

Using real-time phylodynamic analysis to assess and guide public health interventions in an HIV outbreak among people who inject drugs in Scotland



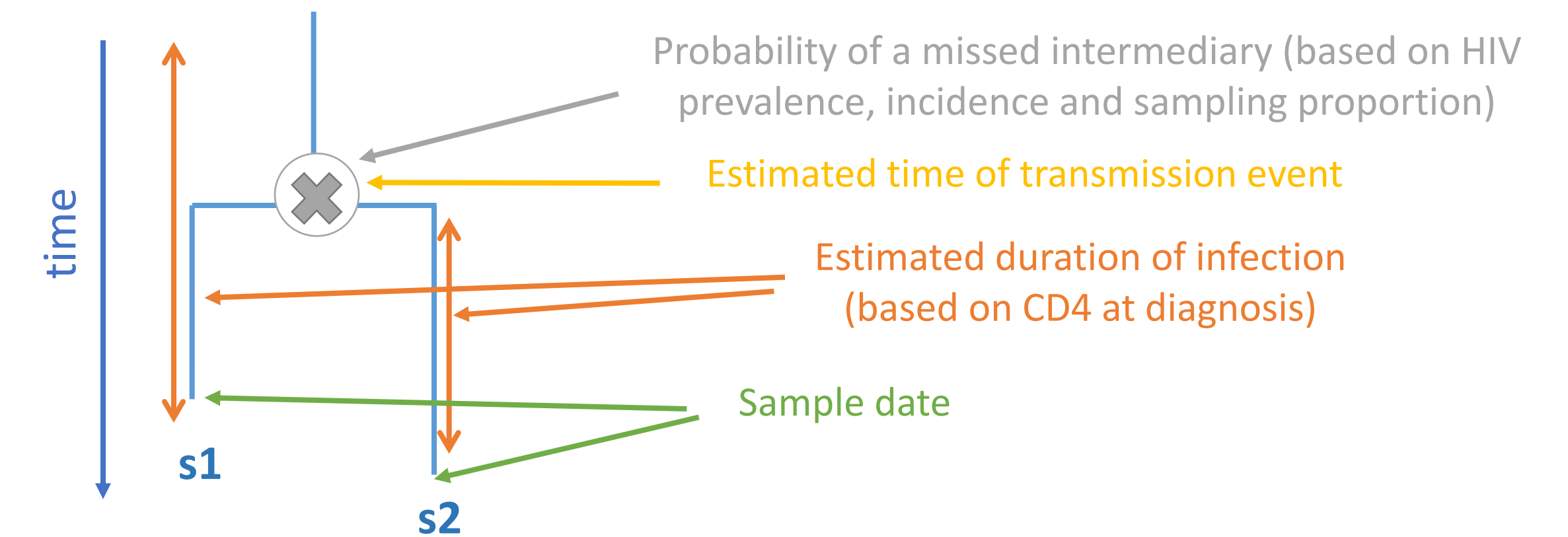
Manon Ragonnet-Cronin^{1,2}, Amanda Bradley-Stewart³, Rebecca Metcalfe^{4,5}, Rory Gunson³, Erica Peters⁴, Andrew McAuley^{5,7}, Catriona Milosevic⁶ and Andrew Leigh Brown¹

background

- People who inject drugs (PWID) are at high risk for HIV acquisition if they share equipment or have unprotected sex
- Harm reduction in the UK and the rest of Europe dramatically decreased incidence in this group in the 1980s
- Recently a number of HIV outbreaks among PWID have been reported in Europe^{1,2} linked to the economic recession, funding cuts, homelessness and the injection of new psychoactive substances
- In 2015 a rise of subtype C HIV diagnoses with two drug resistant mutations among PWID was noted in Scotland
- All 104 sequences were closely linked (≤ 0.01 substitutions per site), had both mutations and mean transmission intervals were < 6 months³
- The utility of phylogenetic analysis to detect clusters of HIV infections and support the subsequent public health response has been demonstrated⁴
- Given the scale of the current outbreak, we want to use molecular epidemiology to help guide public health interventions during an ongoing outbreak⁵ with a particular focus on contact tracing investigations

methods

Figure 1: Source Attribution method

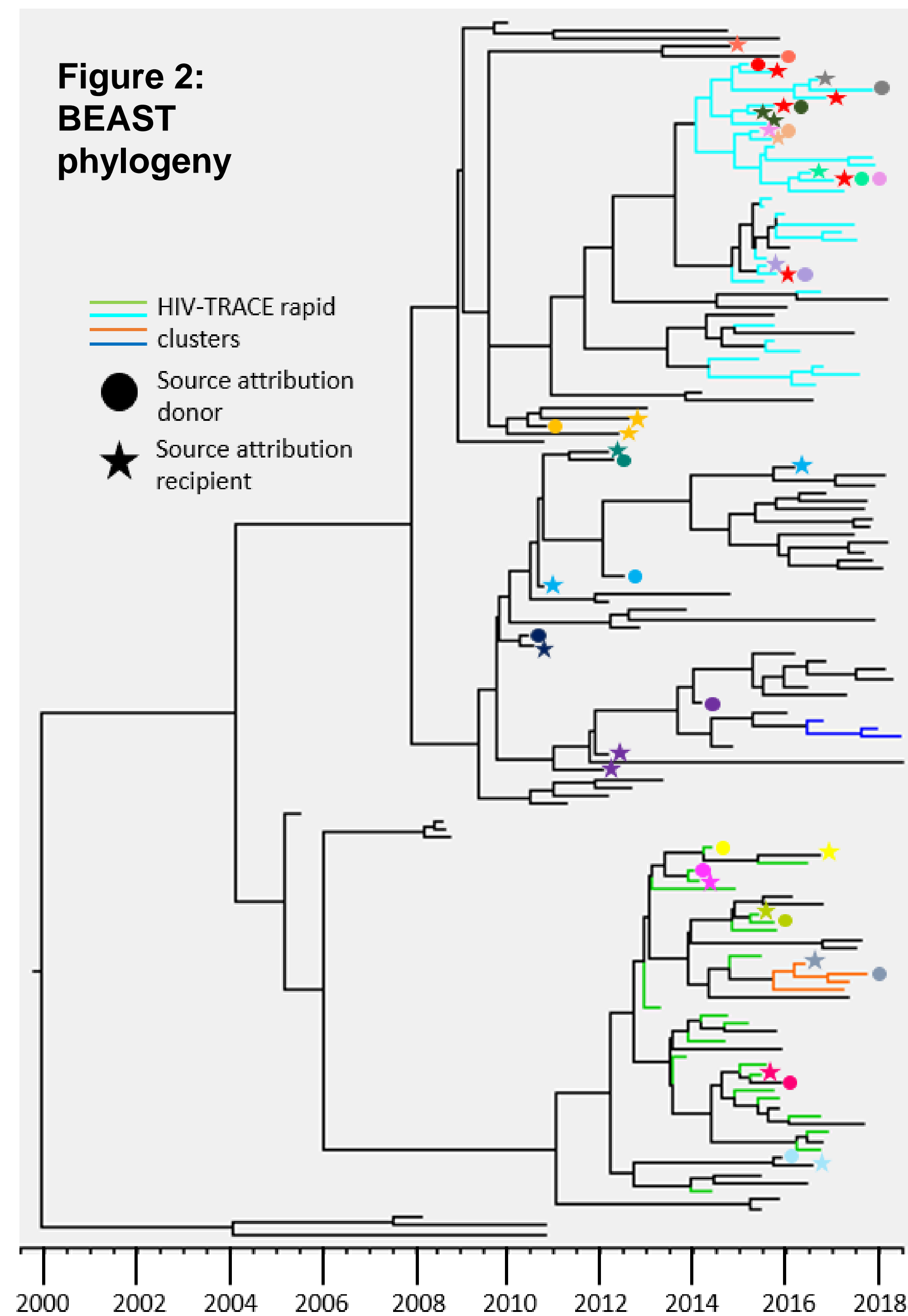


- Phylogenetic analysis of viral sequences provides an alternative and independent route to reconstructing transmission networks
- The West of Scotland specialist virology centre sequences *pol* for all new HIV diagnoses
- The National Health Service portal collects clinical data, including
 - date of last negative test, CD4 count and avidity result
- We time-resolved the phylogeny using BEAST⁶
- Source attribution methods estimate the probability of a direct transmission event between two individuals based on the time-resolved phylogeny, estimated dates of infection, prevalence and incidence⁷ (Figure 1)
- HIV-TRACE can be used to rapidly find clusters based on a genetic distance threshold⁸ and is being used by CDC to detect transmission clusters as they arise⁵

results

1. Time resolved phylogeny of the outbreak

Figure 2: BEAST phylogeny



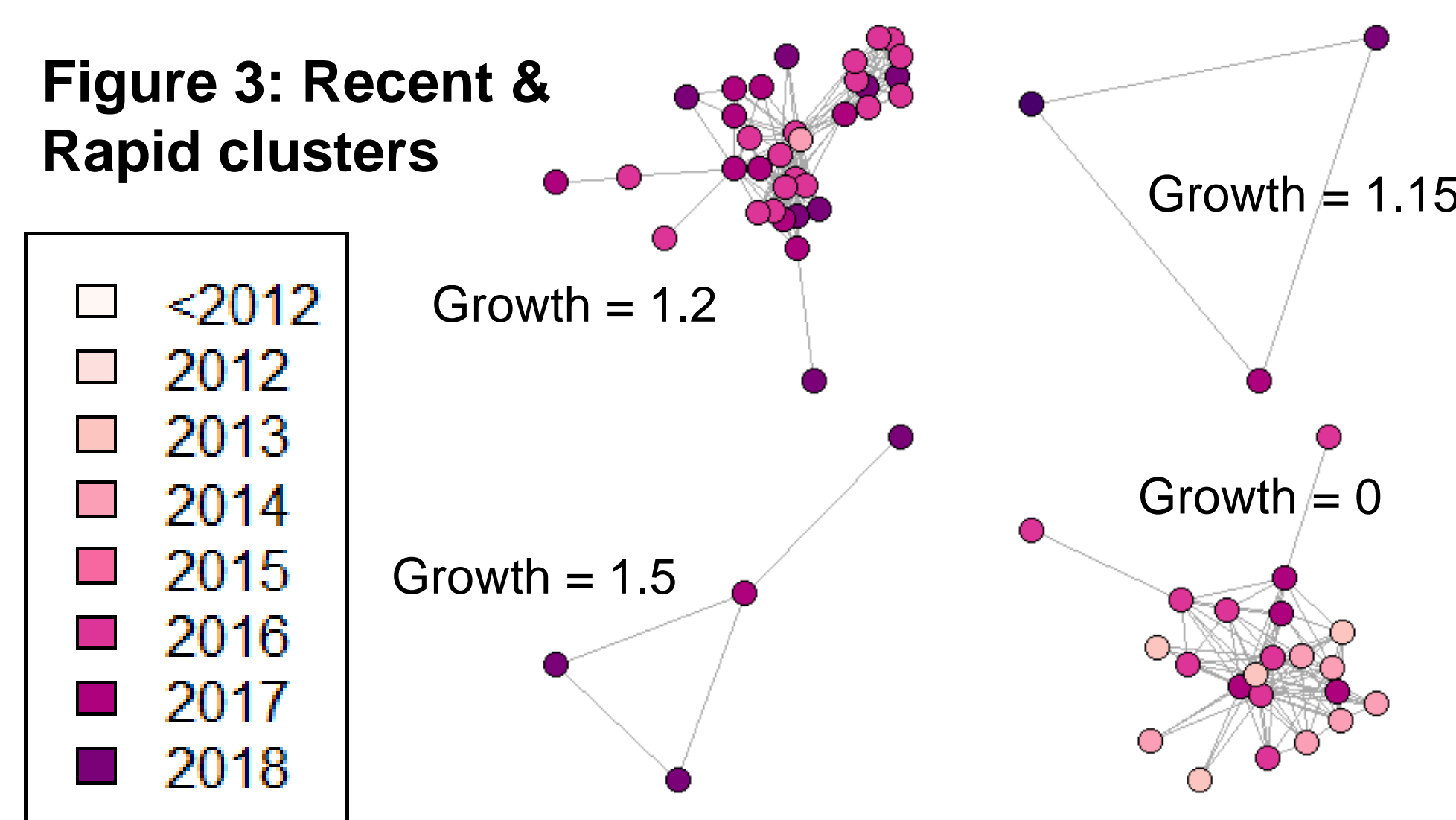
- Single cluster of 145 sequences with both mutations, all from Scotland (Figure 2)
- Origin of cluster is in 2000, first diagnosis in 2005, accelerated transmission after 2014
- Mean genetic distance $< 1\%$
- 3 subclusters, all with recent transmissions
- The coloured branches indicate clusters selected by HIV-TRACE⁸
 - HIV-TRACE does not enforce monophyly
- The circles and stars in the phylogeny indicate the most probable transmission pairs (donors and recipients) based on the Source Attribution method⁷

2. Source Attribution⁷

- We are displaying transmission events $> 70\%$ probability of being direct
- The timing of each transmission event can be estimated from the phylogeny
- Source Attribution can be used to find individuals associated with the highest number of transmissions over time
 - Here, 25% of individuals were responsible for $> 50\%$ of onward transmissions
- Individuals with recent onward transmissions can be contacted to ensure they are on suppressive treatment and their partners are on pre-exposure prophylaxis (PreP) to interrupt further transmission

3. HIV-TRACE⁸

Figure 3: Recent & Rapid clusters



- We used HIV-TRACE to identify clusters with rapid (≤ 0.05 substitutions per site) transmissions, and calculated their recent (2017/2018) growth⁹:
 - $Growth = \frac{\delta N}{\delta t}$ (Figure 3)
- Clusters with recent growth are the most likely to keep growing⁹
- One large cluster had high growth in 2016 but not in 2017/2018
- From a public health perspective, clusters with rapid and recent transmission are termed "priority clusters"⁵
- As such, they serve as a focal point for contact tracing to collect information about partner contacts and social network contacts (to determine the larger risk network)
- This group can then be tested, treated if positive, or provided with appropriate post-exposure prophylaxis

conclusions

- 145 linked HIV cases among PWID in Scotland between 2005 and 2018, the biggest outbreak since the 1980s
- Two different methods for identifying priority cases for public health interventions
- There is some overlap between individuals prioritized by each method but they are calculating different things (probable direct transmissions versus recent cluster growth)
- **LIMITATIONS**
 - Neither method has been tested/evaluated in known transmission chains
 - SA model relies on many parameters (incidence, prevalence, CD4 counts)
- Both methods can be used to:
 - Select specific individuals for enhanced public health interventions (viral suppression, contact tracing, partner notification, partner testing, treatment/HIV PreP for partners)
 - Determine the risk factors for transmission and thus guide public health interventions towards subpopulations at highest risk of transmission/infection
- **ETHICS**
 - The ethics and acceptability of these approaches still need to be ascertained among the HIV+ community

references

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1 University of Edinburgh, UK; 2 University of California, San Diego, USA; 3 West of Scotland Specialist Virology Centre, NHS Greater Glasgow and Clyde, Glasgow, UK; 4 Brownlee Centre for Infectious diseases, NHS Greater Glasgow and Clyde, Glasgow, UK; 5 Health Protection Scotland, UK; 6 NHS Greater Glasgow and Clyde, Glasgow, UK; 7 Glasgow Caledonian University, Glasgow, UK