

# Age and HIV Transmission: Insights from Phylogenetic Analysis

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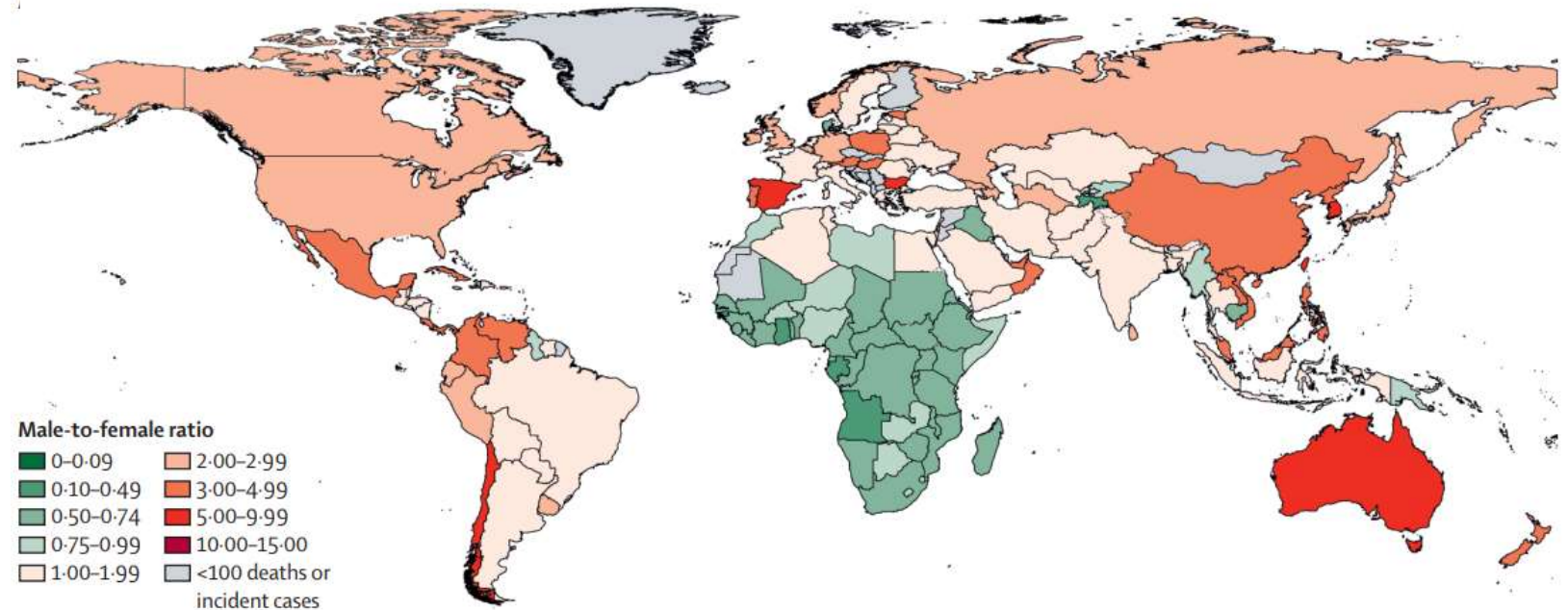
HPTN  
HIV Prevention  
Trials Network

**ANNUAL MEETING**  
2022

# The African HIV epidemic is predominantly female.



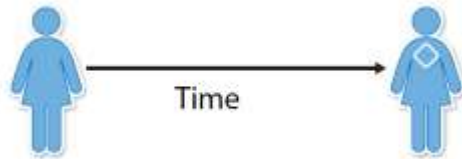
Male to female HIV incidence ratios



GBD 2019 HIV collaborators. *Lancet HIV*. 2021.

# 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.*

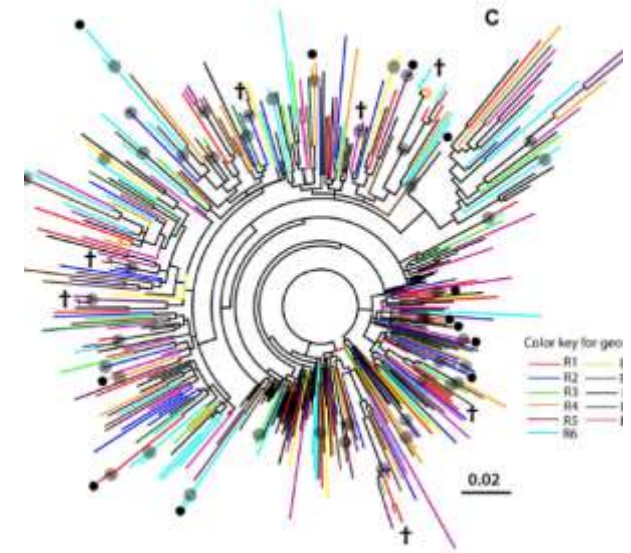


- Less is known about male partner sources of female HIV infection.
  - *Most data come from longitudinal studies of cohabitating stable couples or self-reported partner data .*



Rakai Health Sciences Program PEPFAR  
DREAMS program in south central Uganda

- 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 the age profile of male sources of HIV infection to young women?).
- Approach: Molecular epidemiology/HIV phylogenetics

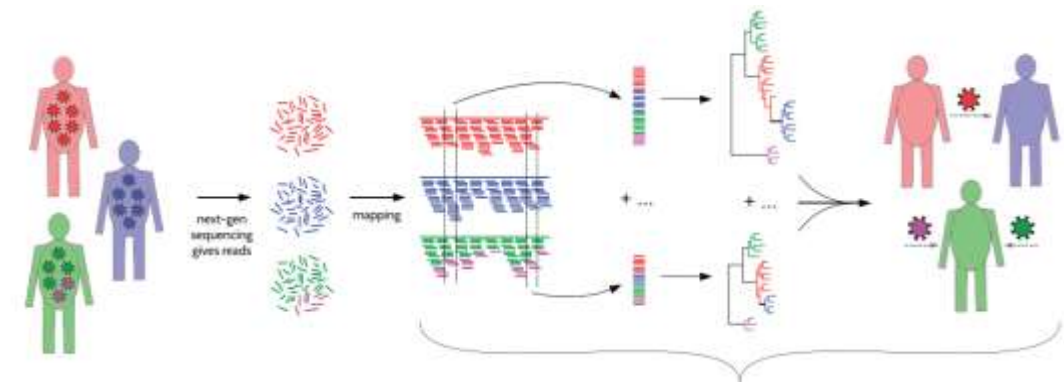


# Phylogenetics and Networks for Generalized Epidemics in Africa (PANGEA-HIV)



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

Cordelia E M Coltart\*, Anne Hoppe\*, Michael Parker, Liza Dawson, Joseph J Amon, Musonda Simwinga, Gail Geller, Gail Henderson, Oliver Laeyendecker, Joseph D Tucker, Patrick Eba, Vladimir Novitsky, Anne-Mieke Vandamme, Janet Seeley, Gina Dallabetta, Guy Harling, M Kate Grabowski, Peter Godfrey-Faussett, Christophe Fraser, Myron S Cohen†, Deenan Pillay‡; on behalf of the Ethics in HIV Phylogenetics Working Group‡

*Lancet HIV* 2018; 5: e656-66

Published Online  
August 30, 2018

[http://dx.doi.org/10.1016/S2352-3018\(18\)30134-6](http://dx.doi.org/10.1016/S2352-3018(18)30134-6)

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appendix

Institute for Global Health  
(C E M Coltart PhD,

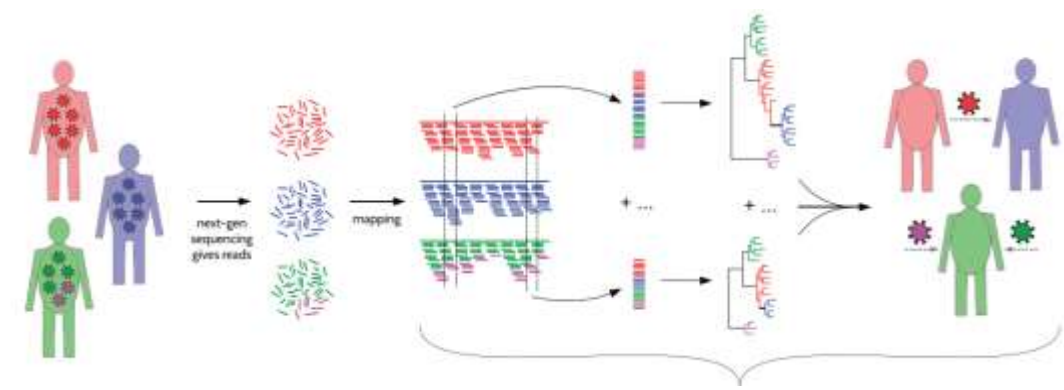
Phylogenetic analysis of pathogens is an increasingly powerful way to reduce the spread of epidemics, including HIV. As a result, phylogenetic approaches are becoming embedded in public health and research programmes, as well as outbreak responses, presenting unique ethical, legal, and social issues 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.

Coltart and Hoppe et al., *Lancet HIV*. 2018

# Phylogenetics and Networks for Generalized Epidemics in Africa (PANGEA-HIV)



## HIV SHIVER and Phyloscanner



Wymant et al. *Virus evolution*. 2018  
 Wymant et al. *Mol. Biol. Evo.* 2018

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

# 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



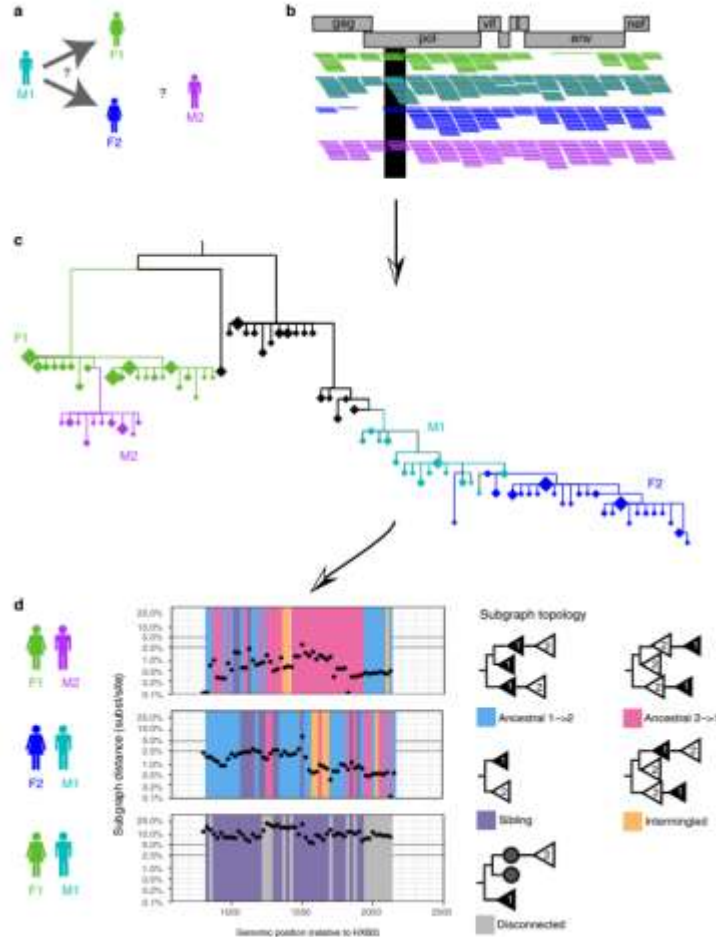
Biospecimens/biometrics



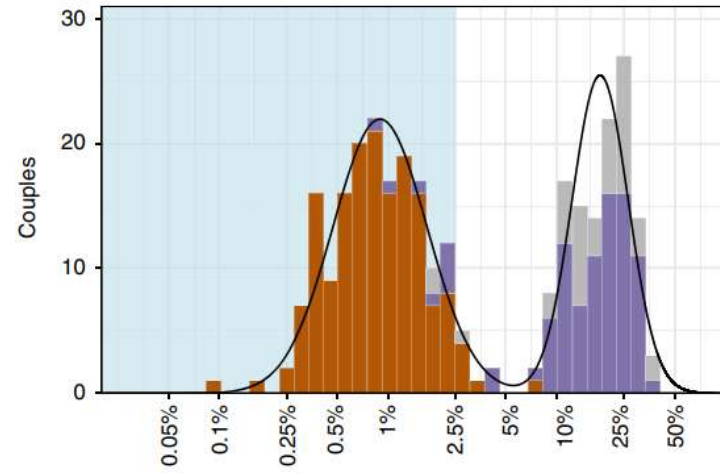
Services



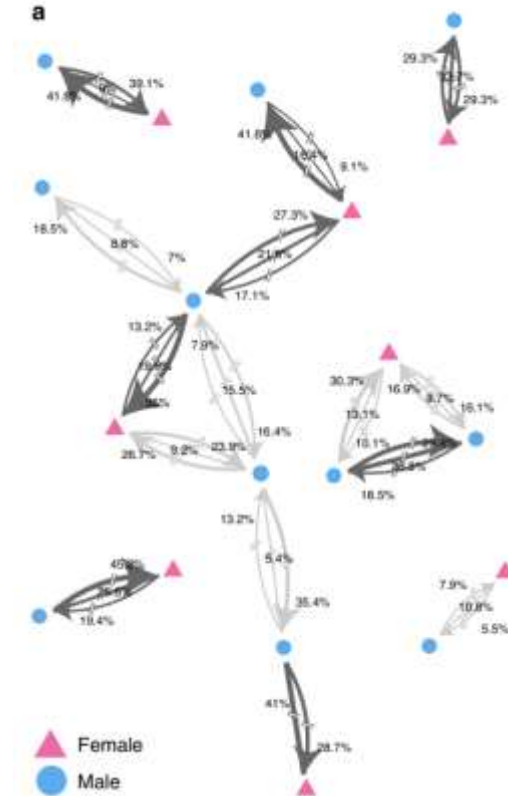
# Inferring African HIV transmission networks with deep sequence phylogenetic analysis



Shiver/Phyloscanner



Genetic pairwise distance distribution in epidemiologically linked couples

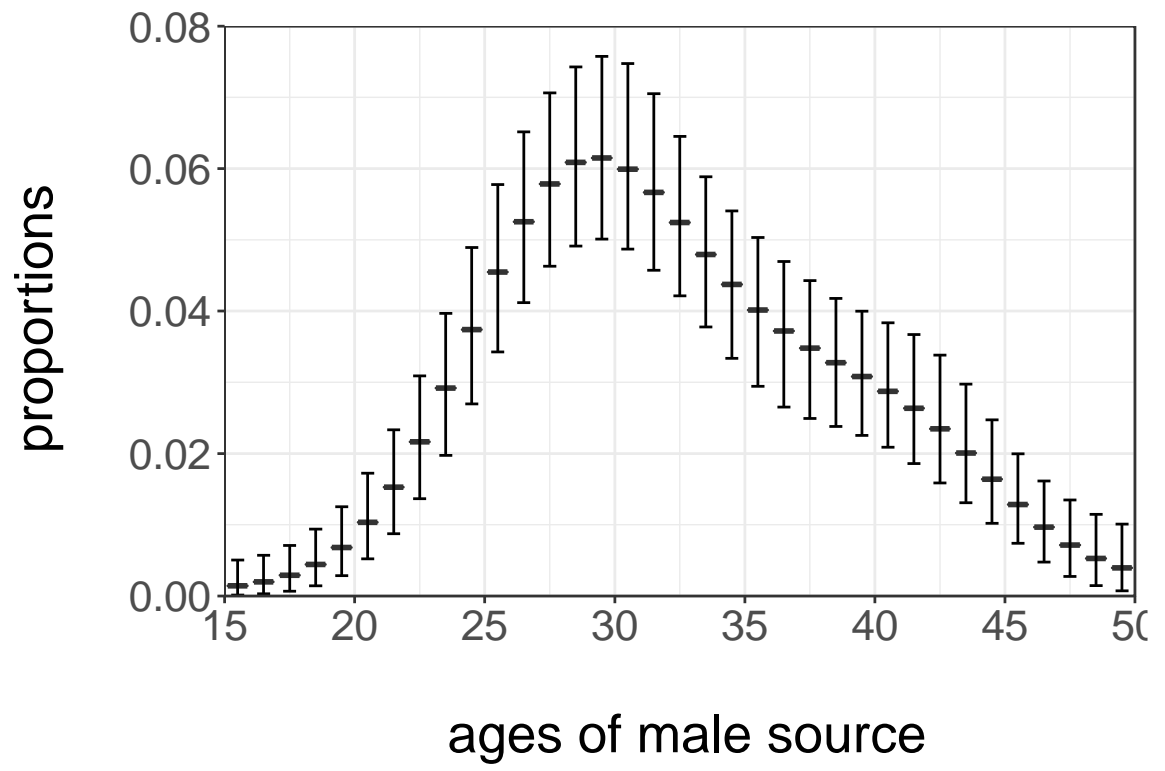


Directed transmission networks with ~900 source-recipient pairs

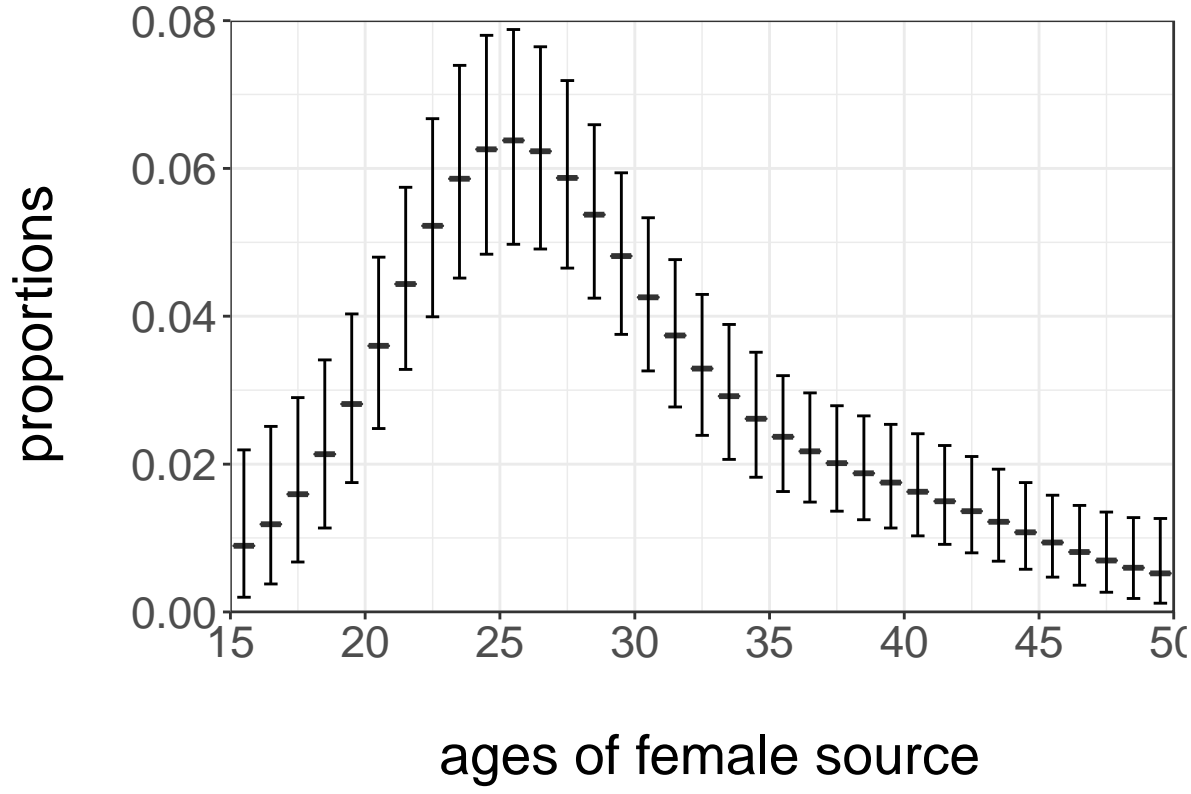
# Sources of transmission by age and gender, 2011-15



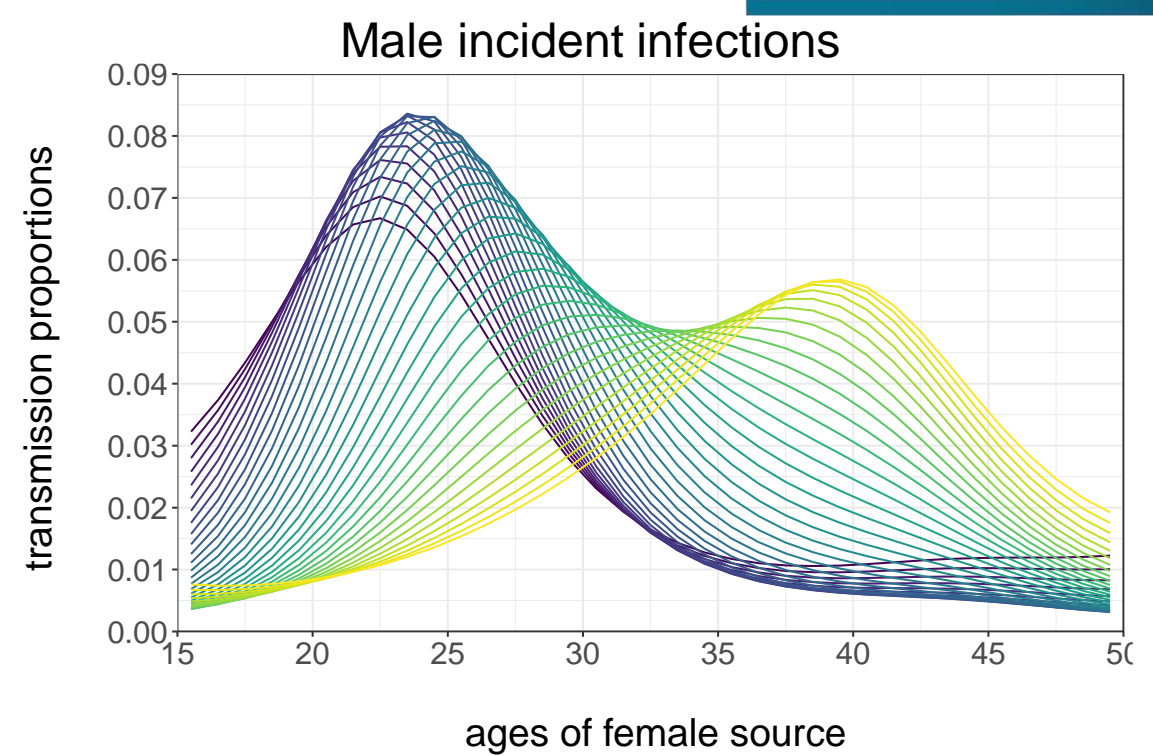
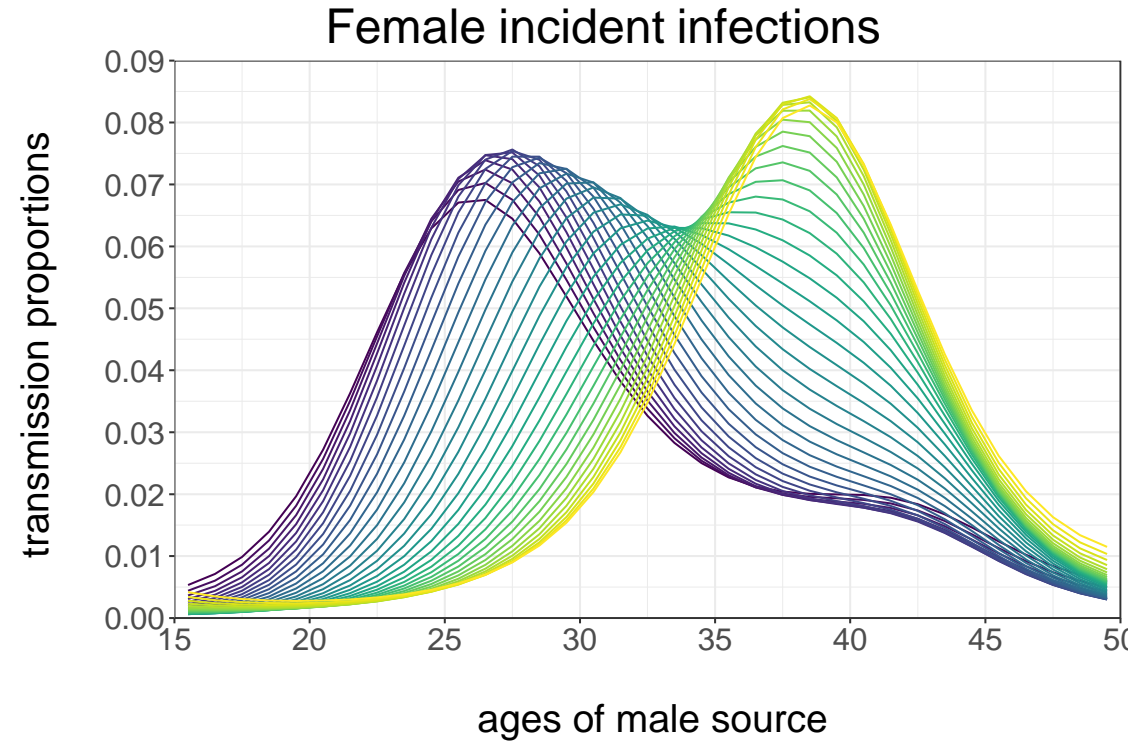
### Incident Female Infections



### Incident Male Infections



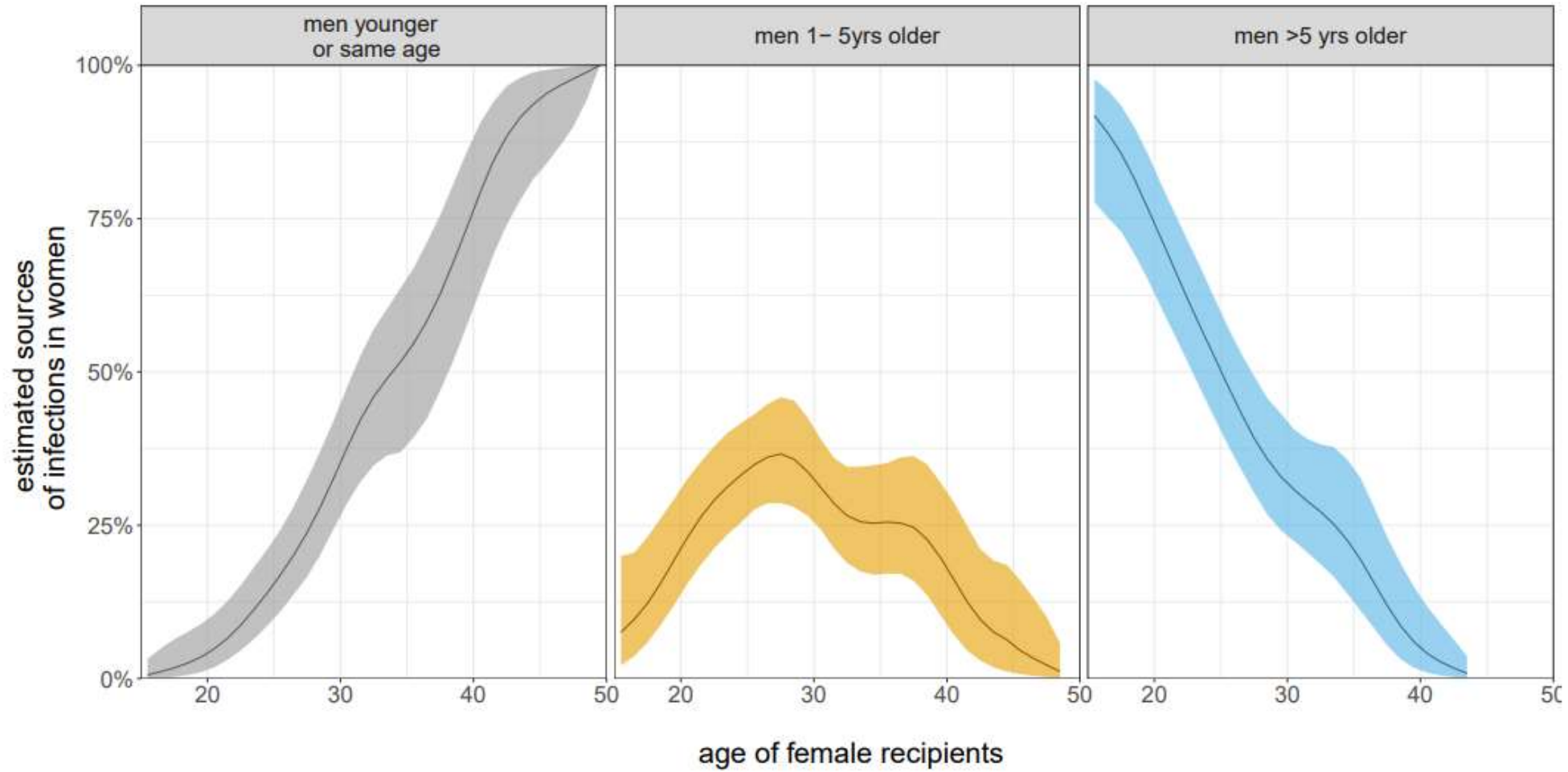
# Sources of transmission by age of recipient and transmitter



Age of recipient

- 15-16 — 16-17 — 17-18 — 18-19 — 19-20 — 20-21 — 21-22 — 22-23 — 23-24 — 24-25
- 25-26 — 26-27 — 27-28 — 28-29 — 29-30 — 30-31 — 31-32 — 32-33 — 33-34 — 34-35
- 35-36 — 36-37 — 37-38 — 38-39 — 39-40 — 40-41 — 41-42 — 42-43 — 43-44 — 44-45
- 45-46 — 46-47 — 47-48 — 48-49 — 49-50

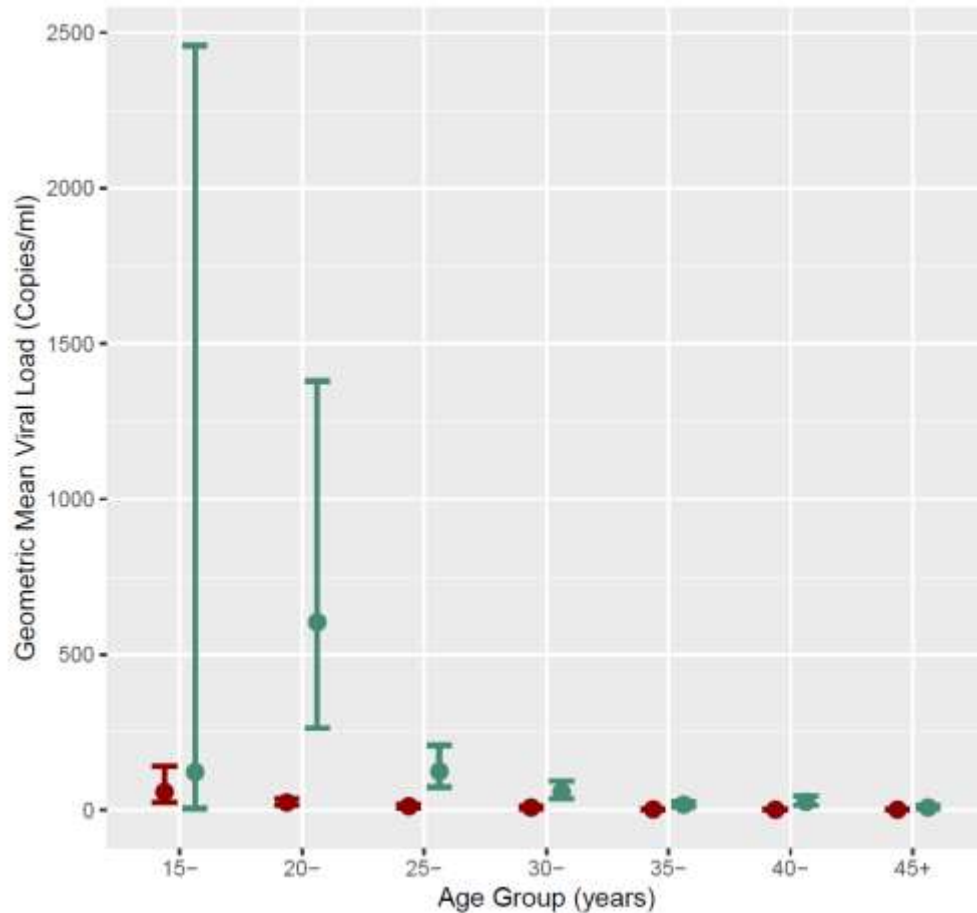
# Male sources of transmission to women



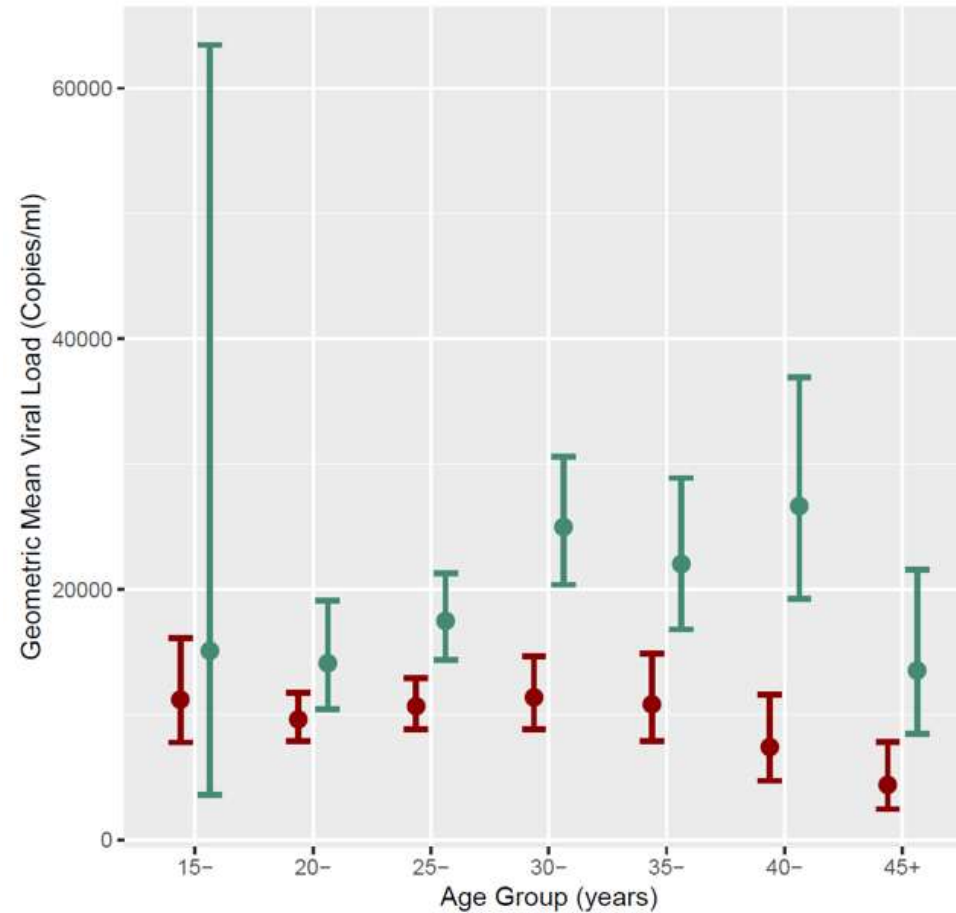
# HIV viremia in the RCCS, 2016-17



All HIV-positive persons

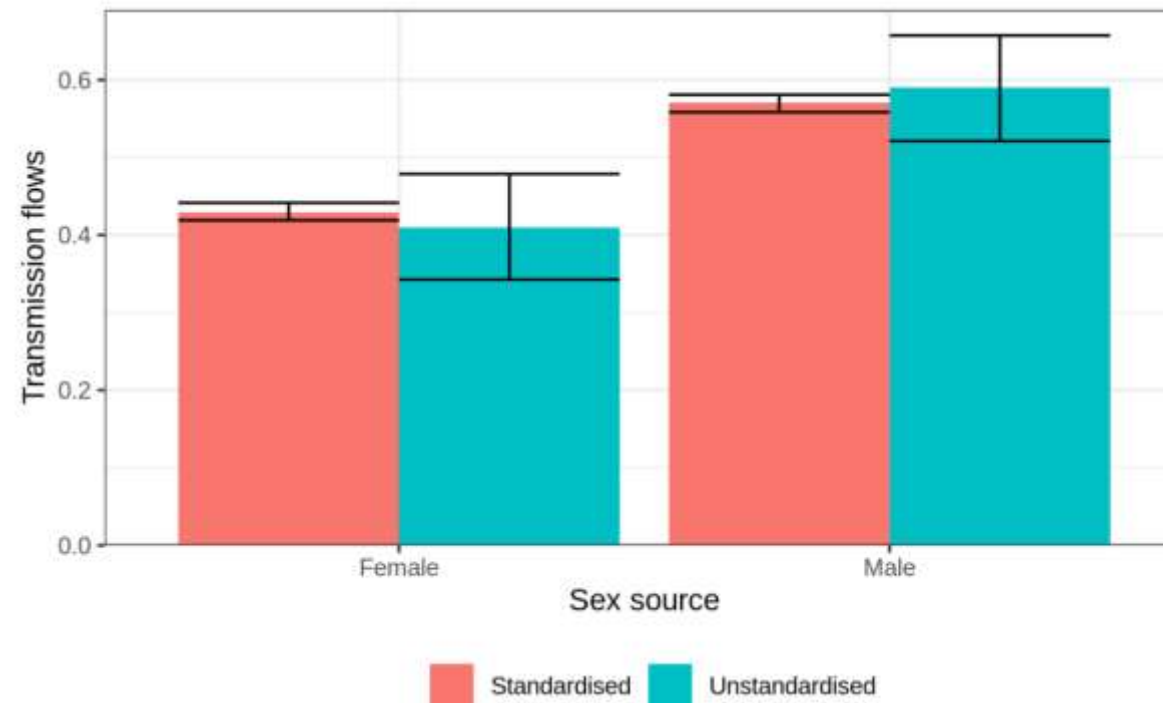


HIV-positive persons with VL>400 copies



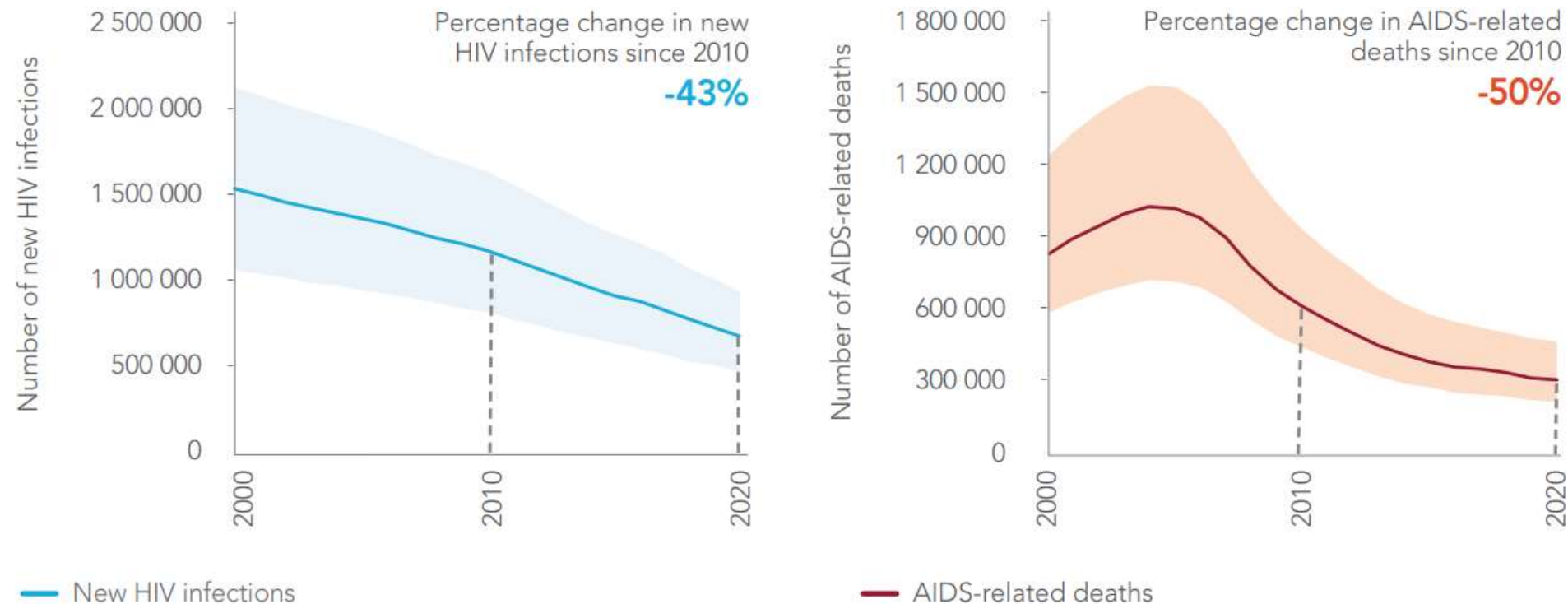
- women
- men

# Transmission cycle



# HIV incidence in sub-Saharan Africa is declining

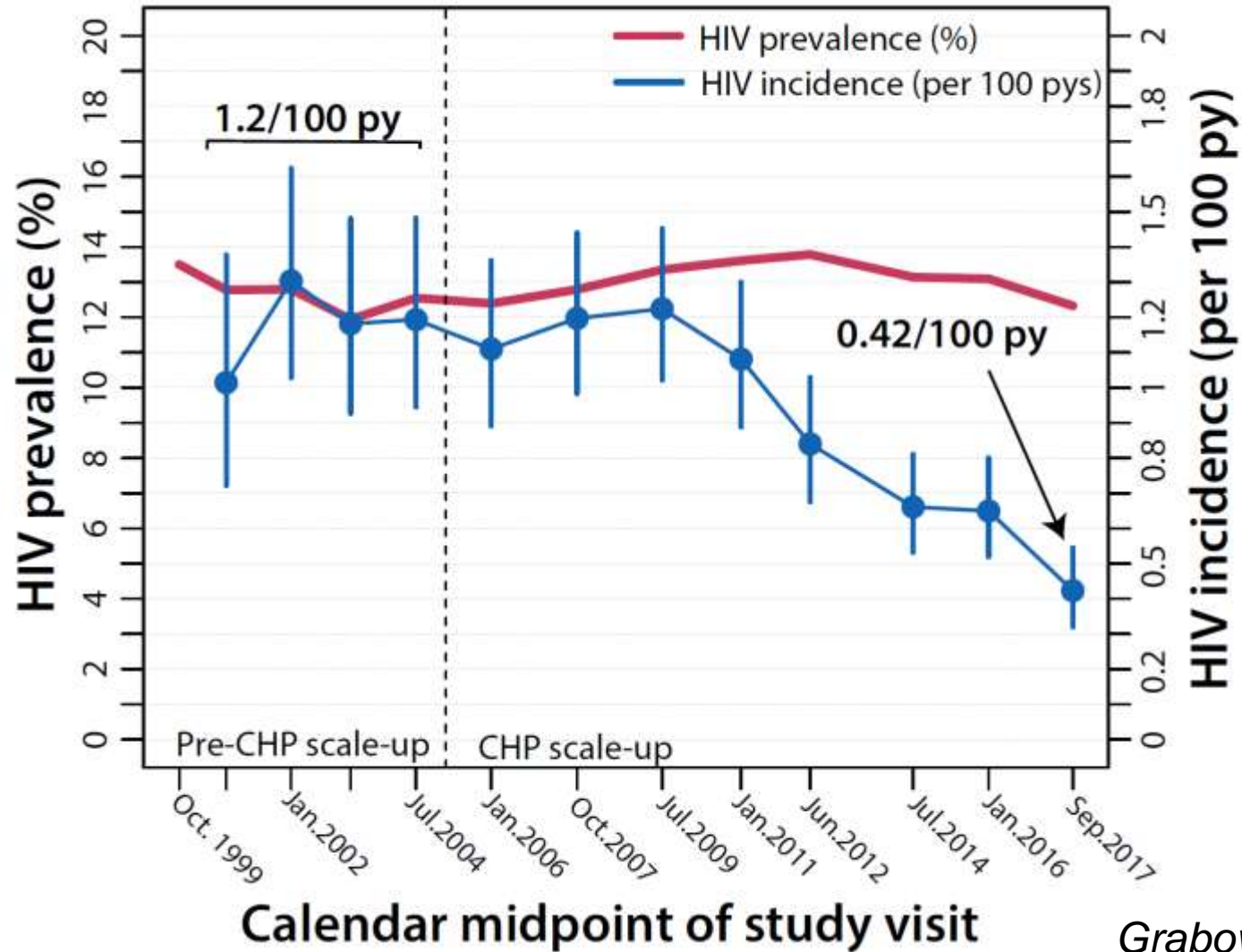
## NUMBER OF NEW HIV INFECTIONS AND AIDS-RELATED DEATHS, EASTERN AND SOUTHERN AFRICA, 2000–2020



Source: UNAIDS epidemiological estimates, 2021 (<https://aidsinfo.unaids.org/>).



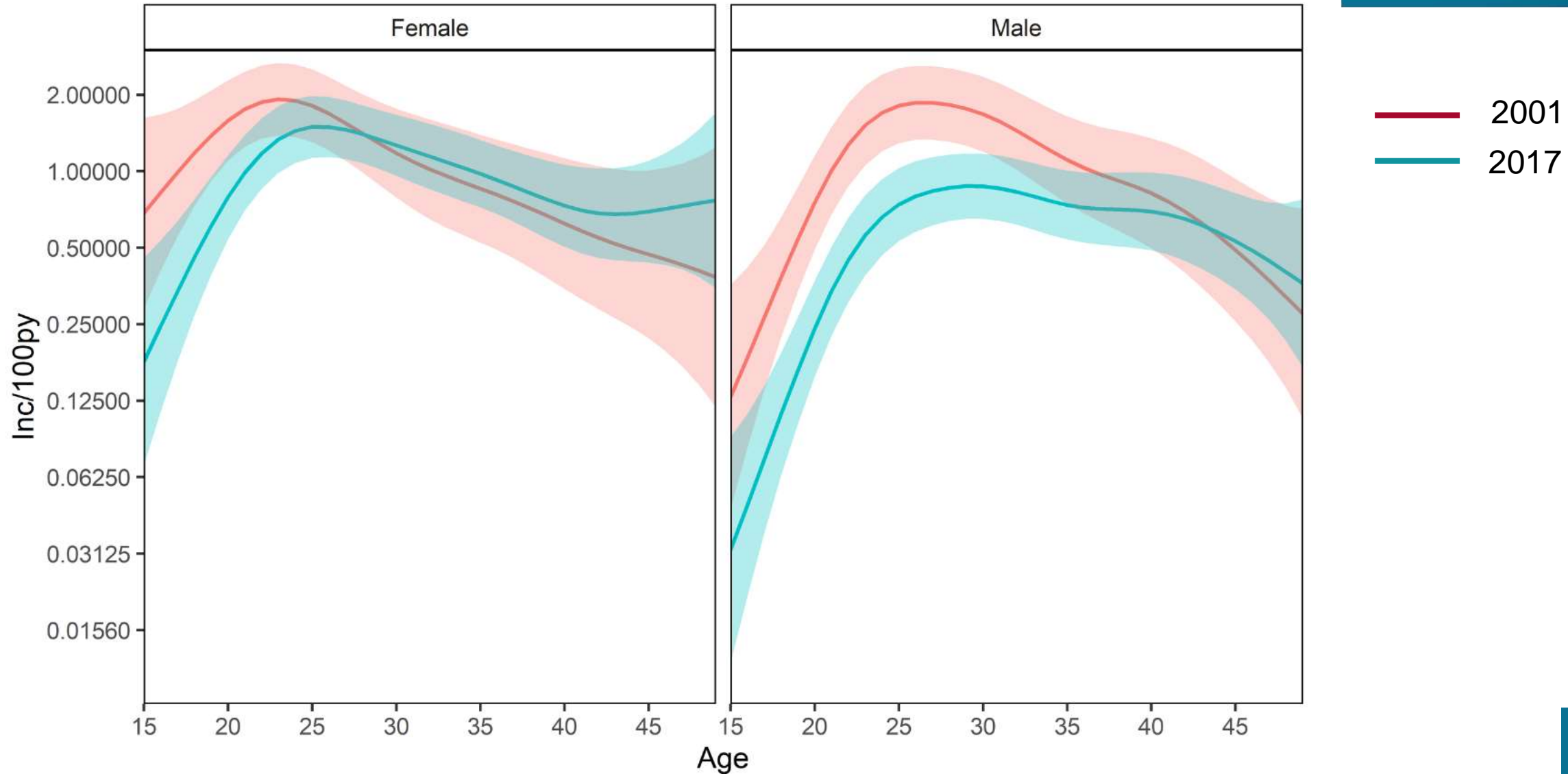
# HIV incidence trends in Rakai, 1999-2017



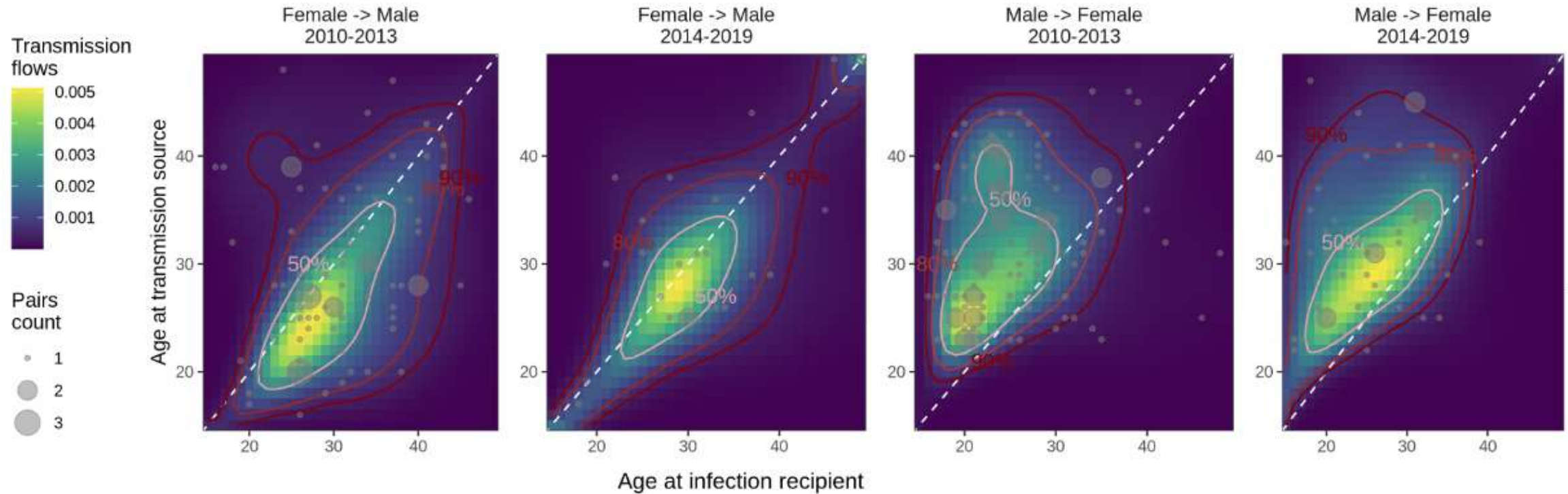
CHP=combination HIV prevention

Grabowski et al. NEJM. 2017  
Grabowski et al. CROI. 2020

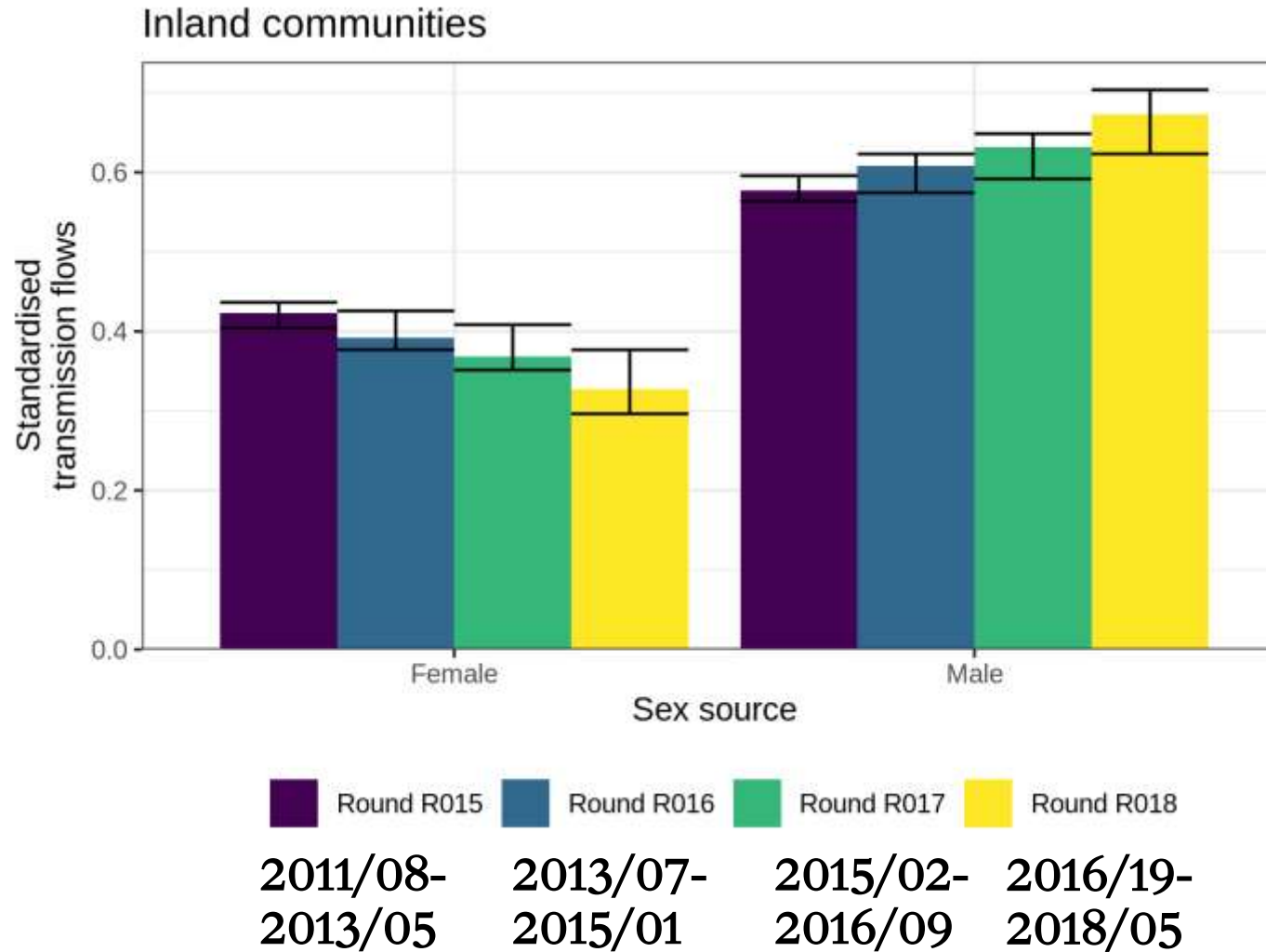
# HIV incidence in Rakai by age, 2001 vs. 2017



# Shifting sources of transmission



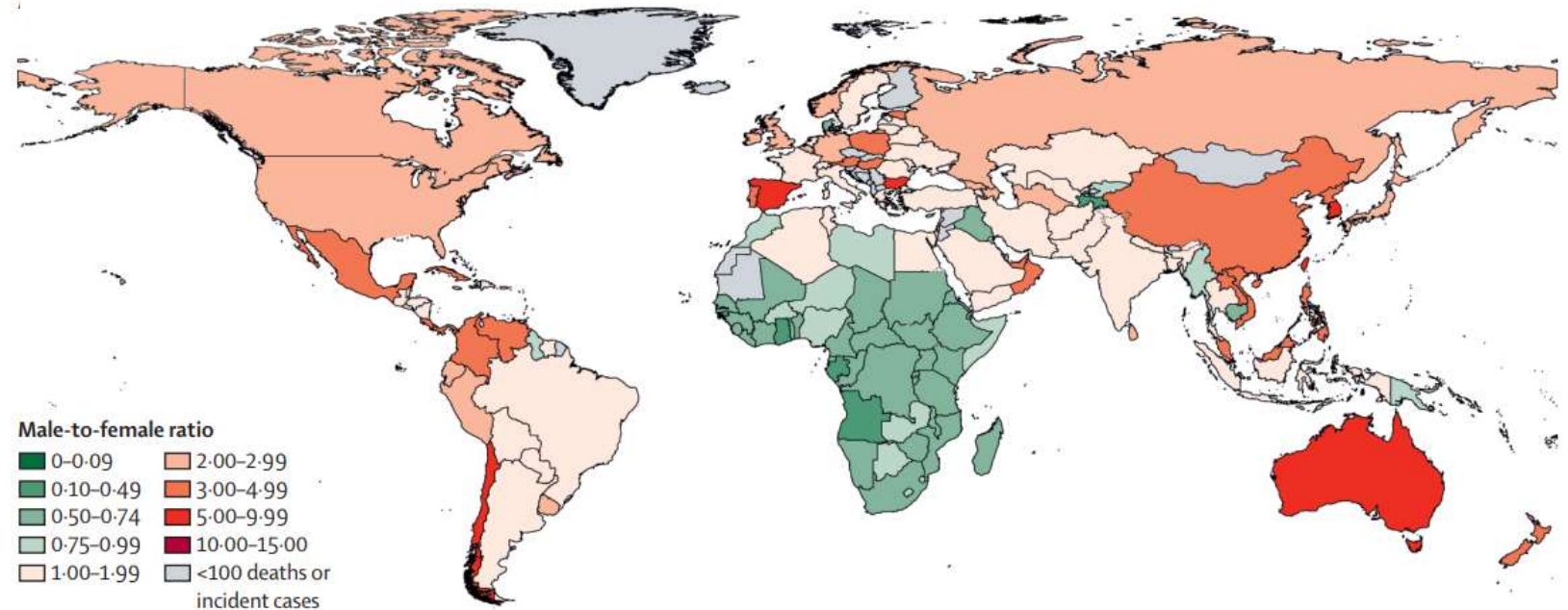
# Increasingly male driven transmission flows



# The African HIV epidemic is predominantly female?



Male to female HIV incidence ratios



GBD 2019 HIV collaborators. *Lancet HIV*. 2021.

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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/HIVptn

# Acknowledgments

## Rakai Health Sciences Program

David Serwadda  
Fred Nalugoda  
Joseph Kagaayi \*  
Godfrey Kigozi  
Gertrude Nakigozi  
Tom Lutalo  
Robert Ssekubugu\*  
Grace Kigozi  
Ronald Galiwango\*  
Anthony Ndyanabo

## Johns Hopkins Bloomberg School of Public Health

Ronald Gray  
Maria Wawer  
Justin Lessler  
Caitlin Kennedy  
Joseph Sekasanyu



/HIVpntn

## Johns Hopkins School of Medicine

Kate Grabowski  
Aaron Tobian  
Larry Chang

## National Institute of Allergy and Infectious Diseases

Thomas Quinn  
Andrew Redd  
Oliver Laeyendecker  
Steve Reynolds

## Oxford University

Christophe Fraser\*  
Matthew Hall  
Chris Wymant  
Tanya Golubchik  
Lucie Abeler Dorner\*  
Rafael Sauter  
Francois Blanquart  
Will Probert

## Imperial College

Oliver Ratmann\*  
Imogen Kyle  
Xiaoyue Xi  
Melodie Monad\*  
Andrea Brizzi

## Institute for Disease Modeling

Adam Akullian

## Rakai Health Science Program Staff and Study participants

## Uganda Ministry of Health

## National Institutes of Health

## Centers for Disease Control

## Bill and Melinda Gates Foundation

