Characterization of large cluster viral networks sustaining the Montreal Men-having-Sex-with-Men (MSM) epidemic

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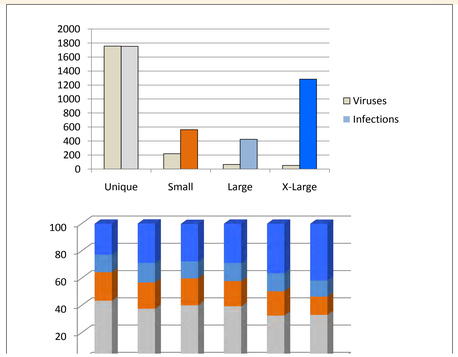
Abstract 251

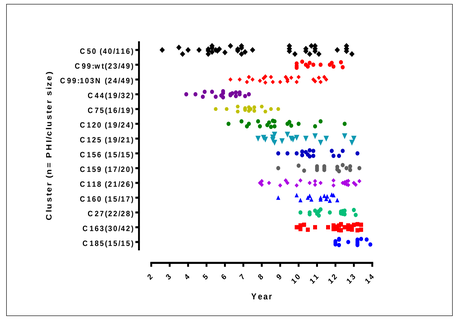
BACKGROUND

The MSM epidemic in Quebec, as reported else
has remained uncontrolled despite widespread
to antiretroviral therapy (ART) and communit
increases in viral suppression (VL< 50 copi
rising from 49% in 2002 to 79% in 2011
phylogenetics findings attribute the cumulative
of the MSM epidemic to frequent onward transm
among newly infected persons, often unaware
HIV-1 status. The cumulative growth of the
epidemic can be ascribed to the episodic gen
large cluster outbreaks that increased from 11 ir
2005 (median cluster size 9) to 118 at the en
(cluster size 25) from 2002-2013. This study co
phylogenetic, sequence-based molecular
assays, virological and behavioural data fron
cohort and SPOT observational cohorts to id
determinants favouring the selection bias towa
cluster outbreaks.

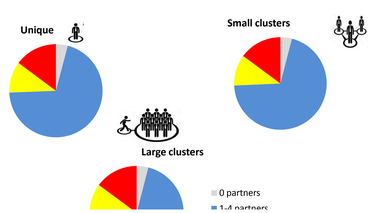
METHODS

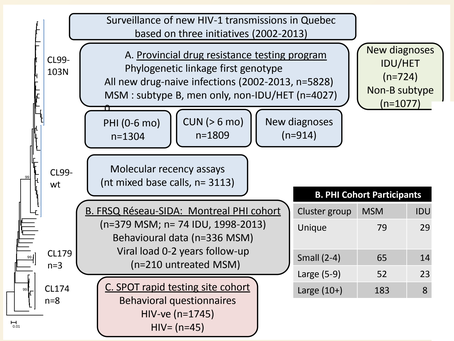
Phylogenetic analysis was performed on *pol*
datasets from all new MSM infections (2002-2
genotyped in primary HIV-1 infection (PHI, 0-6
n=1304), chronic drug-naive stage infec
months, n=2723). Patterns of viral spre
stratified into four groups based on cluster siz
5-9. and 10-119, respectively). Molecular
assays, based on sequence ambiguity (%
base calls) was used to estimate recency of
and genetic diversity over time. Observatio
from the Montreal PHI cohort ascertained s
behaviour and viremia over a 2-year period
individuals belonging to the different cluste
The SPOT rapid testing site initiative as
testing propensity in relation to behavioural ri
MSM.





Reported number of partners three months prior to primary infection
No significant differences in unique, small and large cluster groups





B. PHI Cohort Participants

Cluster group	MSM	IDU
Unique	79	29
Small (2-4)	65	14
Large (5-9)	52	23
Large (10+)	183	8

Testing habits for participants at the SPOT rapid testing sites (2009-2011, n=1745)

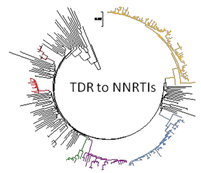
Time of last reported test (months)	% Participants (n=1745)	One-night partners (last 3 months) Mean	Rate ratio	Average number tests
0-3	6	5.1	1	3.8
3-6	16	5.9	1.2	3.4
6-12	27	4.4	0.39	2.4
12-24	25	3.0	0.6	1.4
>24	15	3.2	06	-
Never	11	1.4	0.3	-

*Using a quasi-Poisson model, there is a significant negative association between the number of one-night partners and reporting the time of the last test (p-values are 0.007, 0.034, and <0.001 for 12-24 months, >24 months, and never tested, respectively).

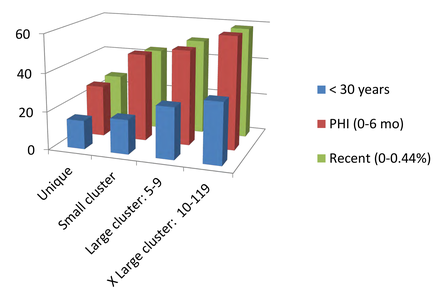
Selection bias in patterns of transmitted drug resistance

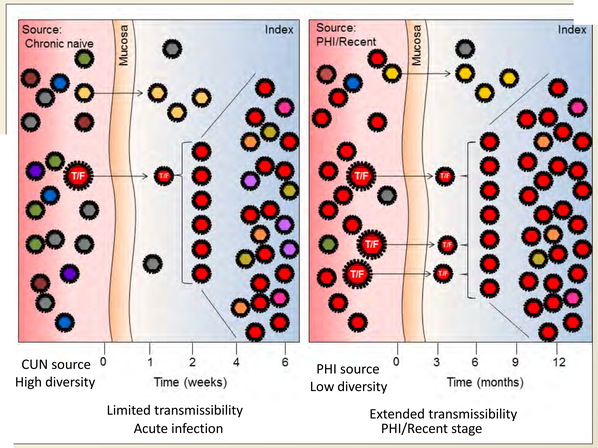
l to 2011, antiretroviral therapy has led to significant increases in viral suppression (42%→76%) and
ı the frequency resistance to NRTIs (78%→37%) and NNRTIs (44%→31%). High rates of transmitted
is sustained though large cluster sub-epidemics spreading among drug-naïve populations.

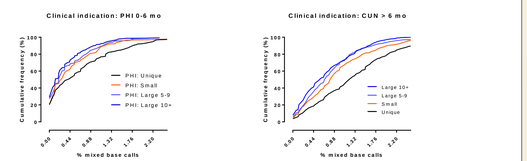
	NRTI TDR	NNRTI TDR	Dual MDR	Triple MDR
	5.4%	5.6%	2.6%	1.6%
2-4	4.3%	5.8%	0.6%	-
-9	7.2%	11.4%	2.9%	-
0-120	2.7%	23.2%	0.4%	-



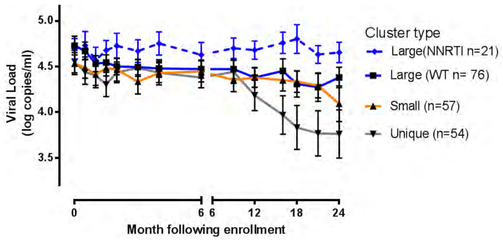
Primary infection (0-6 months) and recent infection (0-0.44% mixed base calls) is the driving force of the MSM epidemic expanding in an increasingly younger population





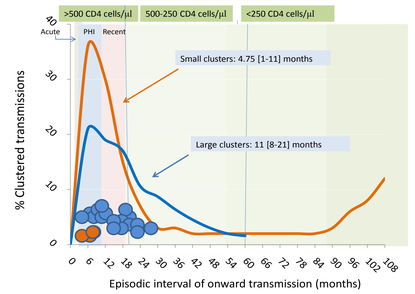


Large cluster lineages show lower genetic diversity and extended viremia over time



	Weighted Ambiguity
Unique	0.40 (0.07-1.07)
Small cluster	0.27 (0-0.74)
Large cluster	0.20 (0-0.67)*u
X-Large cluster	0.13 (0-0.53)*u,s

Treatment as Prevention requires timely diagnosis & earlier treatment of initiation



RESULTS

❖ Large cluster outbreaks were the driving force of epidemic wherein 7% of viral lineages were implicated in 70% onward transmissions. Transmission clustering was related to an increased relative contribution of PHI, accounting for 27%, 46%, 50% and 54% of unique, small and large cluster infections (odds-ratio 1, 2.33, 2.81, 3.33, respectively). Viral variants associated with clusters were qualitatively different showed lower weighted genetic diversity (median sequence ambiguity 0.40%, 0.27%, 0.20%, 0.13%, respectively).

❖ Viral variants associated with clusters were qualitatively different showed lower weighted genetic diversity and elicited extended viremia for two years compared to solitary transmissions where viremia declined to low viral set-points after 6 months.

❖No significant differences were observed in the reported number of one night stand-partners in the four cluster groups.

Cluster networks arose in increasingly younger populations, with 14%, 18%, 27% and 32% in unique, small, large and X-large clusters below 30 years of age.

Large cluster outbreaks were implicated in the enigmatic rise in transmitted resistance to NNRTIs and L5 revertants, despite declines in resistance among treated populations. The frequency of multidrug resistance was negatively correlated with clustering with frequencies of 4%, 0.6%, 2.9% and 0.4%, respectively.

SPOT data showed poor testing habits with 50% of persons untested in the previous year, with an inverse relationship between risk behaviour and testing opensity.

CONCLUSION

Taken together, untimely diagnosis and delayed treatment initiation has contributed to a selection bias towards large cluster viral lineages, showing lower weighted diversity, delayed sequence drift and extended viremia. These findings underscore the potential benefit of expanded testing and Treatment-as-prevention in averting the evolution of large cluster lineages overriding transmission bottlenecks.

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