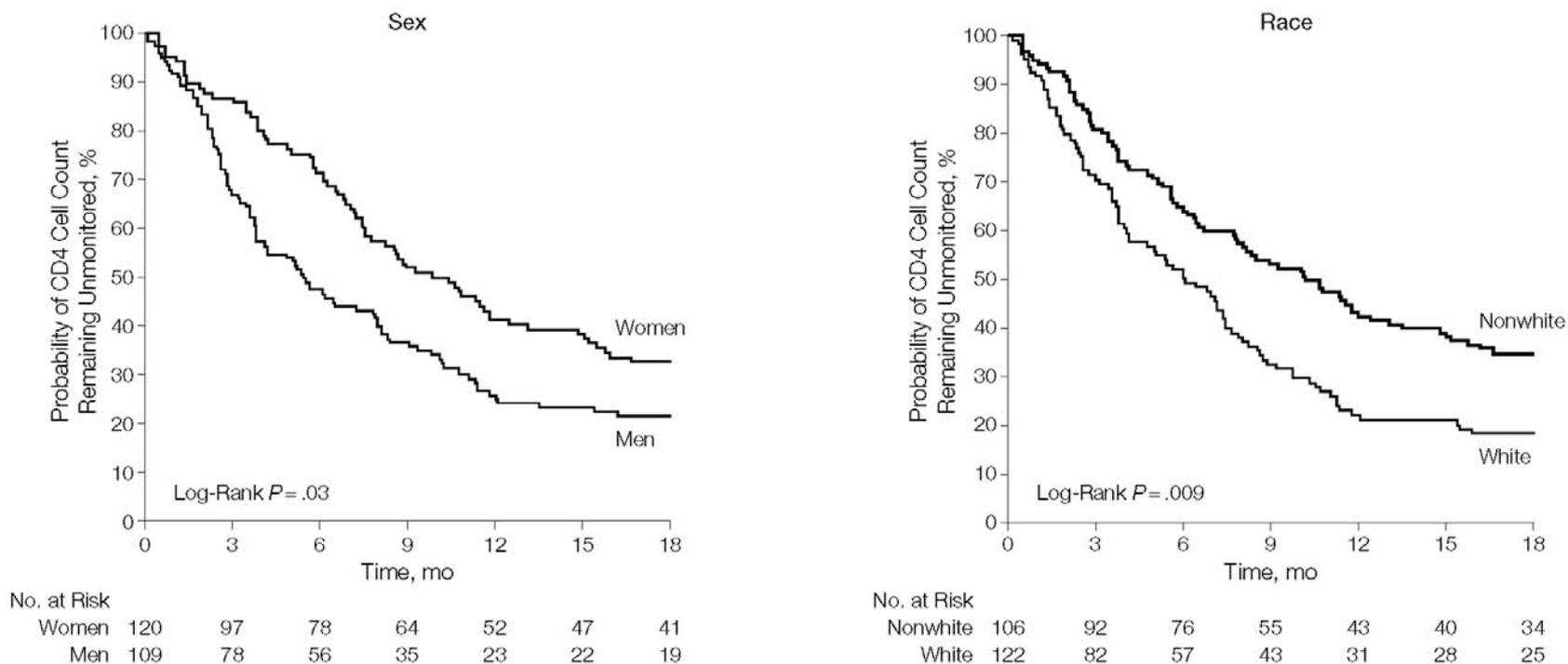
The 18-month period shown approximates a time during which 6 CD4 tests would generally be recommended in human immunodeficiency virus therapeutic guidelines. Because of missing data, 1 person was excluded from the analysis of race.

JAMA, 2004

Table IV. Logistic regression analysis of factors associated with discontinuation of HAART.

	AOR	(95% CI)	P
Age	0.99	(0.9–1.1)	0.811
Frequent heroin injection	1.99	(0.6–6.3)	0.243
Self-regulatory efficacy	0.86	(0.7–0.9)	0.050
Efficacy expectations	0.70	(0.5–0.9)	0.003
Outcome expectation	1.41	(1.2–1.6)	<0.001
Recent incarceration	4.84	(1.2–18.7)	0.022

- 44% HIV-infected IDU discontinued HAART prematurely against medical advice

AIDS Care, 2005

HAART & Incarceration

We identified various forces related to episodes of incarceration that influenced inmates' ability to access and adhere to HAART:

- Short term interruptions in treatment during intake and transfers
- Delays in obtaining medications through institutional healthcare
- Poor relationships between inmates and healthcare staff
- High levels of HIV discrimination and stigma
- Problems ensuring continuity of treatment post-release

Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study

Evan Wood
Thomas Kerr
Brandon D L Marshall
Kathy Li
Ruth Zhang
**Robert S Hogg**
P Richard Harrigan
Julio S G Montaner

Urban Health Research Initiative,
British Columbia Centre for Excellence in HIV/AIDS
Faculty of Medicine, University of British Columbia

British Columbia
Centre *for* Excellence
in HIV/AIDS

URBAN
HEALTH
RESEARCH
INITIATIVE

UHRI

Figure 1: Community plasma HIV RNA among a cohort of injection drug users in Vancouver
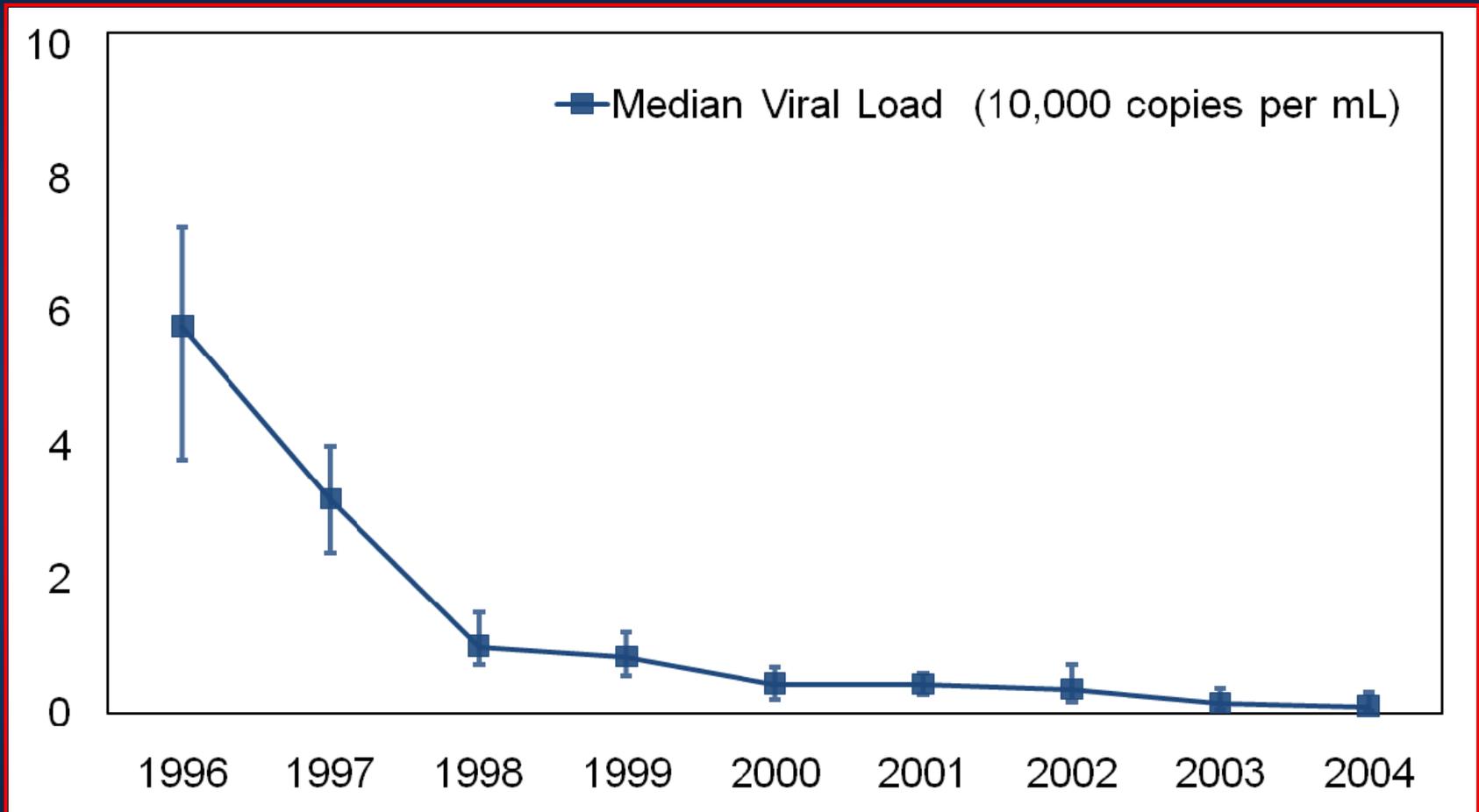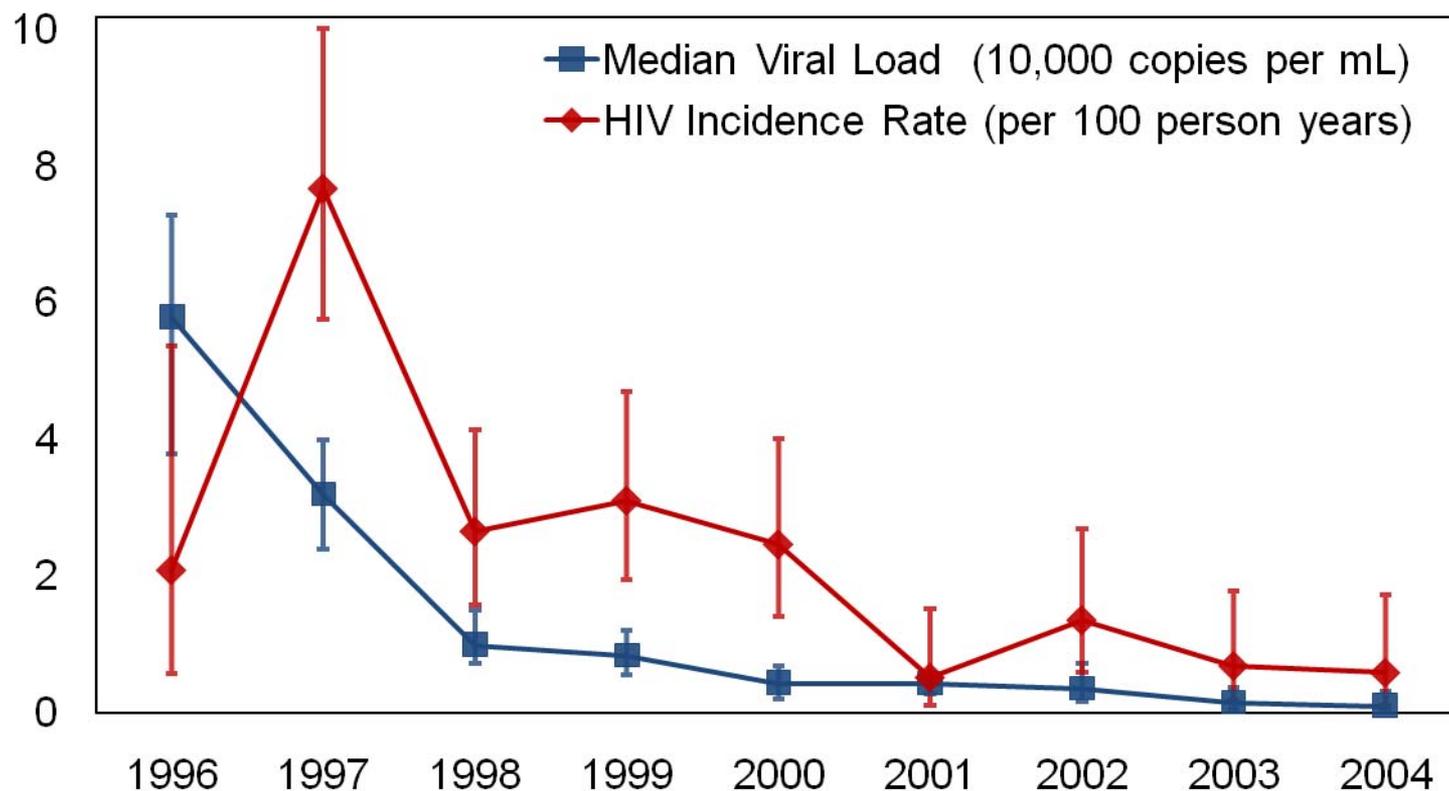

Whiskers represent 95% confidence intervals.

Figure 2: HIV incidence among a cohort of injection drug users in Vancouver
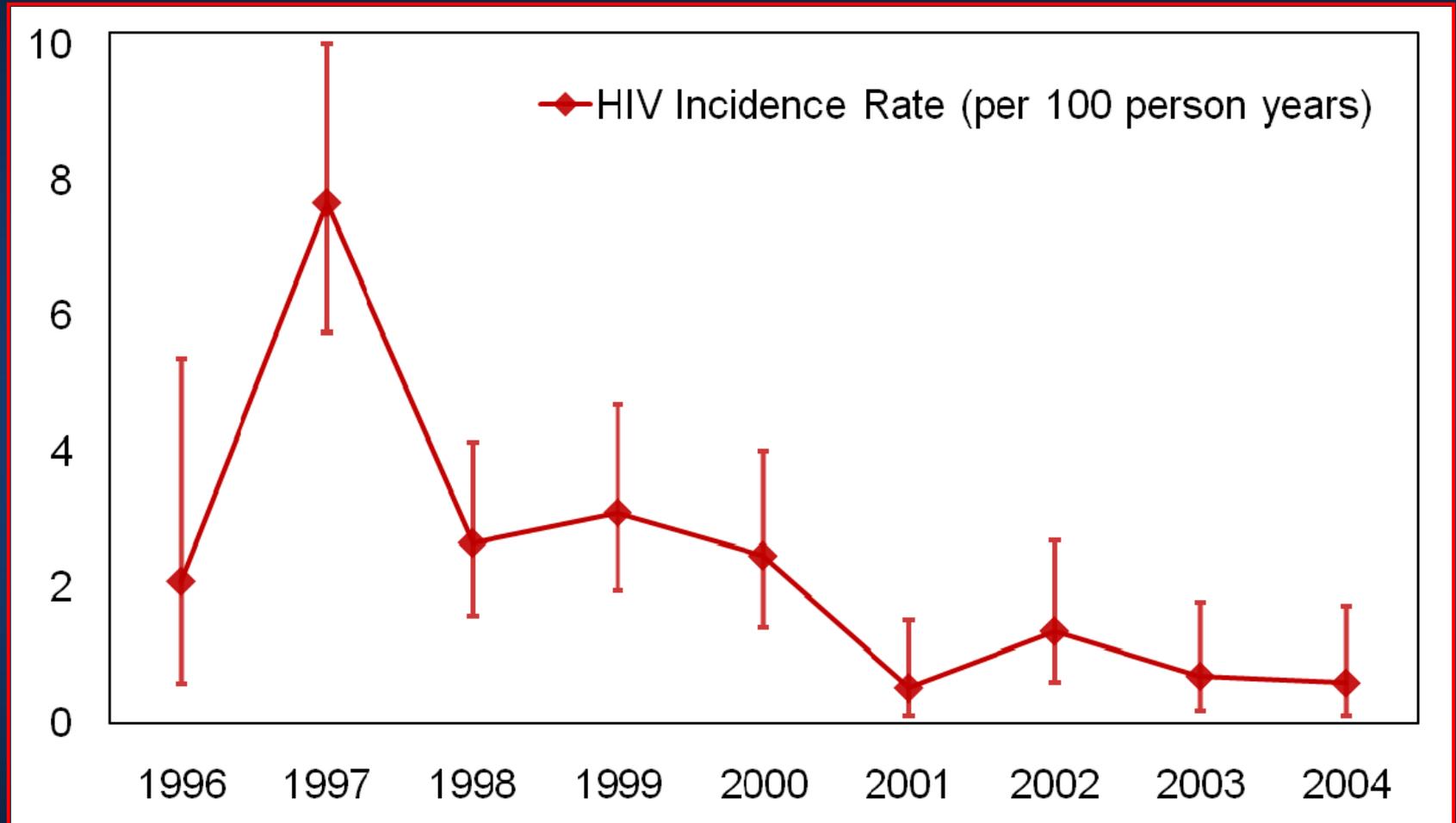
*HIV incidence is expressed as incidence density per 100 person years.
Whiskers represent 95% confidence intervals.

Figure 3: Community plasma HIV RNA levels and HIV incidence among two parallel cohorts of injection drug users.*

*HIV incidence is expressed as incidence density per 100 person years. Whiskers represent 95% confidence intervals.

Table 1: Cox proportional hazards regression of the time to HIV infection among 1,048 HIV negative injection drug users followed between May 1, 1996 and December 31, 2004.

Characteristic	Relative Hazard	95% Confidence Interval	*p*-value
Community Viral Load[†] Per $\log_{10}$ increase	9.40	(4.28 – 20.64)	< 0.001
Unsafe sex Yes vs No	0.82	(0.56 – 1.21)	0.360
Used syringe borrowing Yes vs No	1.70	(1.15 – 2.51)	0.008
Ethnicity White vs Other	0.55	(0.39 – 0.78)	< 0.001
Heroin injection $\geq$ Daily vs < daily	1.19	(0.83 – 1.70)	0.349
Cocaine injection $\geq$ Daily vs < daily	2.88	(1.99 – 4.17)	< 0.001
Unstable housing[*] Yes vs No	1.40	(0.98 – 2.02)	0.067

[†]Plasma HIV RNA was time updated based on median value in the BART cohort during the 6 month period prior to each HIV-negative participant's follow-up visits; [‡]Defined as insertive or receptive vaginal or anal intercourse; *Defined as living in a single room occupancy hotel, shelter, recovery or transition house, jail, on the street, or having no fixed address;

STOP HIV & AIDS =
Interdisciplinary Clinical Research Program

VIDUS >1000 HIV-IDU NIDA	ACCESS >1000 HIV+ IDU NIDA	ARYS >600 Street youth NIDA/CIHR	DTP >2200 HIV+ NIH/CIHR	MAKA >300 Sex workers CIHR

Laboratory and Basic Science Research

Ethnographic and Social Science Research

Policy Research and Knowledge Transfer

Clinical Trials and Intervention Studies

HIV Specialty Treatment and Care

The Future?

Novel Approaches to:

- Extend HIV testing efforts
- Increase uptake of disease monitoring
- Increase access to HAART
- Increase adherence
- Manage toxicities/side effects

Summary

- Prospective cohort studies of IDU have been integrated with clinical HIV programs to enhance the delivery of care and monitoring of HIV infection and treatment

- Cohorts data are linked to a range of clinical databases

- This integrated approach is essential to the "Seek and Treat" initiative focused on expanding HAART for treatment and prevention

- Many challenges remain and will be addressed through ongoing integrated and interdisciplinary clinical and research efforts

Acknowledgements