

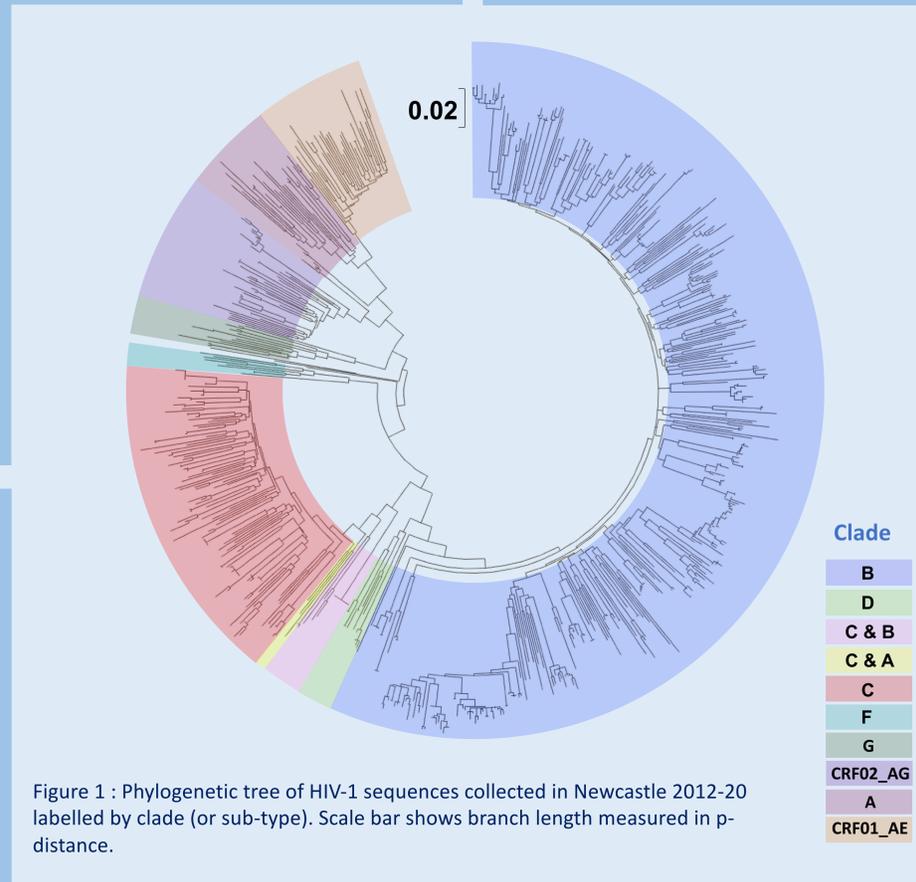
The use of routine diagnostic sequencing data to determine the molecular epidemiology and transmission dynamics of HIV-1 in Newcastle-upon-Tyne

1. Background

- The HIV-1 genome accumulates mutations rapidly, so viruses can differ by an observable amount within the time-scale of one transmission.
- Thus, viruses with very similar sequences are likely to be linked by a transmission event or a short transmission chain.
- Phylogenetic analysis can be used to identify transmission clusters and tracking clusters over time can inform public health measures to reduce transmissions.
- This study aimed to describe the molecular epidemiology of HIV-1 in Newcastle-upon-Tyne, identify potential transmission clusters in the area, and recognise patient characteristics associated with these clusters.

2. Methods

- A section of HIV-1's *pol* gene is routinely sequenced in diagnostic testing. Sequences produced in testing for patients at the Royal Victoria Infirmary and the Newcroft Sexual Health centre from 2012 -2020 were collected.
- These sequences (n=755) were subtyped using the REGA v3 HIV-1 subtyping tool⁽¹⁾ and a phylogenetic tree inferring their evolutionary relationship was produced on MEGAX (v10.2.6)⁽²⁾ (see *fig.1*).



- A set of transmission cluster criteria were developed (see *fig.2*) and putative transmission clusters were identified from the tree using Cluster Picker (v1.2.3)⁽³⁾
- Clinical and demographic data were collected for the patients whose sequences were used to build the tree in order to identify factors associated with belonging to a cluster.

3. Results

- A total of 12 transmission clusters were identified using the criteria, with sizes ranging from 4-15 patients.
- Using data on when the sequences were collected, a line chart was produced which shows the cumulative number of patients in each cluster per year (see *fig.3*).
- On statistical analysis, clusters were found to be associated with young males, infected with B-clade viruses in the UK from sex between men (see *fig.4*). Thus, these demographics are most likely to be implicated in transmission events in Newcastle.

- Through retrospective tracking, the potential for monitoring cluster growth was demonstrated. Addition of further sequences to the analysis over time could allow near-real-time monitoring of transmission clusters.

4. Conclusions

- This study was able to describe the molecular epidemiology and identify clustering of HIV-1 within Newcastle.
- Characterisation of transmission clusters, using socio-demographic and clinical data, could help to inform public health interventions.

Transmission clusters were defined as:



Figure 2 : Criteria developed to identify transmission clusters within our cohort. *Bootstrapping is a statistical method used to assess confidence in tree structure, the higher the % of replicates a cluster is present in the more likely it is in the true, unknown, structure.

Year-on-year growth of transmission clusters

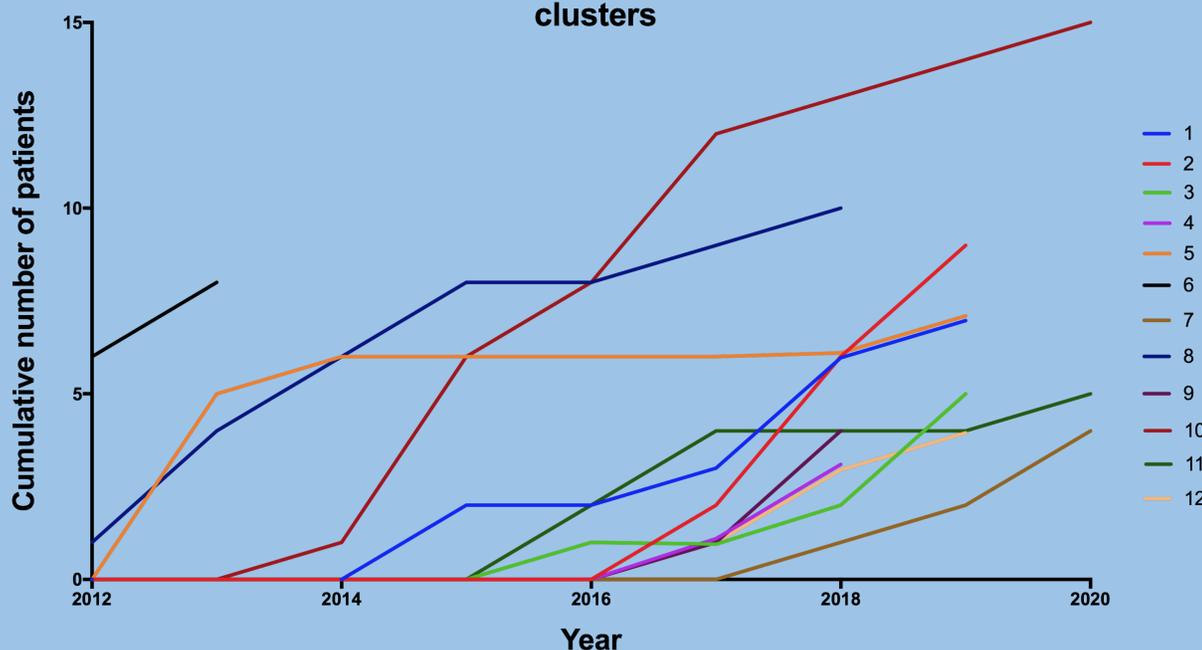


Figure 3 : The cumulative number of patients in each of the 12 transmission clusters per year. The lines are truncated so they finish at the last year where patients were added to the cluster.

	Clustered patients	Non-clustered patients	P-value
% ≤ 25 years-old	82.9	51.9	0.0001
% Male	81.9	63.9	0.0006
% Acquired through sex between men	58.1	35.4	0.0001
% UK acquired infections	62.9	45.2	0.0016

Figure 4: Percentage of clustering and non-clustering patients belonging to different demographic groups. P-values were calculated using a chi-square test.

Works cited

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