



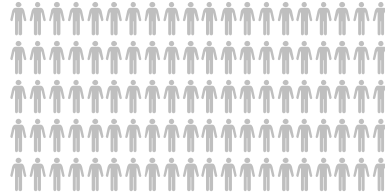
## Phylogenetic clustering of hepatitis C virus among people who inject drugs in Vancouver, Canada

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## The majority of new HCV infections occur among PWID



PEOPLE LIVING WITH HCV INFECTION

1) Hajarizadeh B, et al. *Nature Rev Gastroenterol Hepatol* 2013. 2) Grebely J and Dore GJ *Antiviral Research* 2014.



## The majority of new HCV infections occur among PWID

80% OF NEW INFECTIONS OCCUR AMONG CURRENT PWID



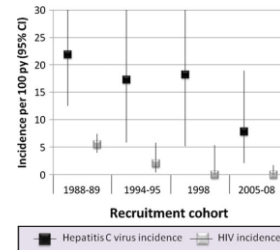
PEOPLE LIVING WITH HCV INFECTION

1) Hajarizadeh B, et al. *Nature Rev Gastroenterol Hepatol* 2013. 2) Grebely J and Dore GJ *Antiviral Research* 2014.



## Harm reduction interventions have been less effective for HCV

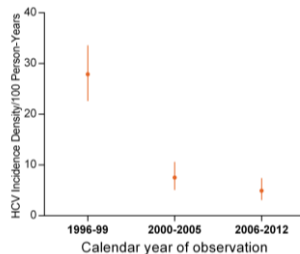
- Higher prevalence of HCV infection (67% vs. 20%)
- Higher risk of infection (3-5% for HCV vs 1-2% for HIV)



Mehta SH, *Journal of Infectious Diseases* 2011.



## HCV transmission among PWID continues



- Factors associated with HCV infection
  - unstable housing, HIV infection, and injecting of cocaine, heroin and methamphetamine

Grebely J, et al *PLoS ONE* 2014



## Limitations of previous work to date

- Traditional epidemiological analyses of HCV incidence measures acquisition, but not transmission of infection
- Identifying characteristics of people at high risk of HCV transmission may provide important information for the design and implementation of targeted strategies
- Phylogenetics provide an opportunity to model underlying transmission patterns that cannot be determined through epidemiological studies<sup>1</sup>, as demonstrated in HIV<sup>2</sup>

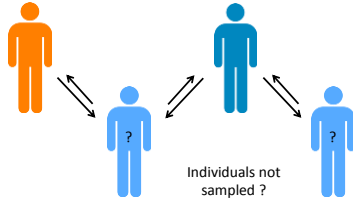
1) Sacks-Davis, *PLoS One* 2012; 2) Brenner BG, *Journal of Infectious Diseases* 2007.



Important caveat....



Two individuals sampled



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Specific Aims



- 1) To investigate phylogenetic clustering of HCV in a longstanding prospective cohort of PWID in Vancouver, Canada
- 2) To examine factors associated with pair/cluster membership

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Study participants



Vancouver Injecting Drug Users Study (VIDUS, 1996-2012):

- Inclusion criteria: PWID residing in the greater Vancouver area who had injected at least once in the previous month

Recruitment:

- Subjects were recruited through self-referral and street outreach efforts

Instrument/Follow-up:

- Baseline and semiannual visits included serological screening for anti-HCV and anti-HIV antibodies
- A questionnaire covered information on subjects' characteristics, injection and non-injection drug use, borrowing and lending of syringes

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Vancouver Injecting Drug Users Study (VIDUS)



- VIDUS I/II Vancouver Injection Drug User Study



Downtown Eastside  
 VIDUS  
 Older pop<sup>n</sup>  
 Longer injecting career  
 HCV prevalence > 80%



Study methodology



Sequencing and phylogenetics

- First HCV antibody/RNA positive sample
- HCV Core-Hypervariable Region-1 nested PCR (1300bp)
- Phylogenetic inference using RAxML maximum likelihood method with 1000 bootstrap replicates
  - 0.05 genetic distance threshold and 90% bootstrap
- Clusters and pairs identified using ClusterPicker

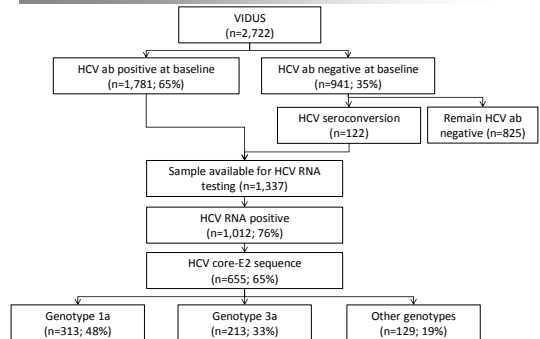
Statistical Analysis

- Factors associated with being in a cluster identified using logistic regression
  - Sensitivity analysis: varied the genetic distance threshold to assess impact on factors associated with clustering

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Participant disposition



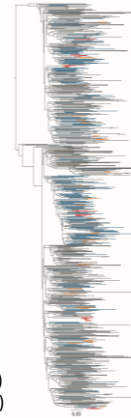


Participant characteristics

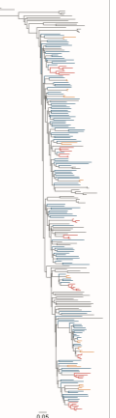
Characteristics	Overall (n=655)
Female sex (vs. male sex)	162 (25%)
Age (median (Q1-Q3))	36 (31-42)
Unstable housing (vs. stable)†	452 (69%)
HCV acute/recent (vs. not)	40 (6%)
HIV infection (vs. none)†	164 (25%)
Syringe borrowing (vs. none)†	268 (41%)
Crack use (vs. none)†	159 (24%)
Cocaine injecting (vs. none)†	546 (83%)
Heroin injecting (vs. none)†	473 (72%)
Genotype	
1a	313 (48%)
3a	213 (33%)
Other (1b, 2a, 2b, 4a, 6a, 6e)	129 (19%)



HCV G1a



HCV G3a

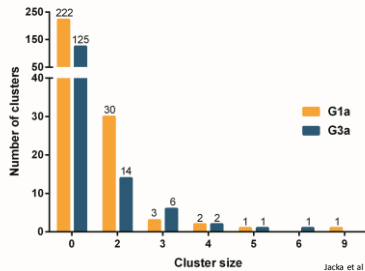


Grey – LANL reference  
 Blue – VIDUS, no cluster  
 Yellow – VIDUS, pair (n=2)  
 Red – VIDUS, cluster (n≥3)



Cluster size distribution – G1a and G3a

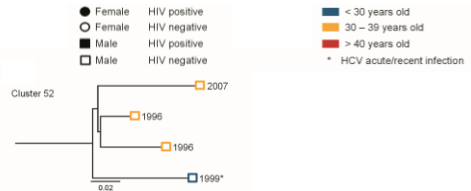
- Among participants with HCV G1a (n=311), 29% clustered
- Among participants with HCV G3a (n=190), 34% clustered



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Examples of interesting clusters – Genotype 1a



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Factors associated with clustering

Characteristic	In cluster /pair (n ≥ 2) (n=156)	Membership in cluster/pair n ≥ 2
Total n (%)	119 (54%)	
Age <40 years (vs. ≥40 years)	52 (40%)	
HIV infection (vs. none)†	15 (48%)	
HCV acute/recent (vs. not)	75 (37%)	

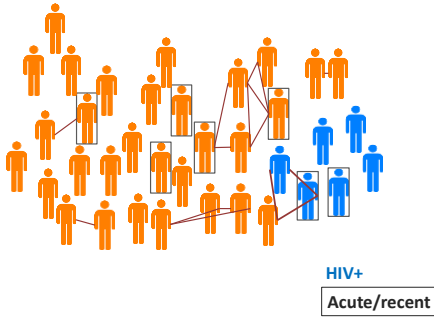
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Conclusions

- One third of participants with either HCV genotype 1a and 3a were genetically related to another
- Being in a cluster/pair independently associated with
  - recent/acute HCV infection
  - HIV infection
  - younger age
  - recent syringe borrowing
- Interventions targeted towards those at greatest risk of transmission

Implications?



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