Sociodemographic Determinants of HIV Drug Resistance in British Columbia, Canada

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Chanson J Brumme[1,2], Melanie Rusch[3], Keith Chan[1], Dmitry Shopin[1], Guillaume Colley[1], Zabrina Brumme[1,4], Robert S Hogg[1,4], Julio SG Montaner[1,2], P Richard Harrigan[1,2]

[1] BC Centre for Excellence in HIV/AIDS, Vancouver, BC, Canada; [2] Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada; [3] Vancouver Island Health Authority, Victoria, BC, Canada; [4] Faculty of Health Sciences, Simon Fraser University, Burnaby, BC, Canada

Presenting Author:
Chanson Brumme
cbrumme@cfenet.ubc.ca

Background

- Baseline clinical factors and adherence to HAART are associated with resistance development after therapy, however, the interplay between sociodemographic and clinical factors influencing resistance development has not been well characterized at a population level

Methods

- A cohort of 11,083 HIV-positive persons accessing treatment from the BC-CfE Drug Treatment Program from 1996-2012 was followed longitudinally
- A subset of 5381 patients were antiretroviral-naïve at HAART initiation
- Patients were grouped by Census Tract (census subdivision comprising ~2000-8000 persons) of residence at time of enrollment in the BC-CfE Drug Treatment Program
- Census level sociodemographic variables were assigned to individual patients based on Census Tract of residence; data from the census conducted closest to each patient's enrollment date was used (1996, 2001, 2006, 2011)
- Uptake of HIV drug resistance testing endpoint:
  - Patients with at least one pVL above the lower limit required for resistance testing (>250 HIV RNA copies/mL) in a calendar year were considered eligible for HIV drug resistance testing
  - Patients for whom a physician-ordered resistance test result was available were considered to have accessed testing in that year
- Drug resistance endpoints in antiretroviral-naïve subgroup:
  - Time from HAART initiation to the first detection of a resistance-associated mutation in HIV Protease or RT as defined by the IAS-USA list (2011)
  - Patients not tested at baseline were assumed to have drug-susceptible HIV at therapy initiation
  - Plasma samples with viral load (pVL) <1000 HIV RNA copies/mL were not systematically tested; untested samples were assumed to harbor drug-susceptible HIV
  - Patients not reaching an endpoint were censored at the earlier of: A) their last pVL measurement, or B) their first untested pVL sample with pVL >1000 HIV RNA copies/Ml
- Census-level sociodemographic predictors of uptake of HIV drug resistance testing were determined using multivariable GEE logistic regression
- The determinants of the emergence and detection of drug resistance in the subset of antiretroviral-naïve persons initiating HAART in BC was assessed with Weibull survival analysis
- Models were adjusted for individual level clinical variables including baseline plasma viral load, CD4, gender, age, risk factors, physician experience and adherence
- All available HIV protease-RT sequences (N~33,000) collected as part of routine HIV drug resistance testing were used, including tests conducted retrospectively on stored plasma samples

Census-Level Sociodemographic Variables Investigated

- % single family vs. multi-family housing
- population density
- % immigrants
- median income
- education (% of population with post-secondary education)
- % unemployment levels

Figure 2: Predictors of Uptake of Resistance Testing

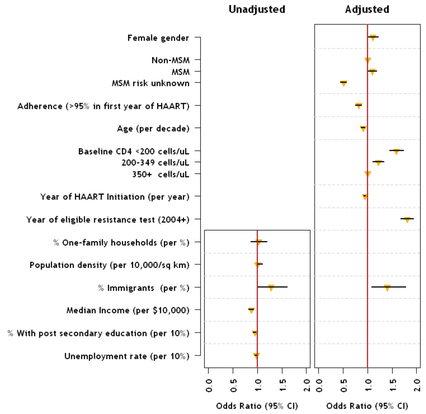


Figure 3: Predictors of Any Resistance

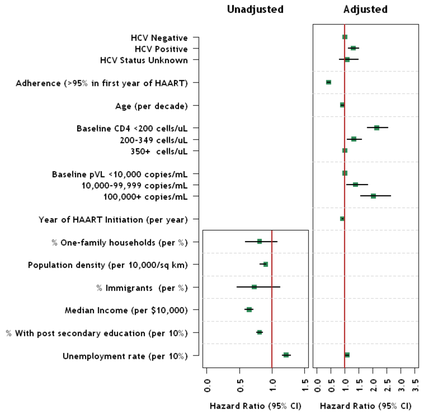


Figure 4: Predictors of NNRTI Resistance

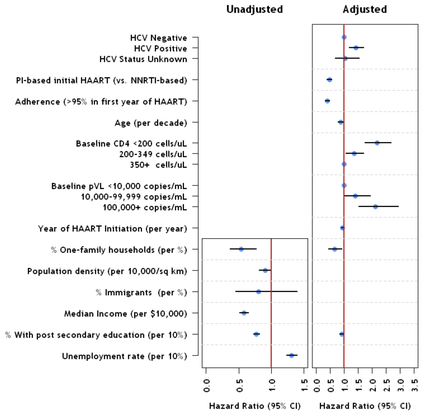
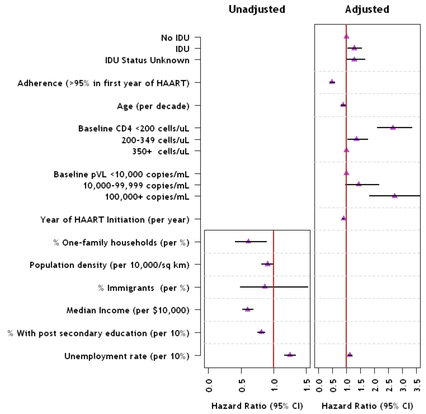


Figure 5: Predictors of 3TC/FTC Resistance



Figures 2-5: Odds Ratios (Access to drug resistance testing) and Hazard Ratios (Time to detection of drug resistance) from univariable (Unadjusted) and multivariable models.
Unadjusted panels show univariable OR/HR of all census-level sociodemographic variables investigated. Univariable OR/HR of individual-level clinical/demographic variables are not shown. *Adjusted* panels show only statistically significant OR/HR in multivariable models corrected for individual-level baseline clinical and sociodemographic variables. OR/HR for continuous variables are shown per unit increment.

Figure 1: Increasing Uptake of HIV Drug Resistance Testing

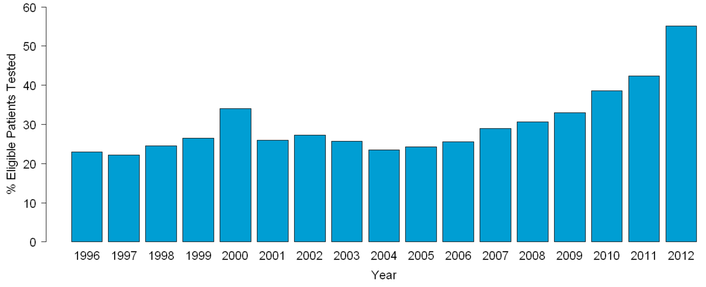


Figure 1: Of the 9310 (84%) patients with at least one post-therapy plasma sample eligible for testing (pVL>250 c/mL) only 4751 (51%) ever had a physician-ordered resistance test; however the proportion of samples tested markedly increased with calendar year (p<0.001)

In univariable models, all census-level sociodemographic variables investigated were significantly associated with either uptake of testing and/or development of HIV resistance.
After adjustment for individual-level clinical variables and adherence, an increased hazard for first resistance event was observed for persons living in census tracts with higher unemployment levels (HR 1.08; p=0.004 per 10% increment; Figure 3) driven largely by the emergence of 3TC/FTC resistance (HR 1.12; p<0.001; Figure 5). However, persons living in census tracts with higher proportions of single family residences (HR 0.65; p=0.01) and post-secondary education (HR 0.92; p=0.009 per 10% increment) were at decreased risk of NNRTI resistance.
No census-level sociodemographic factors were associated with resistance to other NRTIs or PIs

Conclusions

- HIV drug resistance was observed across all sociodemographic strata regardless of adherence levels
- Unemployment rate within a census tract, a surrogate for lower socioeconomic status, was marginally associated with an increased risk of resistance even after adjusting for adherence
- The complex relationship between census-level sociodemographic variables makes it difficult to identify specific social groups or geographic locations at higher risk of developing resistance in BC
- Perhaps surprisingly, no strong associations between census-level sociodemographic parameters and drug resistance were observed; rather the risk of resistance was distributed equally across sociodemographic groups and census tracts

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