Age and HIV Transmission: Insights from Phylogenetic Analysis

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The African HIV epidemic is predominantly female.

Male to female HIV incidence ratios

Lack of data on sources of female infection

• There is abundant information on risk factors for HIV acquisition among African women.
  • *Younger age an historically strong predictor.*

• Less is known about male partner sources of female HIV infection.
  • *Most data come from longitudinal studies of cohabitating stable couples or self-reported partner data.*

Rakai Health Sciences Program PEPFAR DREAMS program in south central Uganda
Study objective and approach

- **Objective**: To characterize sources of HIV transmission by age and gender at the population-level in an African setting with generalized HIV transmission (e.g., what is the age profile of male sources of HIV infection to young women?).

- **Approach**: Molecular epidemiology/HIV phylogenetics
Phylogenetics and Networks for Generalized Epidemics in Africa (PANGEA-HIV)

Abeler-Dörner et al., Curr Opin HIV/AIDS. 2019
Pillay et al., Lancet, 2015

HIV SHIVER and Phyloscanner

Wymant et al. Virus evolution. 2018
Wymant et al. Mol. Biol. Evo. 2018
Ethical considerations in global HIV phylogenetic research

Coltart and Hoppe et al., Lancet HIV. 2018

Phylogenetic analysis of pathogens is an increasingly powerful way to reduce the spread of epidemics, including HIV. As a result, phylogenetic approaches are becoming embedded in public health and research programmes, as well as outbreak responses, presenting unique ethical, legal, and social issues that are not adequately addressed by existing bioethics literature. We formed a multidisciplinary working group to explore the ethical issues arising from the design of, conduct in, and use of results from HIV phylogenetic studies, and to propose recommendations to minimise the associated risks to both individuals and groups. We identified eight key ethical domains, within which we highlighted factors that make HIV phylogenetic research unique. In this Review, we endeavoured to provide a framework to assist researchers, public health practitioners, and funding institutions to ensure that HIV phylogenetic studies are designed, done, and disseminated in an ethical manner. Our conclusions also have broader relevance for pathogen phylogenetics.
Phylogenetics and Networks for Generalized Epidemics in Africa (PANGEA-HIV)

Abeler-Dörner et al., Curr Opin HIV/AIDS. 2019
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The Rakai Community Cohort Study (RCCS)

- Population-based HIV surveillance cohort in south central Uganda conducted by the Rakai Health Sciences Program.
- 28 rural agrarian and semi-urban trading communities under surveillance since 1994
- 4 Lake Victoria fishing communities under surveillance since 2011
- ~20,000 study participants surveyed every 1.5-2 years
Population census

Survey

Biospecimens/biometrics

Services
Inferring African HIV transmission networks with deep sequence phylogenetic analysis

Directed transmission networks with ~900 source-recipient pairs

Genetic pairwise distance distribution in epidemiologically linked couples

Shiver/Phyloscanner

Ratmann et al. Nature Comm. 2019
Sources of transmission by age and gender, 2011-15

Incident Female Infections

Incident Male Infections

Xi et al. JRSSC. 2022
Sources of transmission by age of recipient and transmitter

Female incident infections

Male incident infections

Age of recipient


Xi et al. JRSSC. 2022
Male sources of transmission to women

Xi et al. JRSSC. 2022
HIV viremia in the RCCS, 2016-17

All HIV-positive persons

HIV-positive persons with VL>400 copies

red: women

green: men
Transmission cycle

Ratmann et al. Lancet HIV 2020
HIV incidence in sub-Saharan Africa is declining

NUMBER OF NEW HIV INFECTIONS AND AIDS-RELATED DEATHS, EASTERN AND SOUTHERN AFRICA, 2000–2020

HIV incidence trends in Rakai, 1999-2017

CHP=combination HIV prevention

Grabowski et al. NEJM. 2017
Grabowski et al. CROI. 2020
HIV incidence in Rakai by age, 2001 vs. 2017
Shifting sources of transmission

Monod et al., in preparation
Increasingly male driven transmission flows

Monod et al., in preparation
The African HIV epidemic is predominantly female?

Male to female HIV incidence ratios

Conclusions

1. Young, unsuppressed HIV-positive men, ages 25-34, are linked disproportionately to many transmission events.

2. Adolescent girls and young women, 15-24 years, are typically infected by men many years (5+) older than them.

3. As women age, their transmitting partners tend to be the same age or younger.

4. The HIV epidemic is aging, with incidence becoming more concentrated in older age groups, increasingly male driven transmission flows, and age-disparate partnerships contributing less to virus transmission.

5. Viral phylogenetics are a powerful tool for understanding HIV transmission patterns at a population-level.
Thank you!

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PANGEA