

Phylogenetic Analysis of HIV Transmission among Different Ethnic MSM Groups in the UK

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Introduction

- HIV-1 clades associated with heterosexual transmission in the UK, such as subtypes A or C, are increasingly found in men having sex with men (MSM), suggesting **transmission bridges** between exposure groups. [1]
- Black and minority ethnic** (BME) MSM in the UK and the US are more likely to have **female sexual partners** than white MSM. [2,3]
- We investigated the potential **'bridging' role** of BME MSM in the UK epidemic, by investigating patterns of HIV transmission among different ethnic MSM groups by phylogenetic means.

Methods

- The phylogeny of **2,063** subtype A, **22,507** subtype B and **9,303** subtype C HIV-1 sequences (PR + RT; 1,495nt) sampled in the UK between 1994 and 2008 was reconstructed by approximate maximum likelihood inference, using the software FasTree [4]. These correspond to the first sampling point of each patient, prior to therapy and several years post-infection.
- Transmission clusters** were defined as phylogenetic clades with ≥ 2 sequences, a maximum patristic genetic distance ≤ 0.045 nucleotide substitutions per site and a local branch support $\geq 90\%$. Clusters were identified using an automated method (Lycett S; unpublished).
- The robustness of the clusters was assessed by from the alignment 37 codon positions associated with antiretroviral drug resistance.
- Surveillance data were used to examine **demography and risk behaviour** of persons in clusters that included at least one MSM.
- Transmission clusters including **at least one MSM** were categorised into: (i) clusters where MSM where all BME (**BME MSM clusters**), (ii) clusters where MSM where all white (**white MSM clusters**) and (iii) clusters including both BME and white MSM (**mixed clusters**).
- The characteristics of the latter clusters were statistically compared using chi²-test in SAS v9.1.

Results

- A total of **5,449** transmission clusters were identified, including 374 (**7%**), 3,252 (**60%**) and 1,823 (**33%**) subtype A, B and C viruses respectively.
- In total, the proportion of white MSM (8,360/13,179) and BME MSM (1,078/1700) found in transmission clusters was identical (63%).
- Of the 2,346 clusters (12,602 patients) for which the ethnicity of **all MSM** was known:
 - 1,687 (**71.9%**) included MSM of white ethnicity only (white MSM clusters)
 - 111 (**4.7%**) included MSM of non-white ethnicity only (BME MSM clusters)
 - 548 (**23.4%**) included both white and BME MSM (mixed clusters).
- The average size of the clusters was greater for mixed clusters (median size 5) than for those in a white MSM (median size 3) or BME (median size 2) cluster (**Table 1**)

Table 1: Cluster-level summary statistics; all entries are median (range) unless otherwise stated

		Cluster group		
		White MSM	BME MSM	Mixed
Number of clusters		1687	111	548
Median size of cluster (range)		3 (2,66)	2 (2,12)	5 (2,218)
% of MSM in cluster	$\leq 20\%$	27 (1.6)	6 (5.4)	1 (0.2)
(p-value=0.0001)*	>20%, $\leq 40\%$	154 (9.1)	21 (18.9)	11 (2.0)
	>40%, $\leq 60\%$	409 (24.2)	37 (33.3)	48 (8.8)
	>60%, $\leq 80\%$	270 (16.0)	12 (10.8)	149 (27.2)
	>80%, $\leq 100\%$	72 (4.3)	0 (-)	100 (18.3)
	100%	755 (44.8)	35 (31.5)	239 (43.6)
% of heterosexuals in cluster				
(p-value=0.0001)*	None	1445 (85.7)	70 (63.1)	324 (77.2)
	0 - $\leq 20\%$	103 (6.1)	1 (0.9)	96 (17.5)
	>20%, $\leq 40\%$	60 (3.6)	12 (10.8)	27 (4.9)
	>40%, $\leq 60\%$	68 (4.0)	20 (18.0)	2 (0.4)
	>60%, $\leq 80\%$	10 (0.6)	8 (7.2)	0 (-)
	>80%	1 (0.1)	0 (-)	0 (-)

* Chi² test for heterogeneity

Table 2: Individual-level summary statistics; all entries are n (%)

		Cluster group			
		White MSM	BME MSM	Mixed	
Number of patients		6926	327	5349	
Gender	Male	5216 (75.3%)	237 (72.5%)	4493 (84.0)	
	(p-value =0.0001)*	Female	191 (2.8%)	29 (8.9%)	68 (1.3)
		Not known	1519 (21.9%)	61 (18.7%)	788 (14.7)
Ethnicity	White	5248 (75.8)	19 (5.8)	3496 (65.4)	
	(p-value =0.0001)*	Black African	70 (1.0)	75 (22.9)	102 (1.9)
		Black Caribbean	25 (0.4)	81 (24.8)	187 (3.5)
		Black Other	10 (0.1)	22 (6.7)	101 (1.9)
		IPB	2 (0.0)	7 (2.1)	106 (2.0)
	Other	30 (0.4)	60 (18.4)	504 (9.4)	
	Not known	1541 (22.3)	63 (19.3)	853 (16.0)	
Risk behaviour	MSM	4878 (70.0)	188 (57.5)	4204 (78.6)	
	(p-value =0.0001)*	Heterosexual	352 (5.1)	68 (20.8)	225 (4.2)
		Other	115 (1.7)	2 (0.6)	28 (0.5)
	Not known	1612 (23.3)	69 (21.1)	892 (16.7)	
Clade	A	62 (0.9)	14 (4.3)	27 (0.5)	
	(p-value =0.001)*	B	6777 (97.9)	261 (79.8)	5220 (97.6)
		C	87 (1.3)	52 (15.9)	102 (1.9)

Note BME and white MSM clusters may include individuals of other ethnicities infected via other means
* Chi² test for heterogeneity

- Across all clades, 659/2,346 clusters (28.1%) contained at least one BME MSM.
- Clusters with BME MSM included a greater proportion of **females** and **heterosexuals** compared to clusters with white MSM (**Table 2**).
- Heterosexuals found in BME MSM clusters were more likely to be **Black Africans** (44.1%), **Black Caribbean** (20.6%) or **white** (16.2%) (**Table 3**)

BME were categorized as:

- Black Caribbean (BC)
- Black African (BA)
- Other
- Black Other (BO)
- Indian/Pakistani/Bangladeshi (I/P/B)

Table 3: Individual level summary data for heterosexuals (n=645); all entries are n (%)

		Cluster group			
		White MSM	BME MSM	Mixed	
Number of heterosexuals		352	68	225	
Gender	Male	195 (55.4)	39 (57.4)	165 (73.3)	
	(p-value =0.0001)*	Female	157 (44.6)	29 (42.7)	60 (26.7)
		Not known			
Ethnicity	White	234 (66.5)	11 (16.2)	132 (58.7)	
	(p-value =0.001)*	Black African	63 (17.9)	30 (44.1)	38 (16.9)
		Black Caribbean	21 (6.0)	14 (20.6)	14 (6.2)
		Black Other	5 (1.4)	2 (2.9)	9 (4.0)
		IPB	2 (0.6)	2 (2.9)	12 (5.3)
	Other	20 (5.7)	8 (11.8)	15 (6.7)	
	Not known	7 (2.0)	1 (1.5)	5 (2.2)	
(p-value =0.0001)*	BME- total	111 (31.5)	56 (82.4)	88 (39.1)	
Clade	A	10 (2.8)	10 (14.7)	2 (0.9)	
	(p-value =0.001)*	B	314 (89.2)	36 (52.9)	212 (94.2)
		C	28 (8.0)	22 (32.4)	11 (4.9)

* Chi² test for heterogeneity

Conclusions

- An equal proportion of white and BME MSM are involved in HIV transmission in the UK.
- MSM clusters are ethnically **heterogenous** with 1 in 4 clusters containing a BME MSM.
- Transmission bridges** between HIV-infected BME MSM and heterosexuals were found.
- Phylogenetic analysis of anonymised viral sequences revealed linkages between risk groups only contact tracing could have unravelled.

References:

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