Professor Andrew Leigh Brown
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<th>Speaker Name</th>
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<td>Professor Andrew Leigh Brown</td>
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COMPETING INTEREST OF FINANCIAL VALUE > £1,000:

Date: October 2014
Inferring HIV transmission dynamics from phylogenetics

Andrew Leigh Brown
University of Edinburgh
## Annual UK HIV Diagnoses

### Estimates for 2012

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<th>Adjusted</th>
<th>Observed</th>
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<tr>
<td><strong>MSM</strong></td>
<td>3,250</td>
<td>2,964</td>
</tr>
<tr>
<td><strong>HET</strong></td>
<td>2,880</td>
<td>2,581</td>
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Source: PHE
Transmission dynamics depend on the contact network

- Often reconstructed by interview data
  - Number, gender & identity of contacts in last year
Transmission dynamics depend on the contact network

- Often reconstructed by interview data
  - Number, gender & identity of contacts in last year
- HIV
  - Rapid evolution
  - Similar sequences reveal linked infections
Closely related viral sequences cluster in a phylogenetic tree

- 9 clusters visualised in this tree
The UK national epidemic - subtype B

- Subtype B still >80% MSM
- Data from UK HIV Drug Resistance Database
  - viral sequences from routine resistance assays
- 14,560 subtype B sequences, 1 per individual
  \( \approx \frac{2}{3} \) of diagnosed cases in MSM in 2007
Subtype B:  50% linked to ≥ 1 other

15% linked to 10 or more

1728 (15%) 2408 (20%) 1673 (15%)
97 clusters

N = 14,560
Clusters of up to 100 individuals
Incorporating real time

- Based on “molecular clock”
  - viral mutations occur ~ constant rate
- Scale trees using calendar dates of samples
  - “BEAST” software (Drummond & Rambaut 2007)
BEAST trees show clusters in time

Gives transmission rate within clusters
Time interval between transmissions

• 1 sequence from each patient
  – very dense sample
• Every split in tree (node) tracks a transmission
Subtype B transmission intervals can be short

20% of transmission intervals < 6 months

Acute HIV infection implicated

median = 17 months
Timing of all splits gives a network from the phylogeny
Network of large cluster

Node depth=1 year
2 years
3 years
4 years
6 years
A scale-free network?

“Cumulative distribution of number of different sexual partners decays as a scale-free power law”

Liljeros et al 2001

In a scale free network, new links are preferentially attached to highly-connected nodes
What does this mean?

Does a new network member link at random?

Or to a member with many existing links?

Cluster size distribution reveals social mechanics of partner choice
Partner selection

• Partner selection **independent** of their no. of partners
  – Negative binomial

but if:

• **Preferential**: a new partner connects to one with many existing links
  – Yule/Waring
Preferential attachment in UK Subtype B

- Waring distribution is best fit

- Preferential attachment makes intervention difficult
  – imperfect interventions ineffective if randomly given

- Most transmission interventions are not completely effective…
Preferential attachment means interventions are better if targeted

Using HIV Networks to Inform Real Time Prevention Interventions

Susan J. Little¹*, Sergei L. Kosakovsky Pond¹, Christy M. Anderson¹, Jason A. Young¹, Joel O. Wertheim¹, Sanjay R. Mehta¹, Susanne May², Davey M. Smith¹,³

New heterosexual infections

New UK infections – 2012

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The rest of the UK HIV epidemic

- 65% of UK HIV infections are heterosexual
  - most derived from sub-Saharan Africa
  - mostly **not** subtype B

- Most non-B is subtype C (~60%) & subtype A (12%)

- What has been happening in this epidemic?
Large non-B clusters are MSM/IDU

N = 14,677
Cluster dynamics over time

- Clusters were picked in the 2007 HIV Rdb tree then re-identified in the 2010 tree.
- Cluster growth was calculated as the number of new sequences per initial sequence (for each cluster).


Cluster growth = 60%
Non-B cluster growth depends on risk group

Cluster growth

N = 14,677

p<10^{-6}
Conclusions

• High density sampling and phylogenetic analysis in time has allowed the description of the transmission dynamics for UK HIV for subtype B
  – 29% of clusters are large
  – 20% of their transmission intervals < 6 months
  – fits Waring distribution with parameter ~ 3.0
  • preferential attachment
    – Means random interventions are not very effective

Conclusions

• High density sampling and phylogenetic analysis in time has allowed the description of the transmission dynamics for UK HIV

• for subtype B
  – 29% of clusters are large
  – 20% of their transmission intervals < 6 months
  – fits Waring distribution with parameter ~ 3.0
    • preferential attachment
      – Means random interventions are not very effective


• for non-B HIV
  – far fewer very large clusters
  – largest clusters crossovers to MSM/IDU
  – MSM/IDU clusters growing fastest
  – epidemic not growing within UK heterosexuals
Edinburgh University
• Samantha Lycett
• Manon Ragonnet
• Gonzalo Yebra
• Emma Hodcroft

UK HIV Drug Resistance Database
• Esther Fearnhill (MRC CTU)
• David Dunn (MRC CTU)
• Deenan Pillay