Poster 0597

Epidemic History of Hepatitis C Virus among MSM in Amsterdam, the Netherlands

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Introduction

To strengthen HCV micro-elimination efforts among men who have sex with men (MSM), a better understanding of transmission networks is vital. Insight in the proportion of new HCV infections that result from ongoing transmission of local variants versus new infections via external introductions may further guide specific local elimination efforts. We describe the epidemic history of HCV genotype 1a among MSM in Amsterdam from 1994 to 2018.

Methods

Study population: HCV positive MSM from Amsterdam were included from the Amsterdam UMC (n=136), OLVG (n=8), DC Clinics (n=16), and the municipal health service in Amsterdam (n=16). Sanger sequencing of part of the E1E2 genomic region (525 base pairs) was applied to 174 samples positive for HCV gt1a – the most prevalent genotype in Amsterdam (64%) – from MSM diagnosed between 1994 and 2018. The majority of MSM was HIV positive (86%) and diagnosed during the acute phase of the infection (71%).

Phylogenetic methods: 174 genotype 1a sequences were aligned using *mafft* and manually edited using *BioEdit* until perfect codon alignment was achieved. A maximum likelihood genealogy was inferred using *RaxML* with the GTR+Gamma+I model of substitution. *Phydelity* software was used for statistically supported transmission cluster designation. Clusters larger than 5 were included for subsequent analyses. Time-resolved phylogenetic analyses were performed using *BEAST (v1.10.2)* to estimate the temporal origin and progression of the transmission clusters. The analyses were performed under a relaxed uncorrelated molecular clock model with the GTR+Gamma+I model of nucleotide substitution. The Bayesian SkyGrid model was used as a coalescent tree prior.

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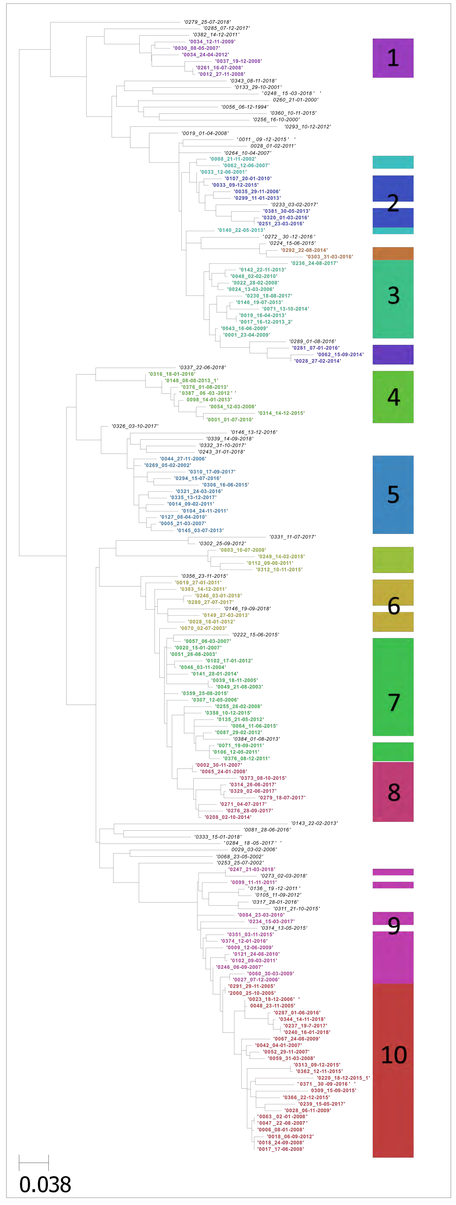

Figure 1. Maximum likelihood tree of 174 HCV genotype 1a sequences. Clusters ≥ 5 sequences are numbered. Colored sequence labels are clustered sequences; black sequence labels indicate unclustered sequences.

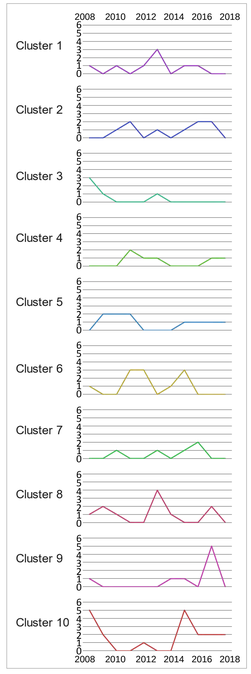

Figure 2.
Cluster activity of clusters with 5 or more sequences. Sample dates of all sequences after 2008 were plotted per cluster. X-axis depicts time in years, y-axis depicts number of new infections is the cluster per year.

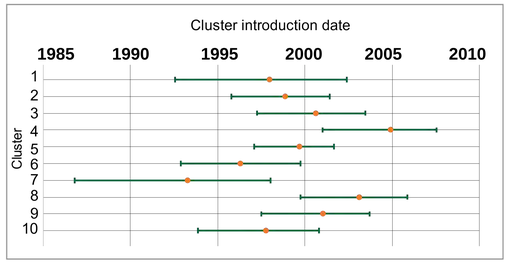

Figure 3.
Introduction dates of clusters containing five or more sequences. Orange dots indicate the date of the most recent common ancestor per cluster. Green bars indicate 95% highest posterior density intervals of these nodes. Cluster numbers correspond Figure 1.

Population characteristics (n=174)		
HIV-status		
Positive	**Negative**	**Unknown**
147	19	8
Acute or chronic infection		
Acute	***Chronic***	***Unknown***
122	26	26
PrEP usage		
PrEP	***No PrEP***	***Unknown***
19	147	8
Primary or reinfection		
Primary	***Reinfection***	***Unknown***
130	43	1
SVR12		
Yes	***No***	***Unknown***
58	9	107

Table 1. Population characteristics. 174 HCV genotype 1a positive samples were obtained from 4 institutes in Amsterdam, the Netherlands.

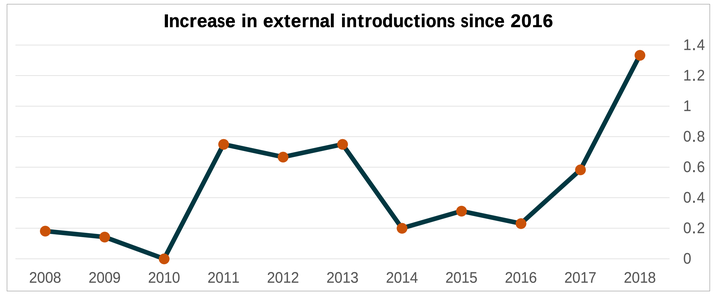

Figure 4. Ratio external introductions over clustered infections**.** Separate phylogenetic trees were constructed each year with sequences up to that year. The number of external introduction and number of local transmission events were quantified.

Results

130 sequences (75%) grouped into thirteen transmission clusters and one transmission pair; introduction dates ranged from 1994 to 2005. Ten clusters with more than 5 sequences were found, the largest cluster (10) containing 26 sequences. The ratio external introductions to clustered sequences was relatively high between 2011-2013 and from 2017 onwards. The external introduction outnumbered the clustered infections for the first time in 2018. Most clusters showed activity in recent years suggesting local transmission within the communities in Amsterdam continue to contribute to the epidemic. However, the recent increase in external introductions may indicate a shift in the sources of new infections.

Conclusions

- Both external introductions and ongoing transmission within existing clusters continue to fuel the HCV epidemic among MSM in Amsterdam.
- Between 2011-2013, the proportion of external introductions compared to local transmissions seems relatively high and in 2018, external introductions outnumbered local transmission for the first time.
- The recent increase in external introductions seem to coincide with universal access to HCV antiviral treatment in the Netherlands.
- Prospective, phylogenetic analyses combined with collection of transmission network could guide targeted prevention interventions and stresses the need for real-time HCV sequence monitoring in the Netherlands.