Hepatitis C Virus Phylogenetic Clustering And Latent Class Analysis Of Drug Use Among People Who Use Drugs In Vancouver Canada

Jacka B, Bray B, Applegate TL, Marshall BDL, Lima VD, Hayashi K, DeBeck K, Raghwani J, Harrigan PR, Krajden M, Montaner J, Grebely J

6th International Symposium on Hepatitis Care in Substance Users
Jersey City/New York, United States; 8th September 2017

Disclosures

- None.

Overview

- Brief background
- Study population and methods
- Outcomes and conclusions

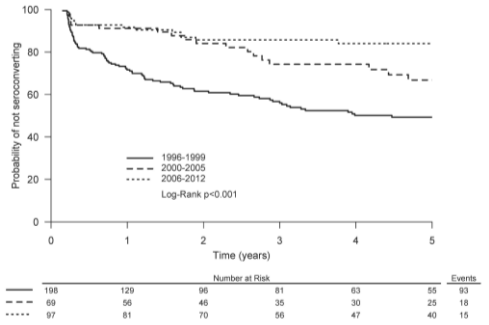
Context

- Factors associated with HCV seroconversion provide information about those at risk of becoming infected with HCV
- It is common to investigate close viral genetic relationships and factors associated with HIV infection, but less common for HCV[1,2]
- Studies of HCV genetic relationships have identified social networks, age, location and acute/recent infection as being associated with clustering[3,4]

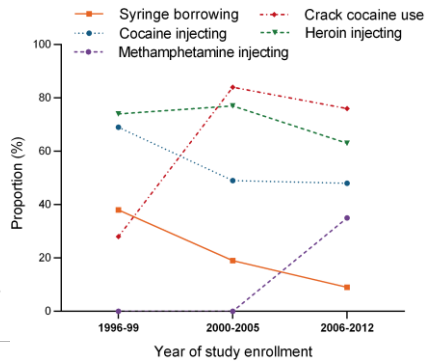
1 Kouyos et al Journal of Infectious Diseases 2010, 2 Chalmet BMC Infectious Diseases 2010
3 Sacks-Davis PLoS One 2012, 4 Jacka Hepatology 2014

HCV in Vancouver cohort 1996-2012

VIDUS time to seroconversion



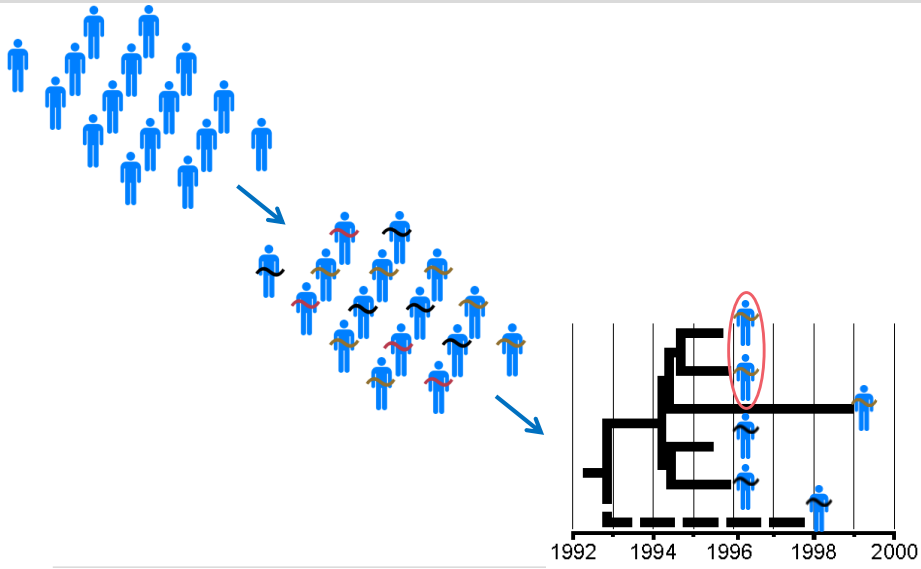
VIDUS recent drug use



5

Grebely PLoS One 2014

Phylogenetic analysis, abridged



6

Previous results from phylodynamic studies

Logistic regression	No cluster	Cluster	Adjusted analysis	
	(n=591)	(n=108)	OR (95% CI)	P-value
Age quartiles				
<27	118 (21%)	26 (26%)	3.01 (1.44, 6.29)	0.003
27 – 34	152 (27%)	38 (38%)	2.53 (1.35, 4.77)	0.004
35 – 39	113 (20%)	20 (20%)	1.87 (0.93, 3.78)	0.080
>40	172 (31%)	16 (16%)	1.00	-
HIV coinfection	128 (22%)	37 (34%)	1.97 (1.22, 3.18)	0.005
ARYS cohort	58 (10%)	7 (6%)	0.39 (0.15, 1.00)	0.049
HCV subtype				
1a	307 (52%)	40 (37%)	1.00	-
1b	36 (6%)	8 (7%)	2.13 (0.90, 5.03)	0.086
2b	43 (7%)	9 (8%)	1.67 (0.75, 3.76)	0.212
3a	205 (35%)	51 (47%)	2.12 (1.33, 3.38)	0.002
Recent HCV infection	60 (10%)	13 (12%)	1.45 (0.72, 2.93)	0.302

7

Jacka et al Journal of Hepatology 2016

Latent class analysis

Variable-centred	Person-centred
Regression and factor analysis	Cluster and latent class analysis
• Identify predictors of outcomes • Dependent-independent variable relationships	• Classification into distinct groups • Focus on relationships of variable outcomes

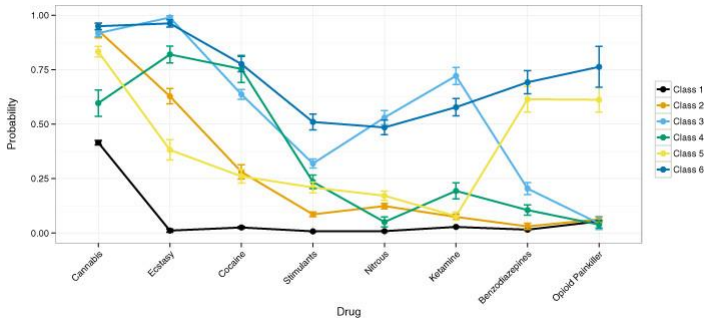
LCA identifies *clusters* which group together individuals who share similar characteristics in a heterogeneous setting

Produces a *K*-category latent variable, where each category represents a cluster with greater similarity than difference

8

Example latent class analysis

- The 2012 Global Drug Survey included 15 000 participants from USA, UK and Australia
- Online questionnaire regarding past-year drug use and sociodemographics
- Latent class analysis to identify polydrug use



Morley et al Drug and Alcohol Review 2015.

Overview

- Brief background
- Study population and methods
- Outcomes and conclusions

Aim

- To identify patterns of poly-drug use using latent class analysis and evaluate the association between drug class and HCV phylogenetic cluster membership

Method

- Phylodynamic reconstruction and time to most common recent ancestor (tMRCA) cluster analysis
- Latent class analysis of drug use, and multivariate logistic regression of clustering

11

Study population

VIDUS I/II ***Vancouver Injection Drug User Study***

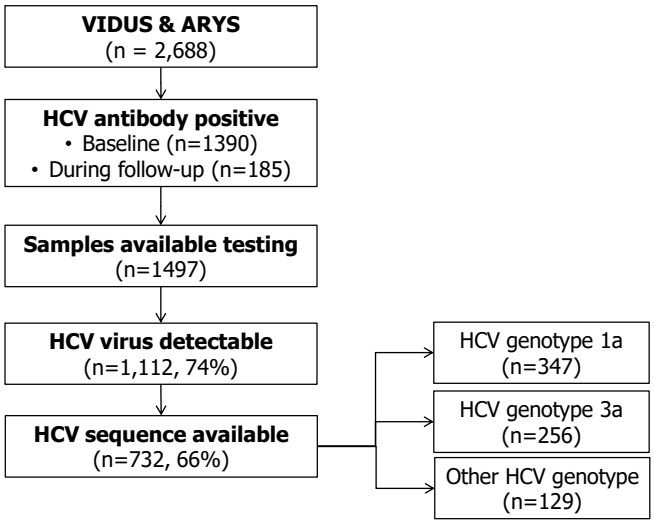
- Open prospective recruitment from 1996 onwards
- Greater Vancouver based, >18 years of age, current injecting risk
- Biannual behavioural survey & research blood sample

ARYS I/II ***At Risk Youth Study***

- Street-involved youth (<26 years of age)
- Recent illicit drug use (other than marijuana)
- Harmonised survey with VIDUS, recruitment from 2005

12

Participant Disposition



13

Overview

- Brief background
- Study population and methods
- Outcomes and conclusions

Participant characteristics

Characteristics	Total (n=699)
Female sex	179 (26%)
High school education or higher	165 (24%)
Unstable housing†	494 (71%)
ARYS cohort	65 (9%)
Recent HCV seroconversion	73 (10%)
HIV infection	165 (24%)
HCV subtype	
1a	347 (50%)
1b	44 (6%)
2b	52 (7%)
3a	256 (37%)

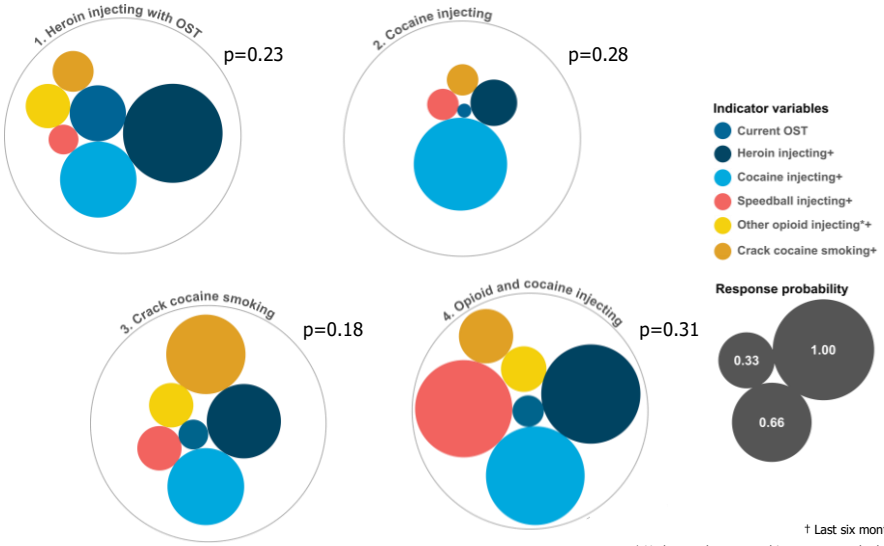
Characteristics	Total (n=699)
Syringe borrowing†	271 (39%)
Currently receiving opioid substitution therapy	89 (13%)
Crack use†	195 (28%)
Cocaine injecting†	556 (80%)
Heroin injecting†	490 (70%)
Speedball injecting†	264 (38%)
Methamphetamine injecting†	51 (7%)
Other opioid injecting*†	102 (15%)

† Last six months

* Hydromorphone, morphine, street methadone

15

Latent class analysis outcomes



† Last six months

* Hydromorphone, morphine, street methadone

16

Phylogenetic clustering logistic regression

	No cluster (n=591)	Cluster (n=108)	Adjusted logistic regression OR (95% CI)	P value
Latent class				
1. Heroin injecting with OST	175 (30%)	23 (21%)	Ref	-
2. Cocaine injecting	120 (20%)	48 (44%)	3.05 (1.71, 5.46)	**<0.001**
3. Crack cocaine smoking	109 (18%)	1 (<1%)	0.06 (0.01, 0.46)	**0.007**
4. Opioid and cocaine injecting	187 (32%)	36 (33%)	1.38 (0.77, 2.48)	0.288

Adjusted for age, HIV co-infection, HCV genotype, cohort and recent HCV infection

Limitations

- As there were differences in the inclusion and exclusion criteria for the two cohorts included, enrolment cohort was controlled for in logistic regression
- Care should be taken when interpreting the outcomes of latent class analysis, particularly when concluding that the classes identified represent actual individuals in the population.
- Nonetheless, latent class analysis provides a useful mechanism for representing the heterogeneity of factors across the population
- Only specimens at first positive visit (baseline or during follow up) were included. Therefore secondary infections, reinfection or superinfection, could not be analysed

Outcomes and conclusions

- This heterogeneous population can be categorised based on drug use behaviours
- Combining latent class analysis and phylogenetics provides insight into groups related to but not necessarily responsible for HCV transmission
- Improved understanding of complex populations is necessary in developing informed and effective interventions and public health strategies
- Overcoming barriers for marginalised and stigmatised populations will be necessary in eliminating HCV

19

Acknowledgement and thanks

- Study participants for their time and contribution to the research. Study investigators and coordinators.
- Funding from Canadian Institutes of Health Research, National Institutes of Health
- *The Kirby Institute*
  - Prof. Greg Dore
  - Ms. Sofia Bartlett
  - Dr. Tanya Applegate
  - Mr. Francois Lamoury
  - A/Prof. Jason Grebely
- *VIDUS & ARYS investigators*
  - UBC Centre for Excellence in HIV/AIDS
  - British Colombia Centre for Disease Control
  - Department of Zoology, University of Oxford
  - The Methodology Center, Penn State University

20

Latent class analysis outcomes

Latent class	Class prob.	Item probabilities					
		Current OST	Heroin injecting	Cocaine injecting	Speedball injecting	Other opioid injecting	Crack cocaine smoking
1. Heroin injecting with OST	0.23	0.32	**1.00**	0.59	0.09	0.20	0.17
2. Cocaine injecting	0.28	0.02	0.22	0.88	0.10	0.00	0.10
3. Crack cocaine smoking	0.18	0.09	0.56	0.60	0.20	0.20	0.64
4. Opioid and cocaine injecting	0.31	0.10	**1.00**	**0.99**	**0.96**	0.21	0.30

Conditional probabilities in **bold** refer to one-third larger than overall and underline one-third smaller than overall

21

Adjusted logistic regression

	No cluster (n=591)	Cluster (n=108)	Adjusted logistic regression OR (95% CI)	P value
Latent class				
1. Heroin injecting with OST	175 (30%)	23 (21%)	Ref	-
2. Cocaine injecting	120 (20%)	48 (44%)	3.05 (1.71, 5.46)	**<0.001**
3. Crack cocaine smoking	109 (18%)	1 (<1%)	0.06 (0.01, 0.46)	**0.007**
4. Opioid and cocaine injecting	187 (32%)	36 (33%)	1.38 (0.77, 2.48)	0.288
HIV	128 (22%)	37 (34%)	1.58 (0.96, 2.58)	0.070
Age (continuous)			0.93 (0.91, 0.96)	**<0.001**
ARYS Cohort	58 (10%)	7 (6%)	0.45 (0.17, 1.19)	0.108
Recent HCV infection	60 (10%)	13 (12%)	1.44 (0.67, 3.09)	0.704
HCV genotype				
1a	307 (52%)	40 (37%)	Ref	-
1b	36 (6%)	8 (7%)	1.97 (0.80, 4.86)	0.142
2b	43 (7%)	9 (8%)	1.90 (0.82, 4.41)	0.132
3a	205 (35%)	51 (47%)	2.20 (1.36, 3.56)	**0.001**

22