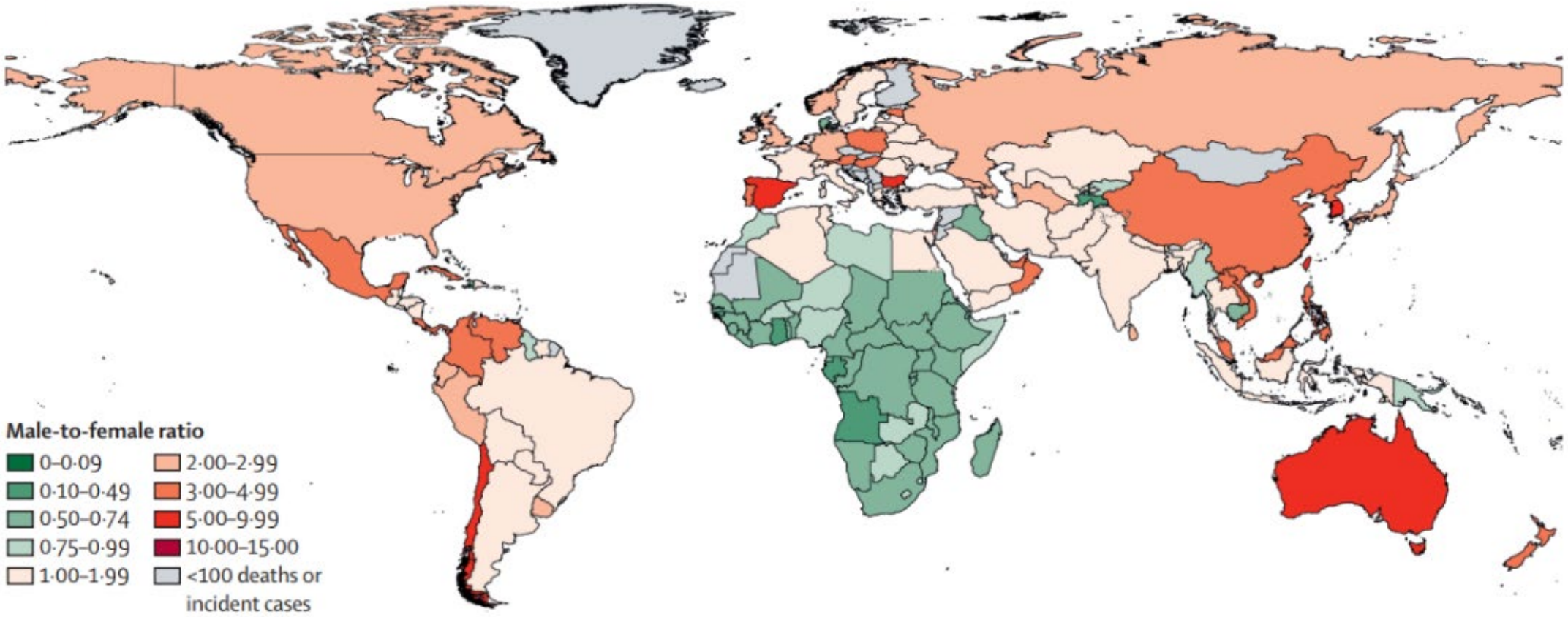
Growing gender disparity in HIV infection in Uganda and policy implications

M. Kate Grabowski

on behalf of Oliver Ratmann, Joseph Kagaayi, Melodie Monad, Rakai Health Sciences Program and PANGEA-HIV Consortium

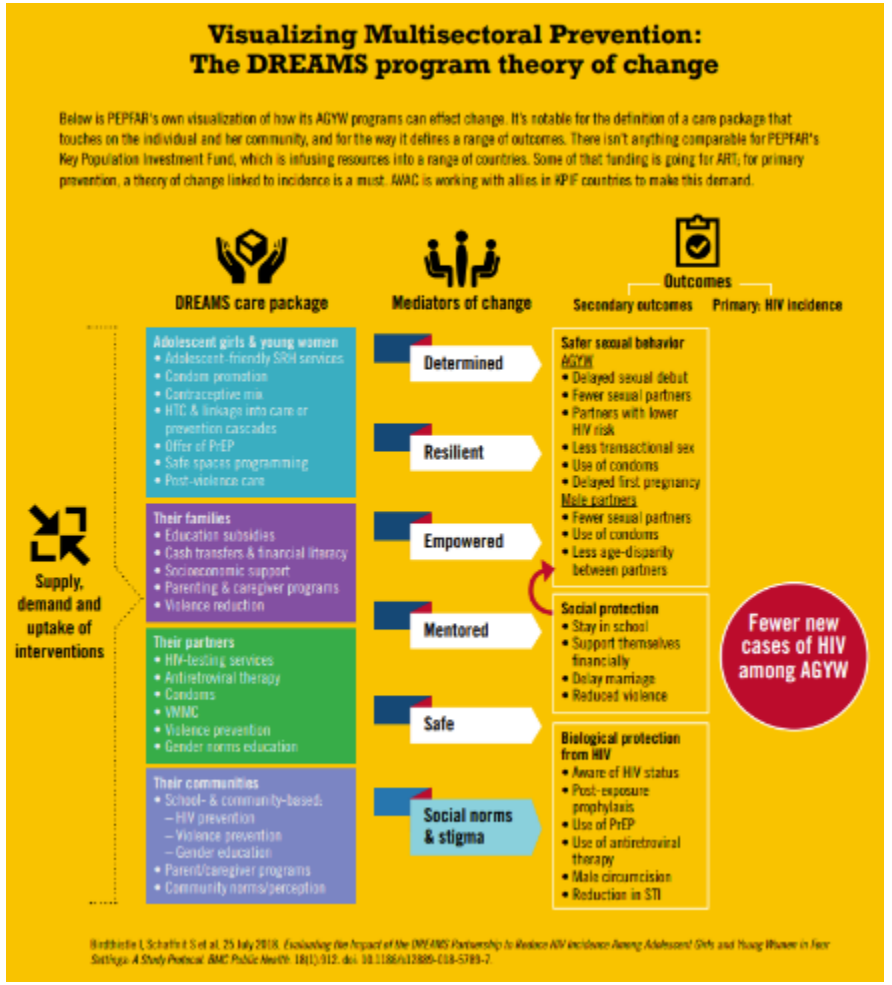
Gender disparities in HIV incidence



Jahagirdar et al. *Lancet HIV*. 2021

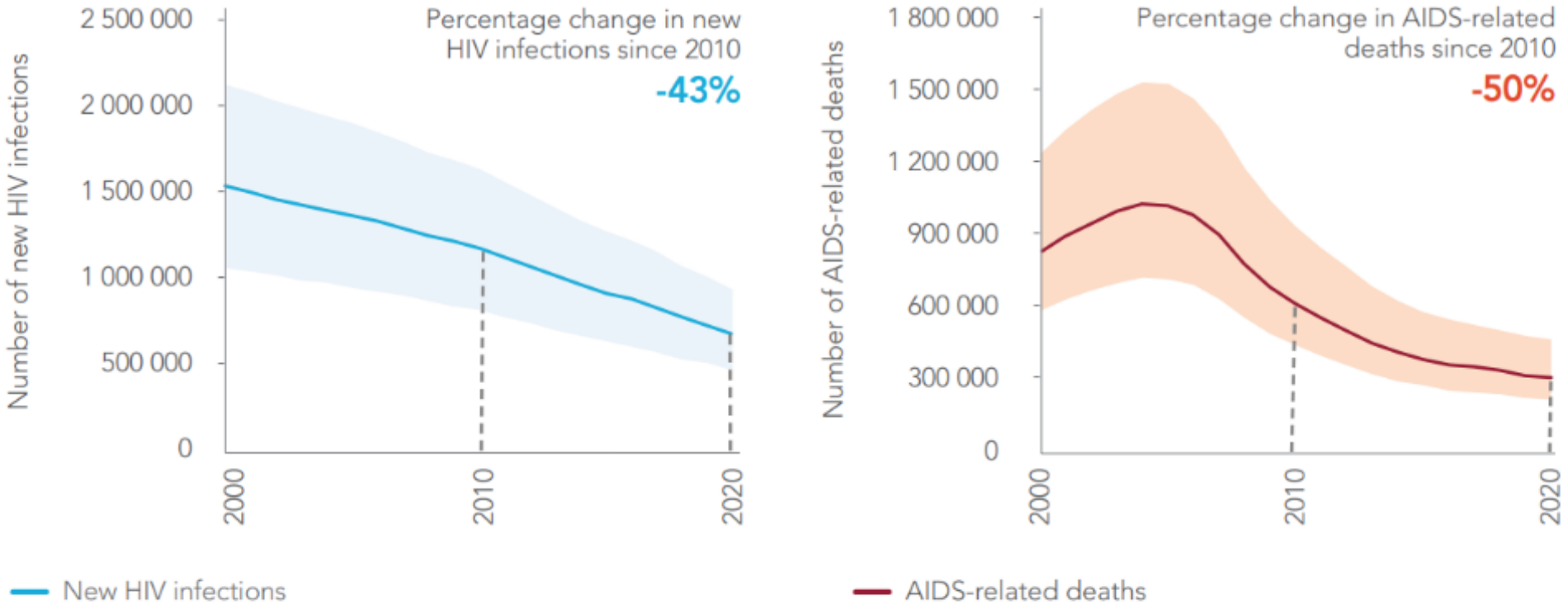
Age and gender targeted HIV programming

DREAMS
WORKING TOGETHER FOR AN AIDS-FREE FUTURE FOR GIRLS & WOMEN



Changing HIV epidemic dynamics

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



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

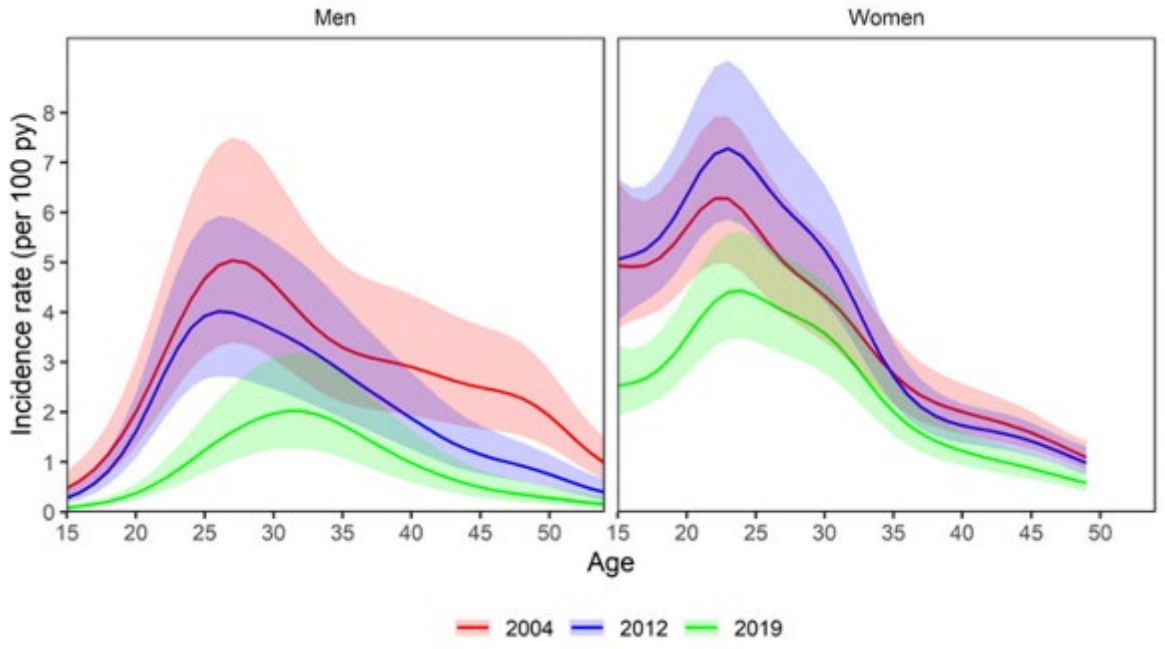
Shifting patterns in HIV incidence

Articles

Age patterns of HIV incidence in eastern and southern Africa: a modelling analysis of observational population-based cohort studies

Kathryn A Risher, Anne Cori, Georges Reniers, Milly Marston, Clara Calvert, Amelia Crampin, Tawanda Dadirai, Albert Dube, Simon Gregson, Kobus Herbst, Tom Lutalo, Louisa Moorhouse, Baltazar Mtenga, Dorean Nabukalu, Robert Newton, Alison J Price, Maitebogo Tlhajoane, Jim Todd, Keith Tomlin, Mark Urassa, Alain Vandormael, Christophe Fraser, Emma Slaymaker, Jeffrey W Eaton, on behalf of the AI PHA Network

Risher et al. *Lancet HIV*. 2021

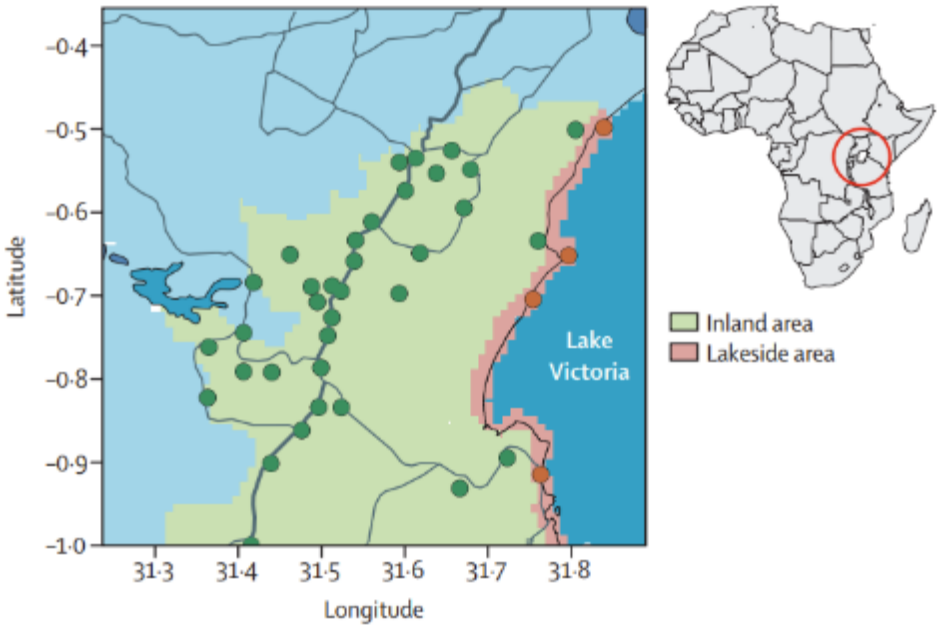


Akullian et al. *PNAS*. 2021

Shifting patterns in HIV transmission?

1. What are the recent trends in HIV incidence in women?
2. Are disparities between men and women closing or widening?
3. Which male populations drive incidence in women, and vice versa?
4. What are the best strategies to close gaps and improve population health?

HIV surveillance framework: The Rakai Community Cohort Study (RCCS)



African HIV surveillance efforts

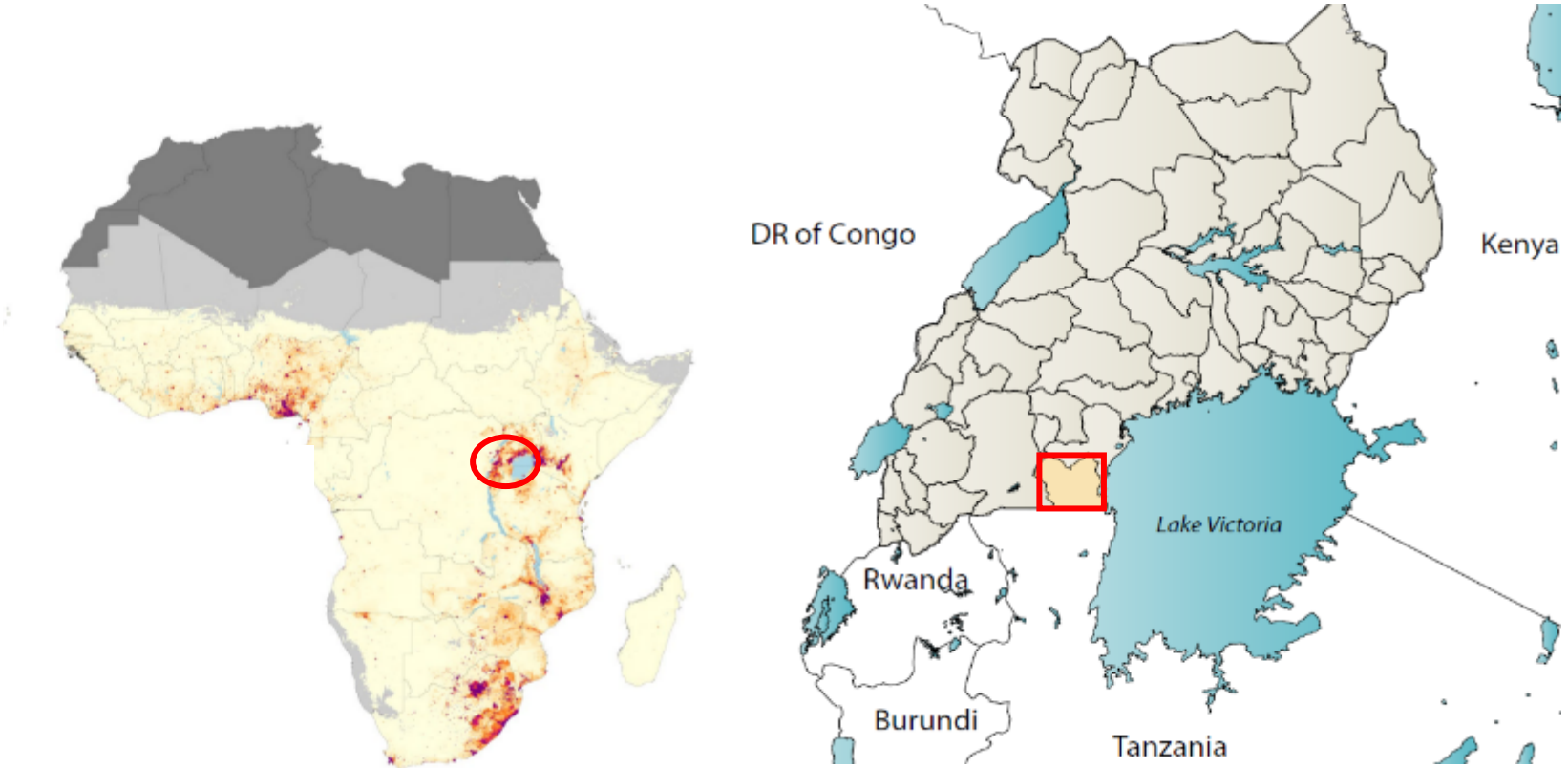
- Clinical and programmatic data
  - Antenatal care clinics
  - Adult and child HIV care clinics
- National surveys (e.g. Population based HIV Impact Assessment Surveys [PHIAs])
- Clinical trials
- Key population programs/cohorts
- Longitudinal population-based HIV cohorts (e.g., the Rakai Community Cohort Study)

Utility of longitudinal population surveillance cohorts

DETAILS AND DENOMINATORS!

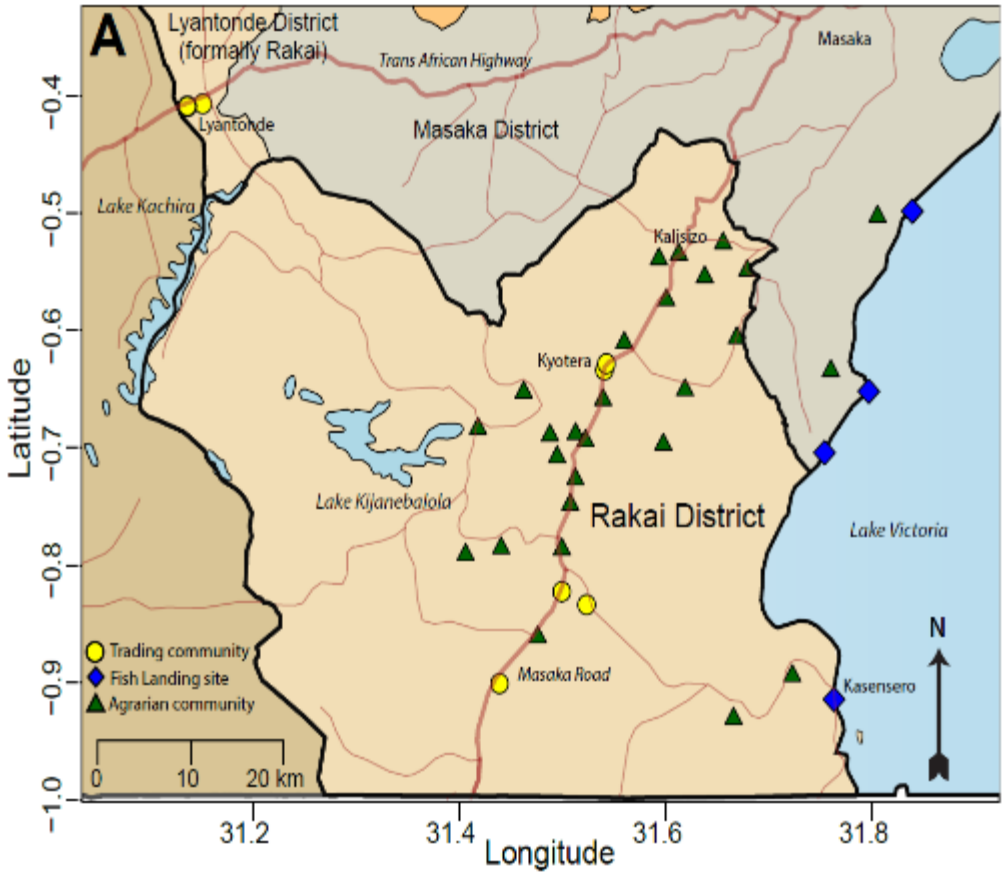
- Fine scale information on who is acquiring and transmitting virus at a population-level
- Longitudinal trends on key metrics
- Impact evaluation
- Nested studies with adequate control groups

Rakai, Uganda



The Rakai Community Cohort Study (RCCS)

- Adolescents and adults 15+ residing in 34 communities
- 30 rural agrarian and semi-urban trading communities communities under surveillance since 1999 (28 since 1994)
- ~20,000 study participants surveyed every 1.5-2 years
- >300k participants contributing >1 million bio specimens



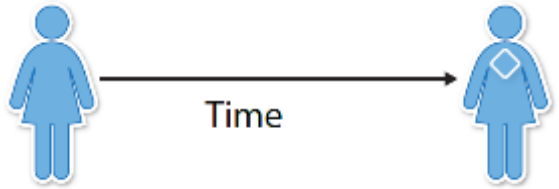
Population census

Survey

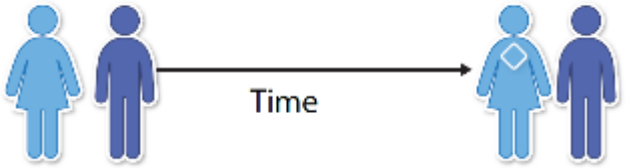
Biospecimens/biometrics

Services

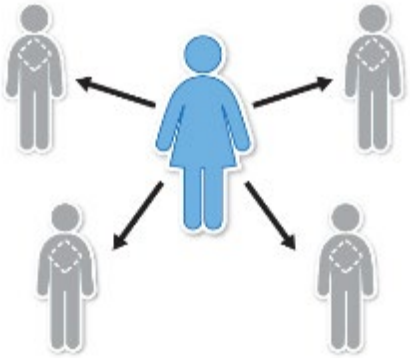
Cross sectional/longitudinal studies of individuals



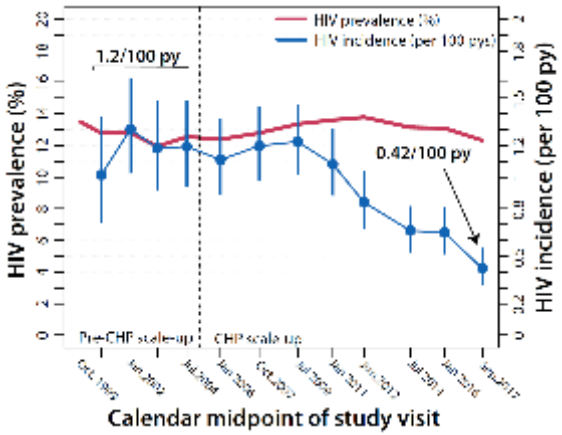
Cross/sectional longtidudinal studies of cohabitating couples



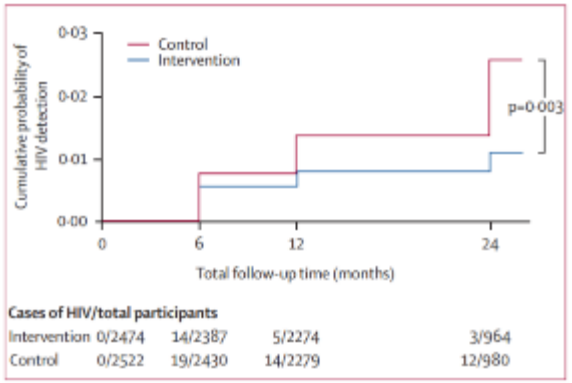
Egocentric network data



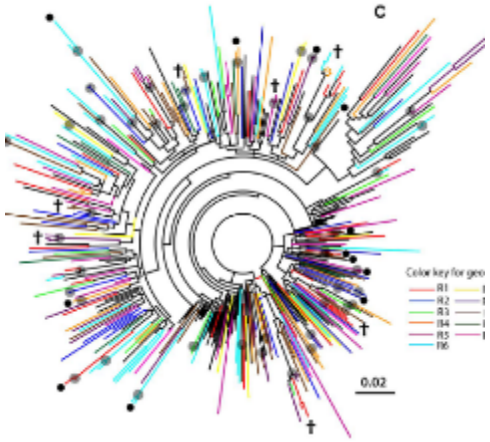
Population trends



Randomized clinical trials (individual and community)



Molecular epidemiology



Basic laboratory research

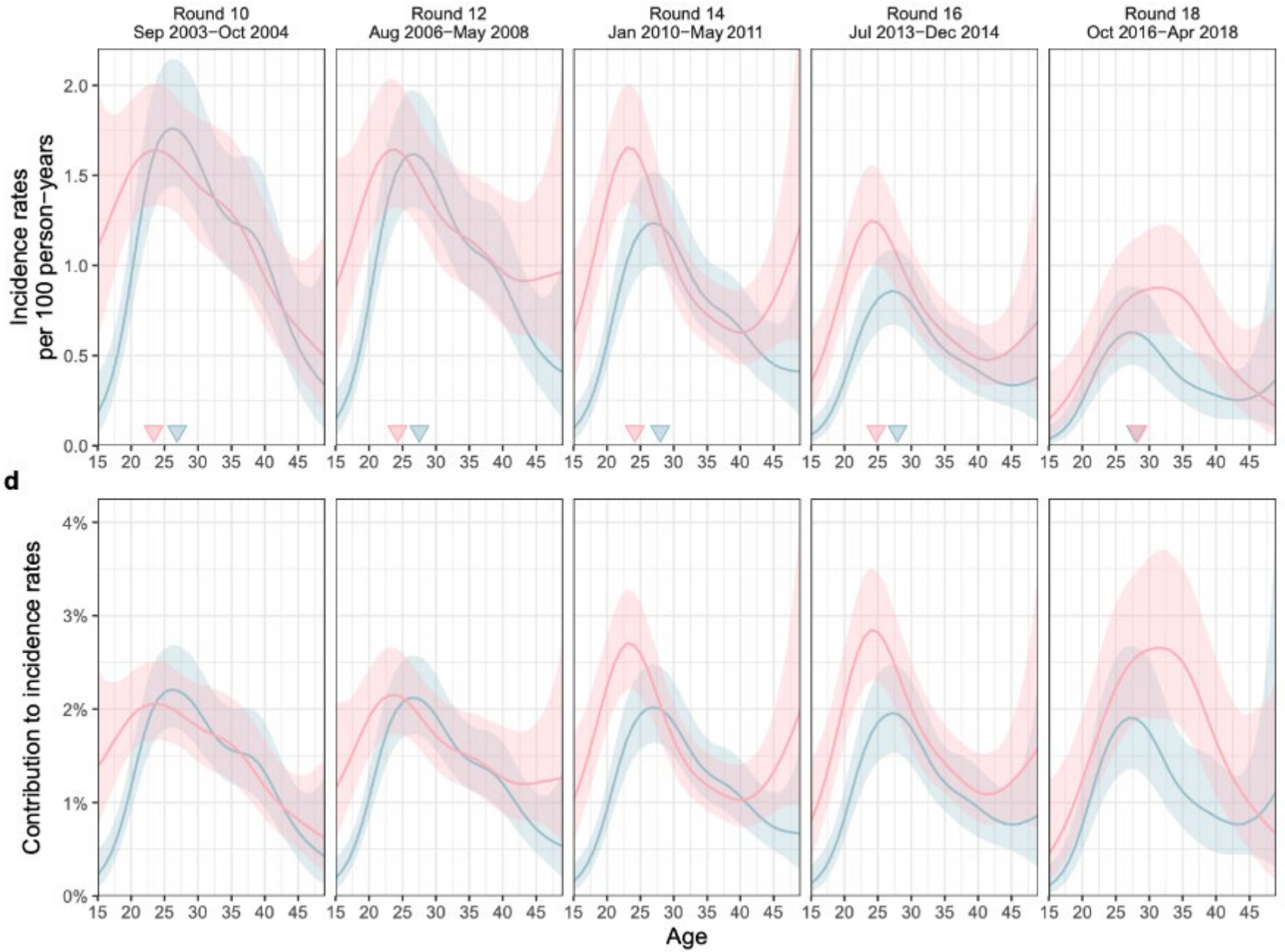
Growing gender disparity in HIV infection in Africa: sources and policy implications

Mélodie Monod, Andrea Brizzi, Ronald M Galiwango, Robert Ssekubugu, Yu Chen, Xiaoyue Xi, Edward Nelson Kankaka, Victor Ssempijja, Lucie Abeler Dörner, Adam Akullian, Alexandra Blenkinsop, David Bonsall, Larry W Chang, Shozen Dan, Christophe Fraser, Tanya Golubchik, Ronald H Gray, Matthew Hall, Jade C Jackson, Godfrey Kigozi, Oliver Laeyendecker, Lisa A. Mills, Thomas C. Quinn, Steven J. Reynolds, John Santelli, Nelson K. Sewankambo, Simon EF Spencer, Joseph Ssekasanvu, Laura Thomson, Maria J Wawer, David Serwadda, Peter Godfrey-Faussett, Joseph Kagaayi, M Kate Grabowski, Oliver Ratmann
Rakai Health Sciences Program and the PANGEA-HIV consortium

doi: https://doi.org/10.1101/2023.03.16.23287351

Trends in HIV incidence in the RCCS, 2003 - 2018

- 1100 incident cases observed over 127k PY, 2003-2018
- Faster declines in HIV incidence in men than women, ages 25 and above.



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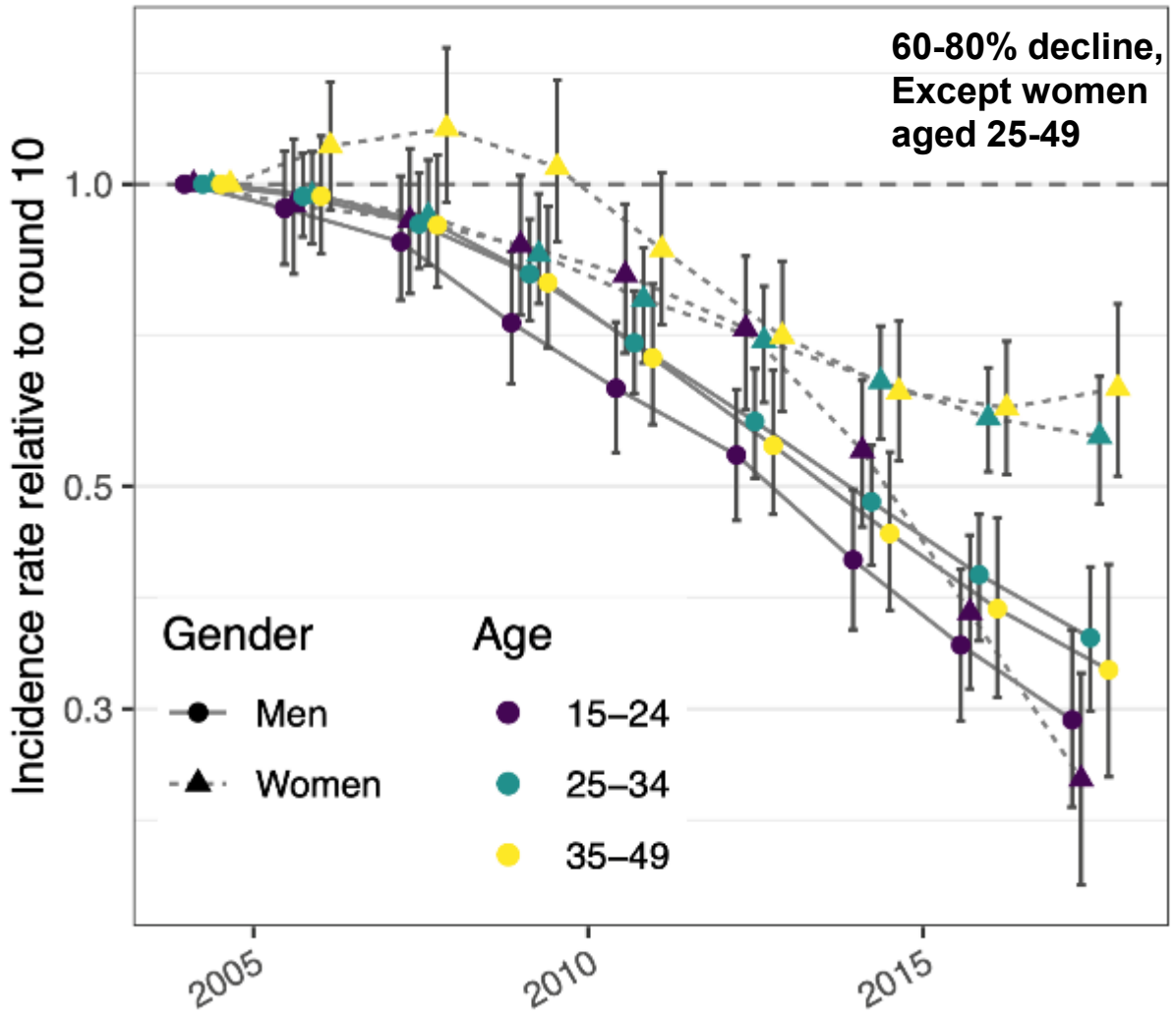
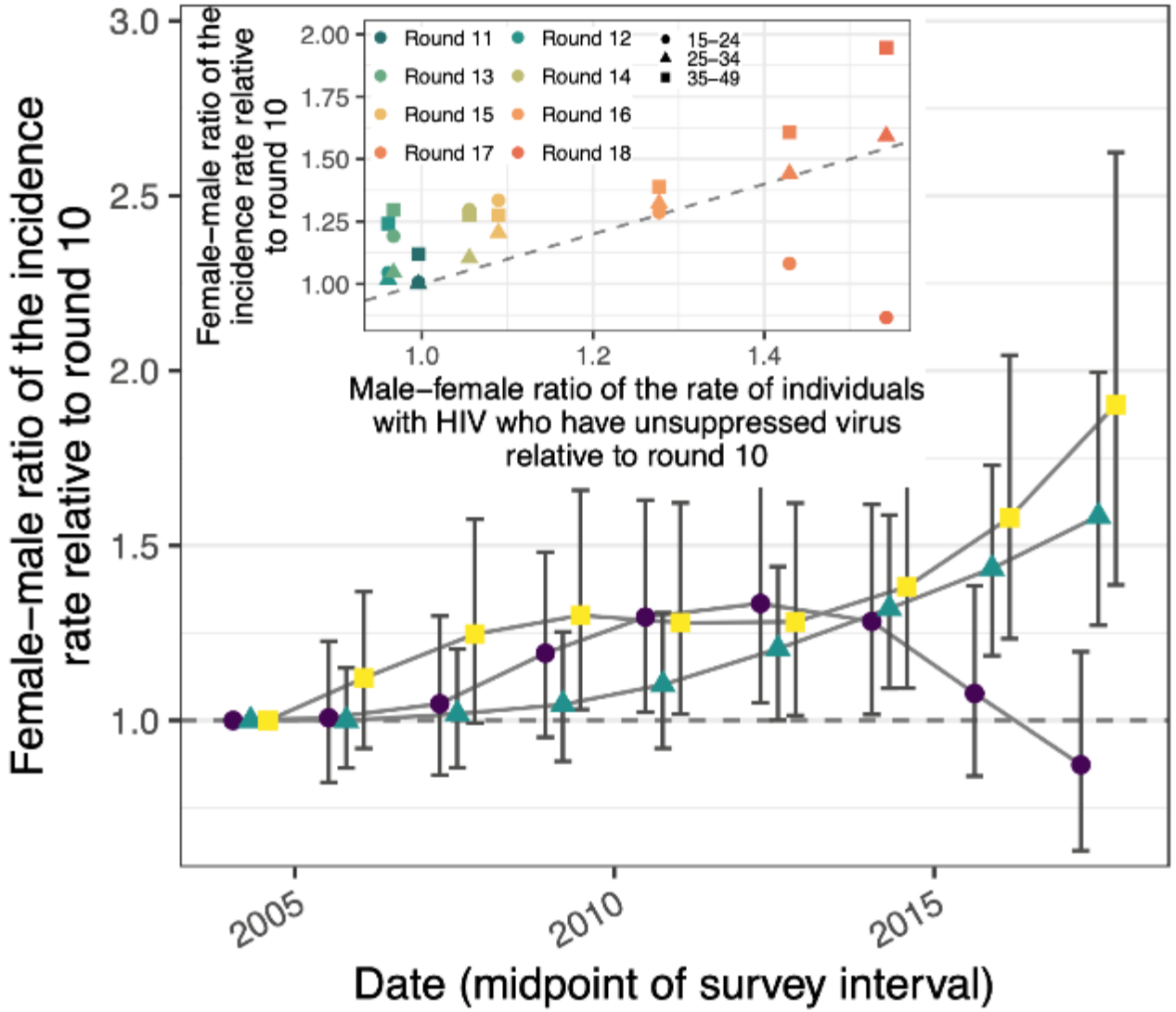
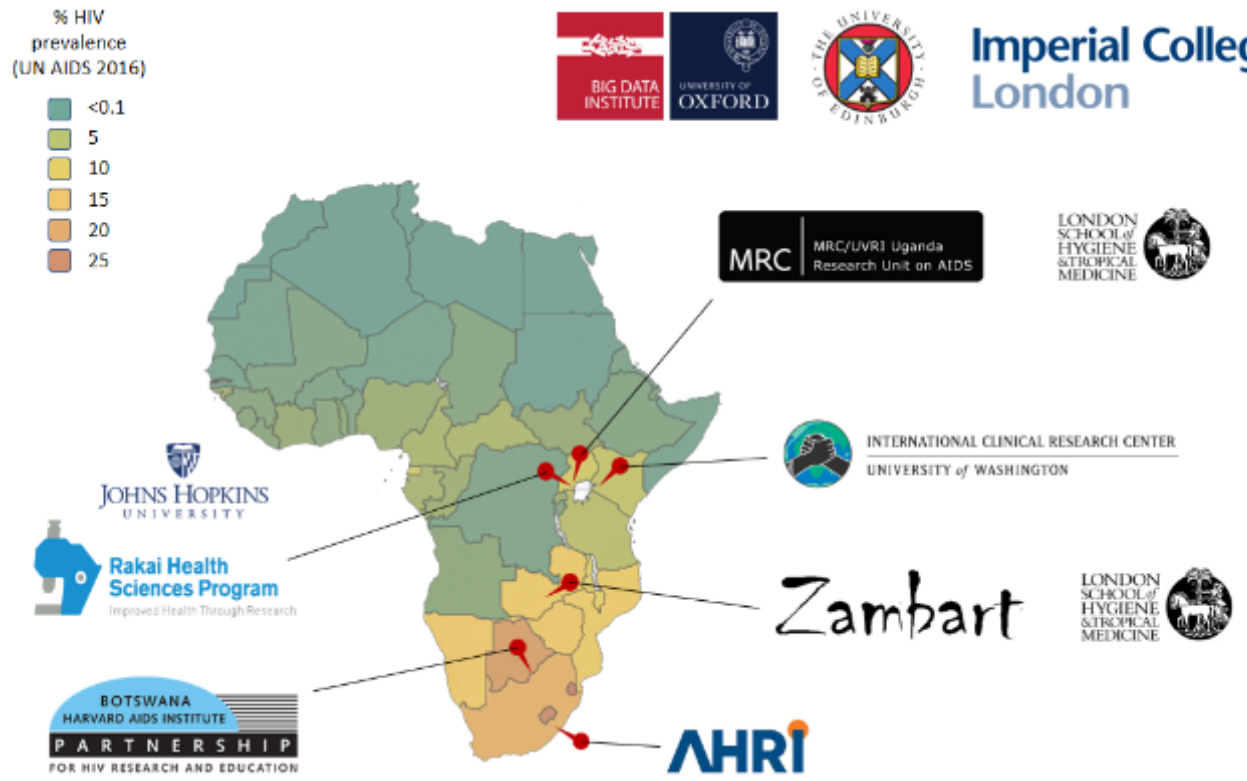
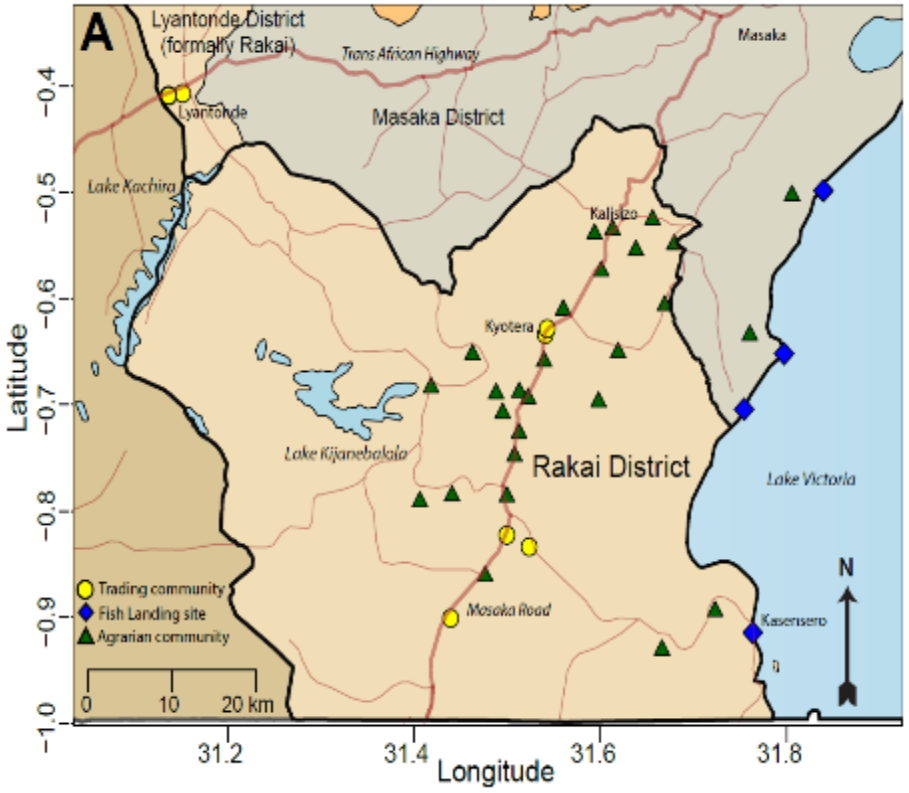

60-80% decline,
Except women
aged 25-49
Incidence rate relative to round 10
1.0
0.5
0.3
Gender
Men
Women
Age
15–24
25–34
35–49
2005
2010
2015


Female–male ratio of the incidence rate relative to round 10
3.0
2.5
2.0
1.5
1.0
Round 11
Round 12
Round 13
Round 14
Round 15
Round 16
Round 17
Round 18
15–24
25–34
35–49
Female–male ratio of the incidence rate relative to round 10
2.00
1.75
1.50
1.25
1.00
1.0
1.2
1.4
Male–female ratio of the rate of individuals with HIV who have unsuppressed virus relative to round 10
2005
2010
2015
Date (midpoint of survey interval)

- **PANGEA-HIV: pan-African HIV pathogen genomics program integrated with population surveillance**

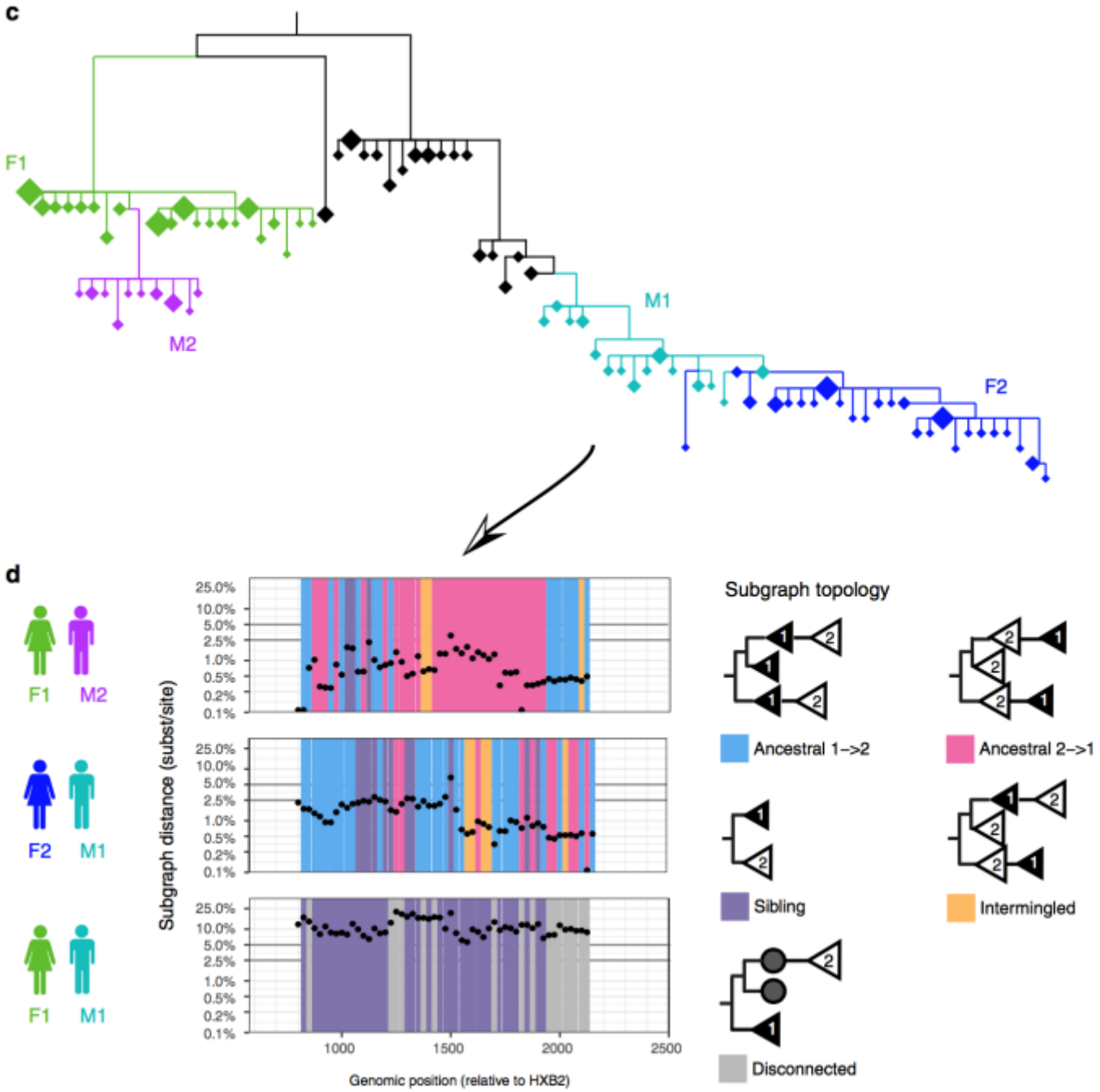


- **PANGEA-HIV: pan-African HIV pathogen genomics program integrated with population surveillance**



	Participants with HIV (n)	Participants with HIV reporting no ART use at first visit (n)	(n)	Participants with HIV and with virus ever deep-sequenced † (%)
Total	5682	4341	2174	38 %
Female (Total)	3817	2836	1291	34 %
Age				
15-24	1066	817	424	40 %
25-34	2074	1488	740	36 %
35-49	1446	826	411	28 %
Male (Total)	1865	1506	883	47 %
Age				
15-24	272	220	157	58 %
25-34	955	782	499	52 %
35-49	984	670	436	44 %
Round‡				
10	884	–	115	13 %
11	1002	884	176	18 %
12	1105	912	234	21 %
13	1160	900	368	32 %
14	1741	1392	820	47 %
15	1944	1331	1085	56 %
16	1875	868	892	48 %
17	2015	646	933	46 %
18	1860	432	848	46 %

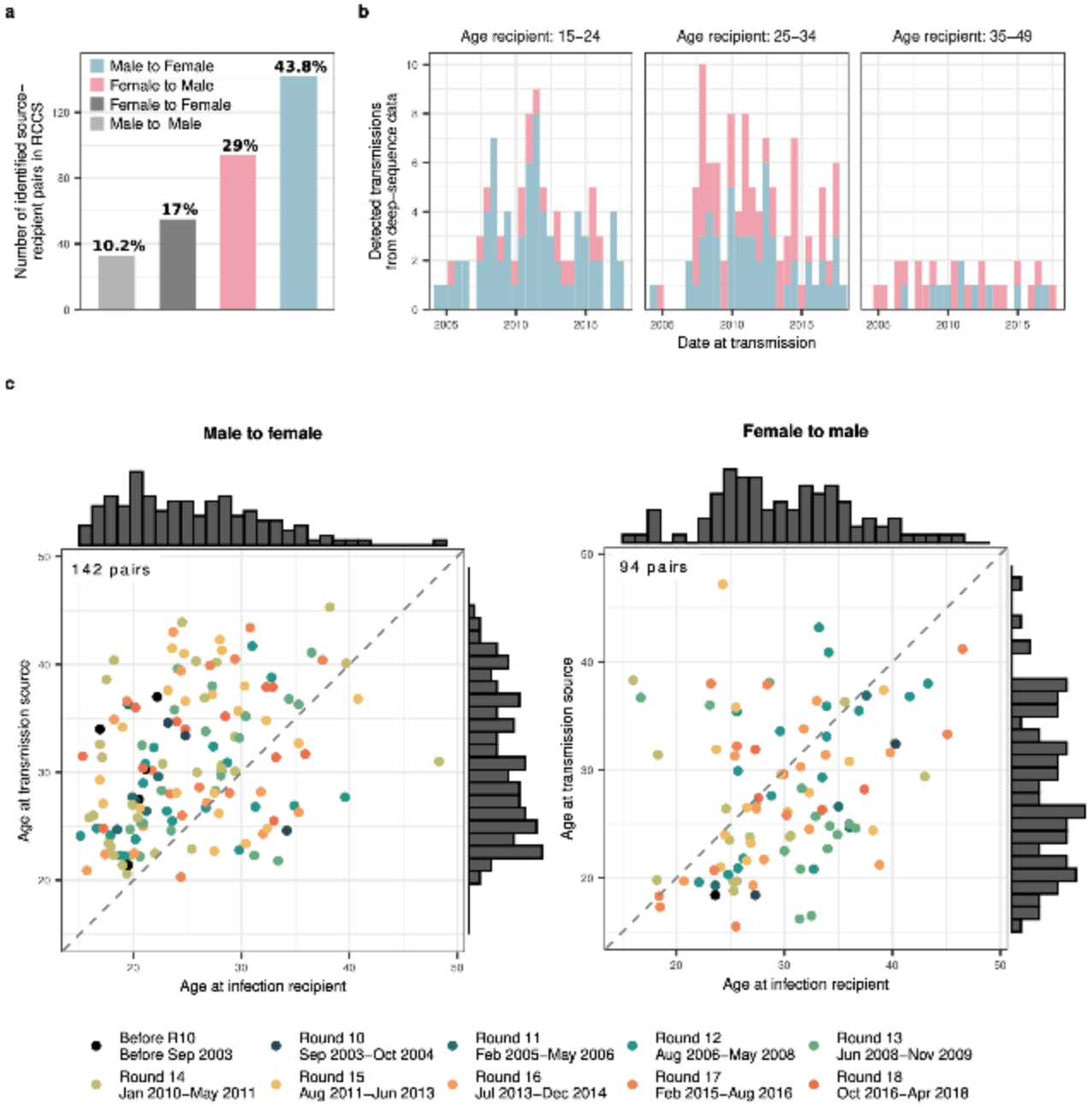
† Individuals with virus ever deep-sequenced were defined as HIV-positive individuals with deep-sequence output meeting minimum quality criteria, see Methods. ‡ Totals by round include individuals seen in other rounds.



PANGEA-HIV: Reconstructing source recipient pairs from deep sequence data

- HIV deep sequencing provides multiple sequence fragments per person
- Think: phylogeography between individuals
- Inference of transmission direction

Wymant et al. MBE 2017
Hall et al. Elife 2019
Ratmann et al. Nature Communications 2019
Ratmann et al. Lancet HIV 2020
Xi et al. JRSSC 2022



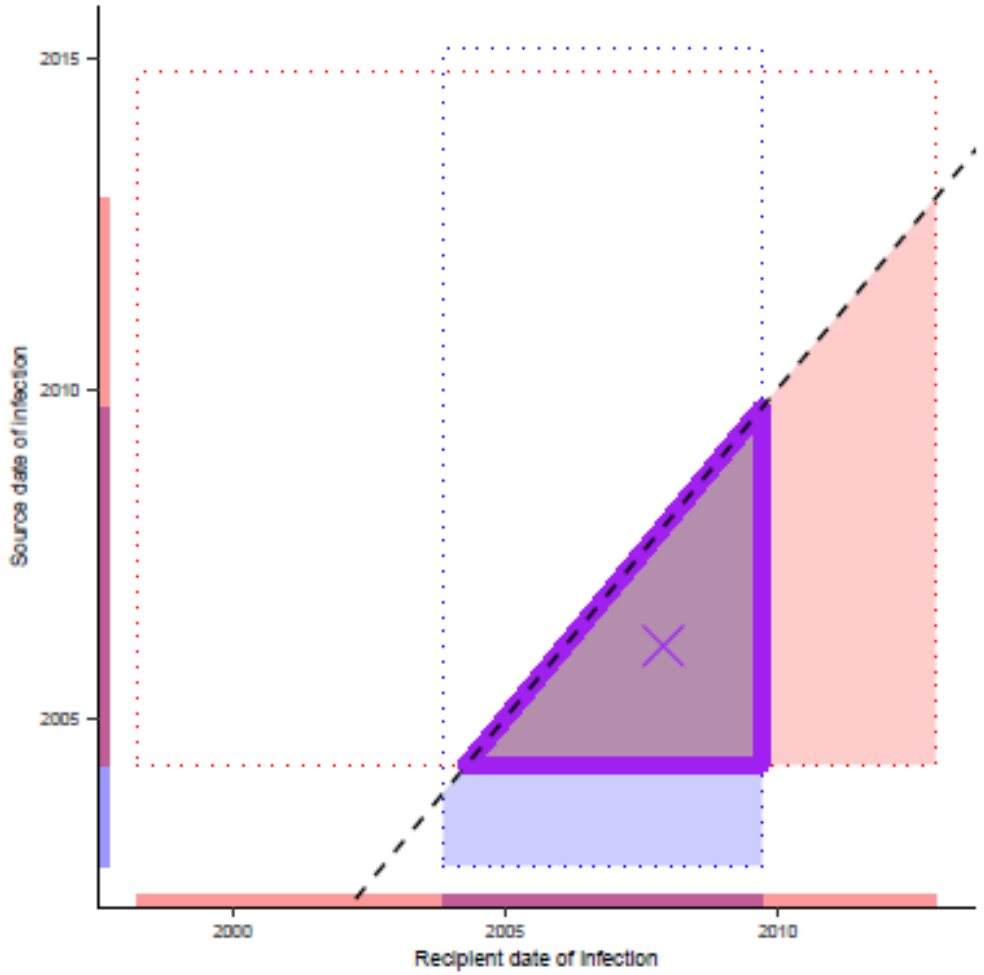
Transmission cohort, 2013-2018

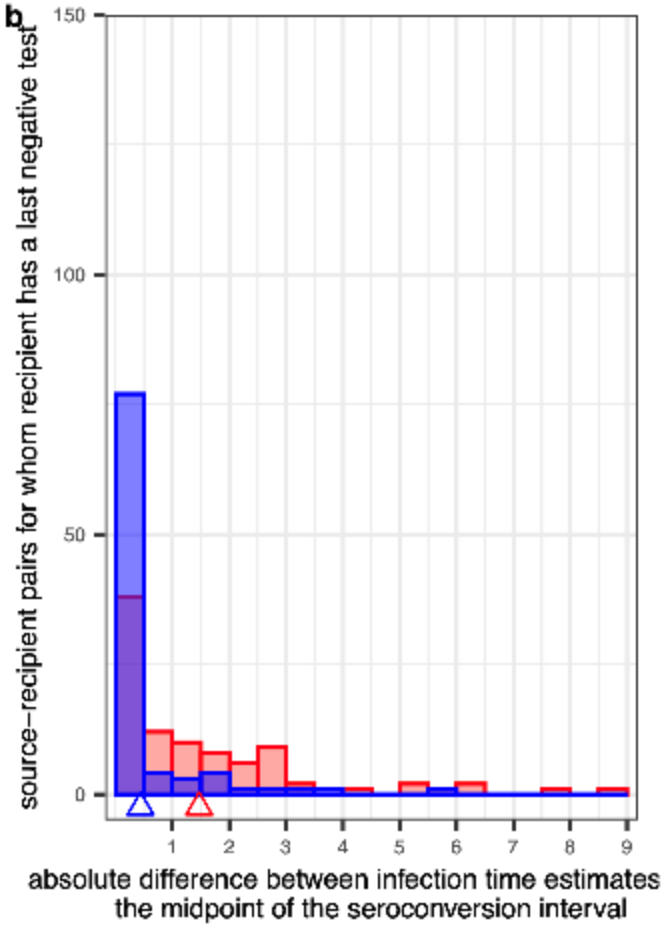
Identified 236 heterosexual source-recipient pairs

Retained 227 in whom transmission was estimated to have occurred during the study period.

Dating the likely infection time with deep-sequence data

- Used phyloTSI algorithm
- Augmented infection time estimates with epidemiologic data



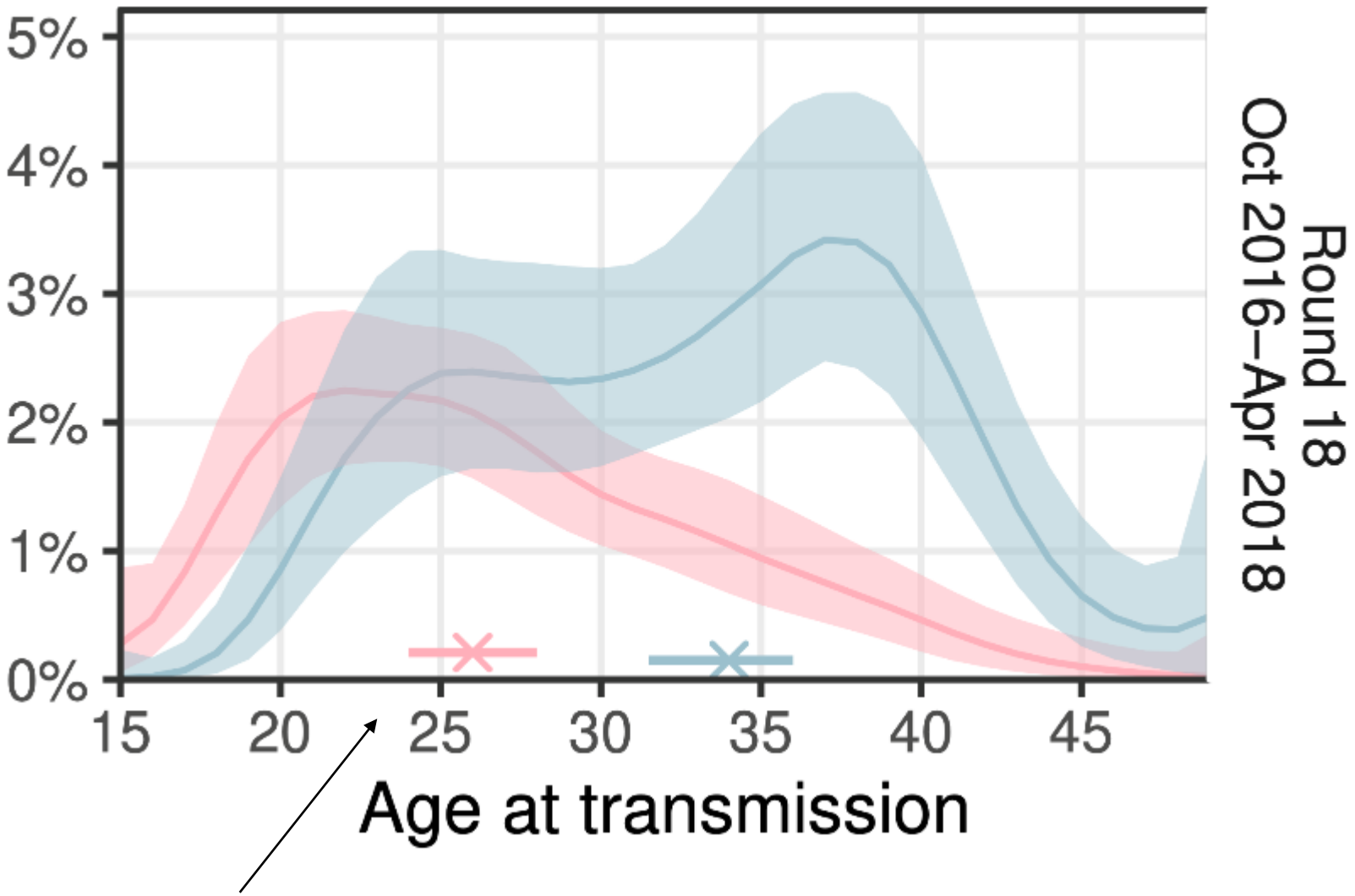


phyloTSI on deep sequence data

refined infection time estimates accounting further for serohistory and transmission direction

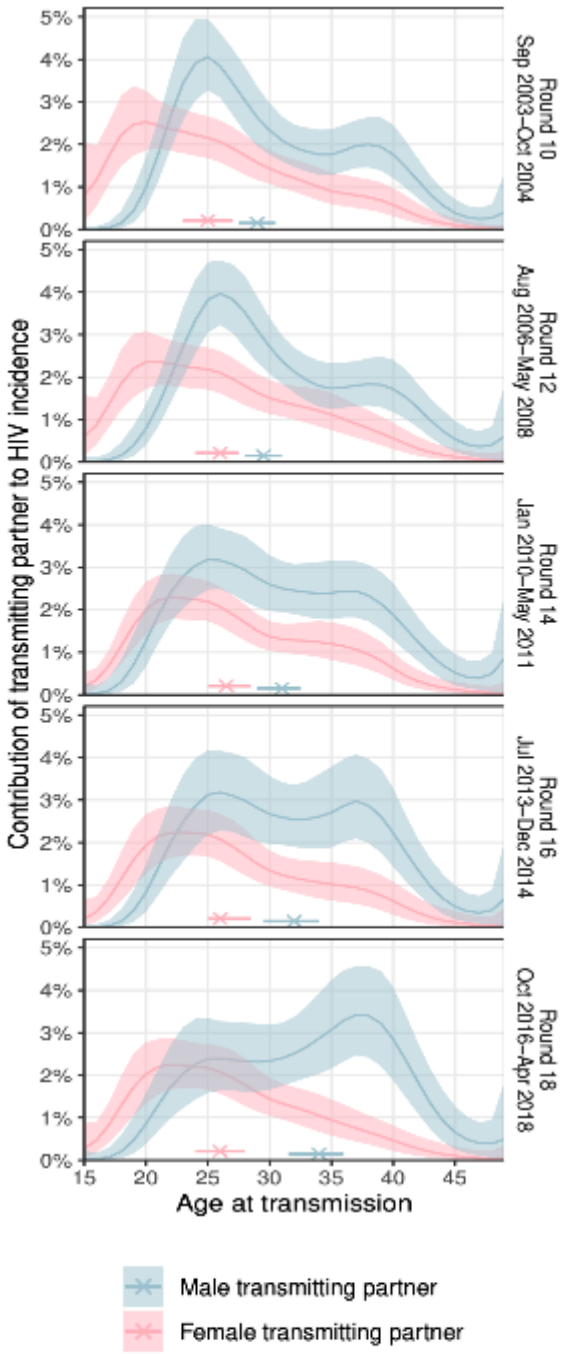
Golubchik et al. Medxriv. 2022

- **Age profile of male sources (blue), and female sources (pink)**
- **Blue + red = 100%**



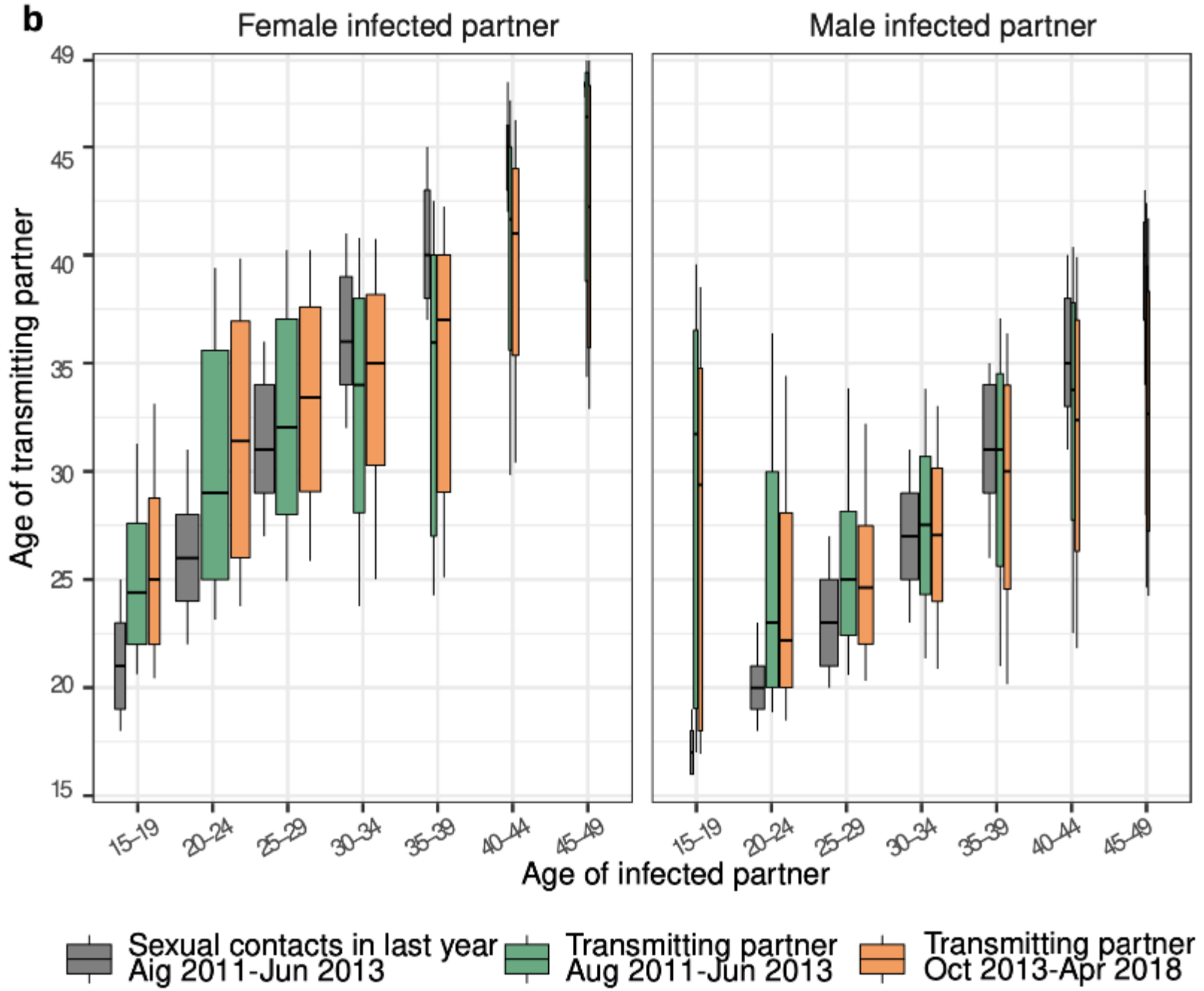
median age of sources

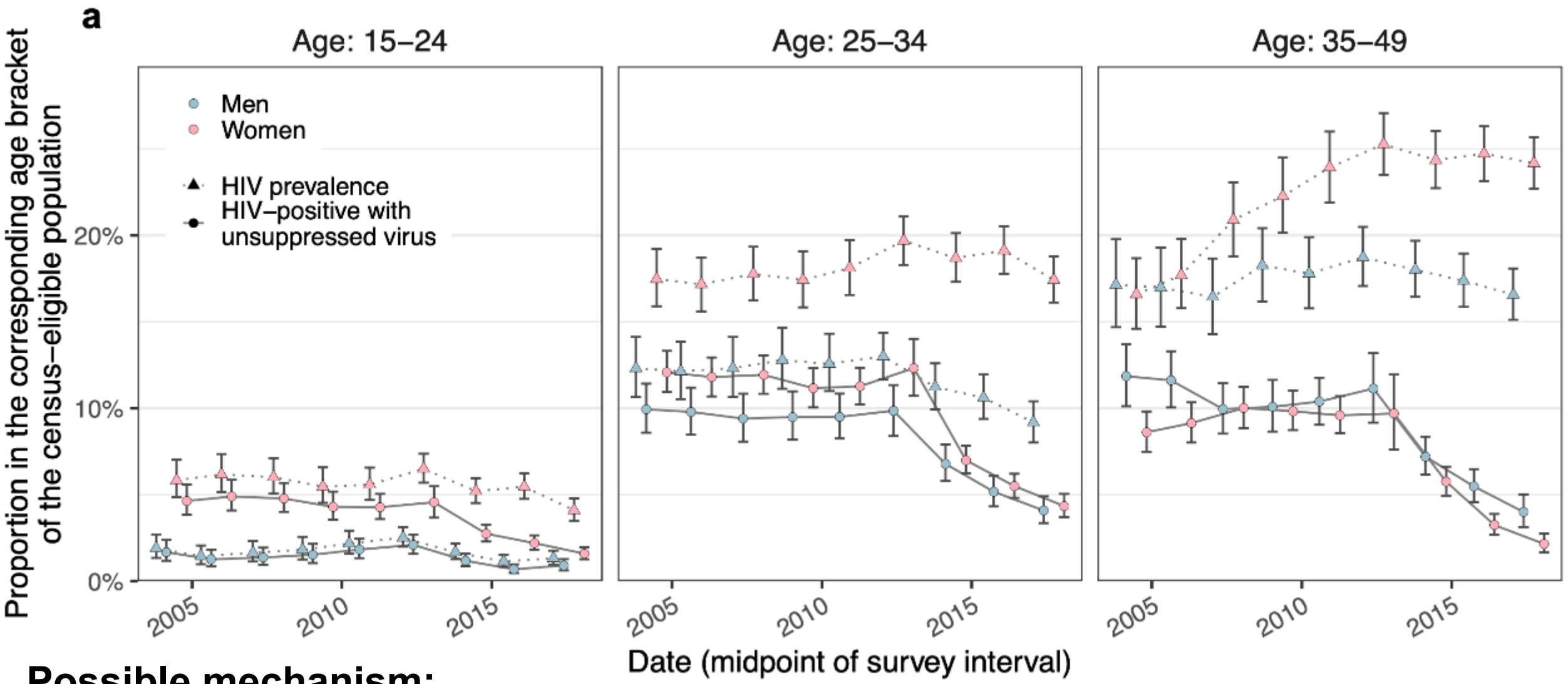
%transmission from men
57.9% [56.1-59.6]
61.9% [60.2-63.7]
62.8% [60.2-65.2]



- Proportion of transmissions from men is increasing
- Transmissions from men are shifting to older ages

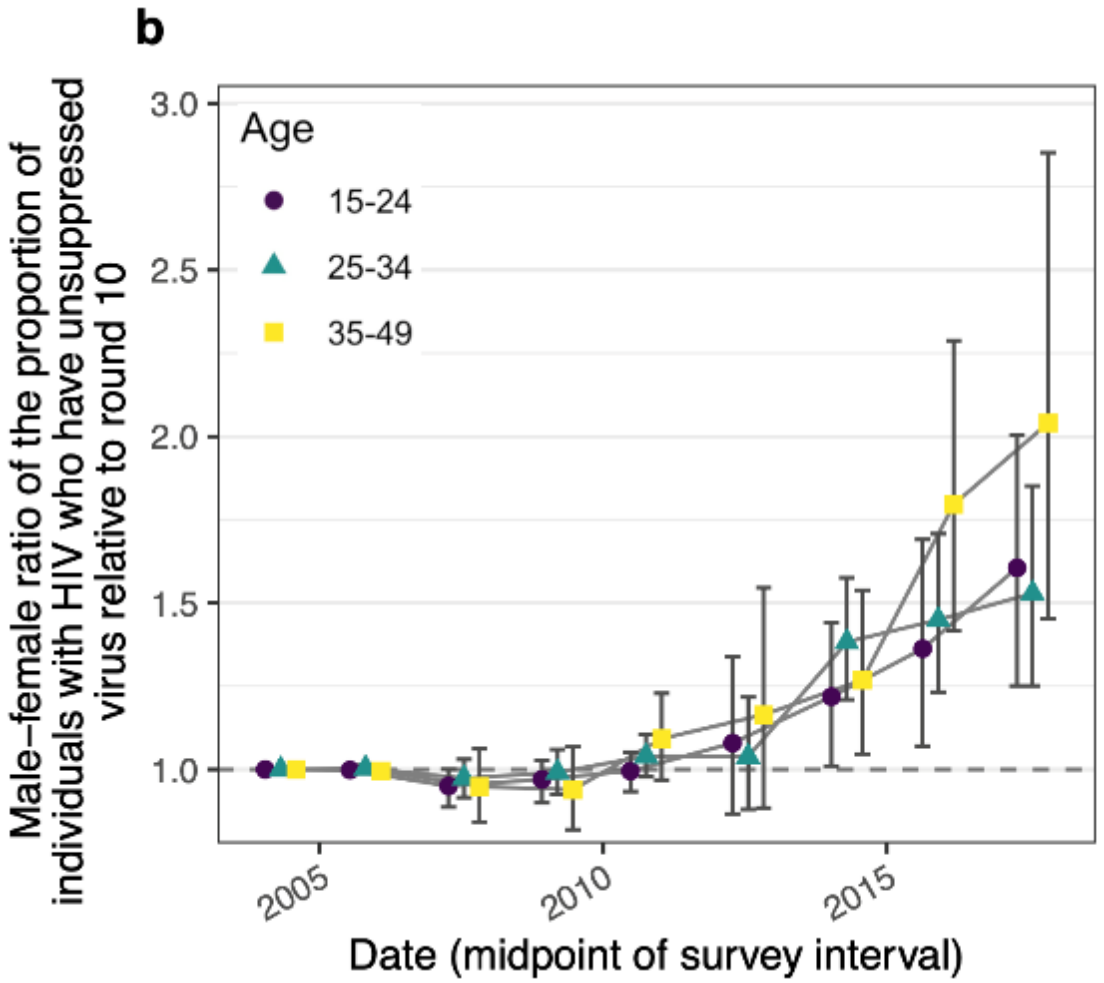
- Adolescent girls and young women are infected by unusually older male partners.
- As women age, age difference between woman and infecting partner decreases.

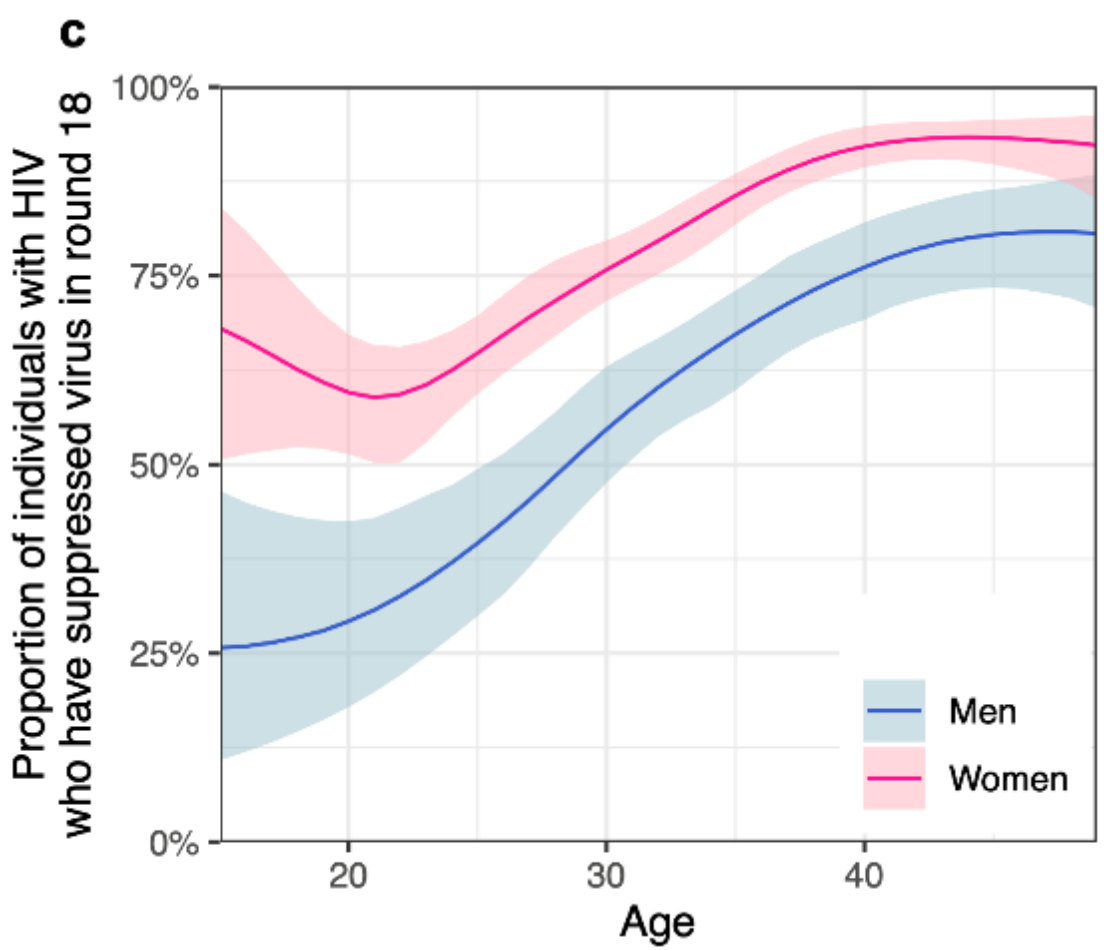




Possible mechanism:

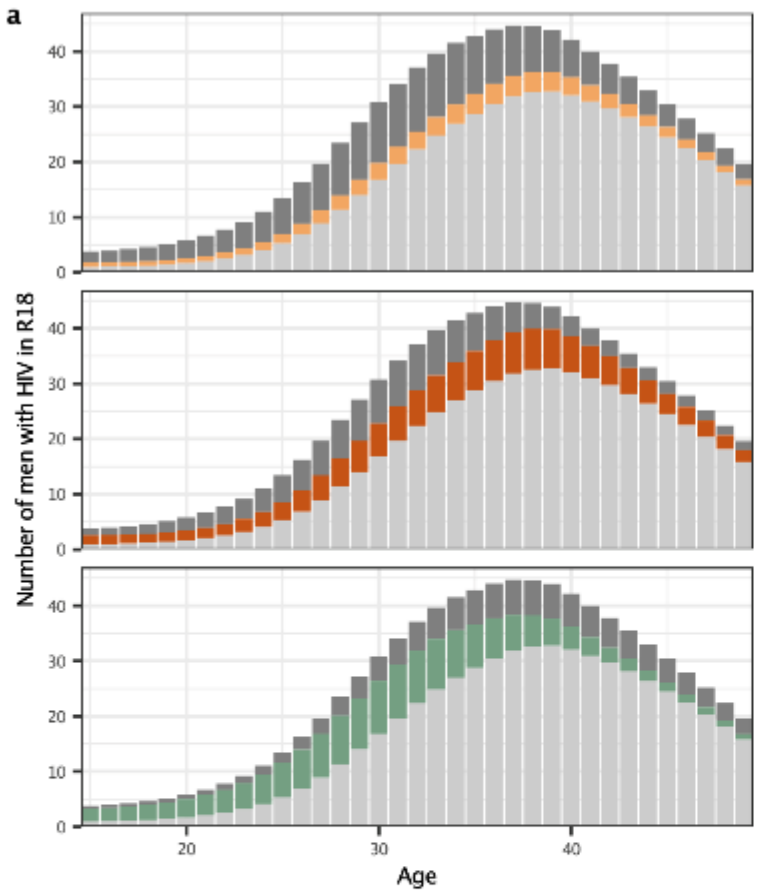
- Decoupling of prevalence and population-level viral load (~ still infectious).

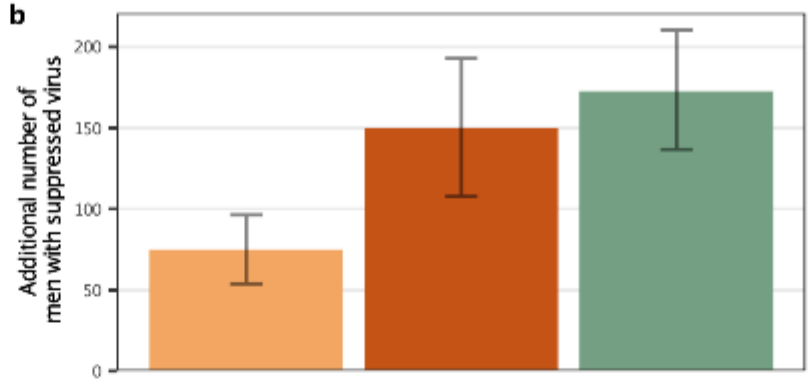


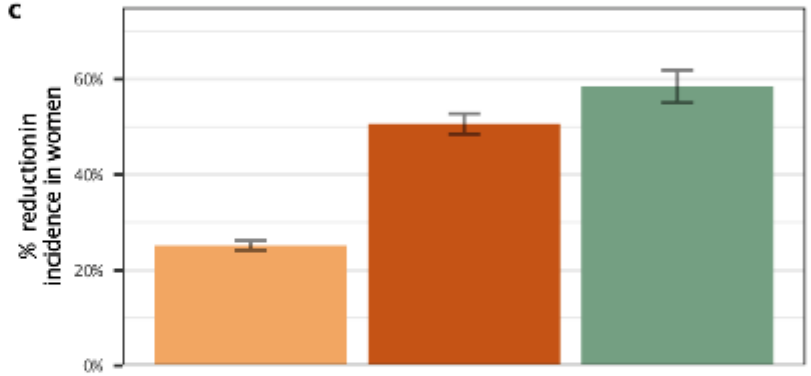


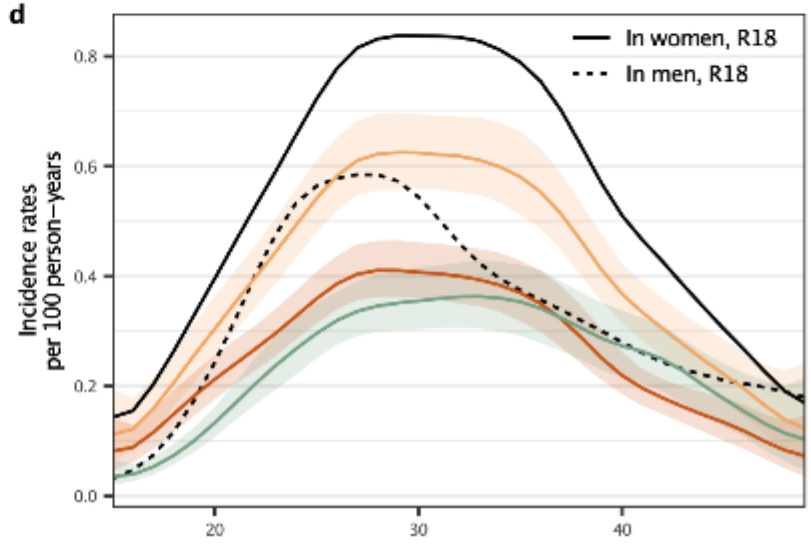
- Faster declines in population-level viral load in women.
- Substantial suppression gap by 2018 in men vs women

- Counterfactual simulations of modelled intervention scenarios on inferred transmission flows

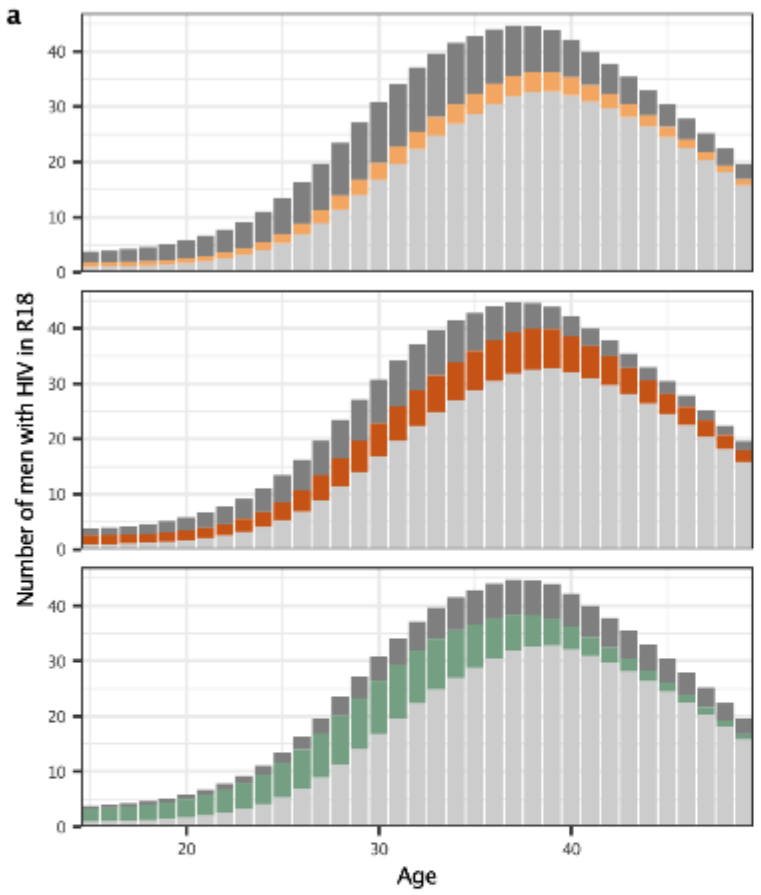


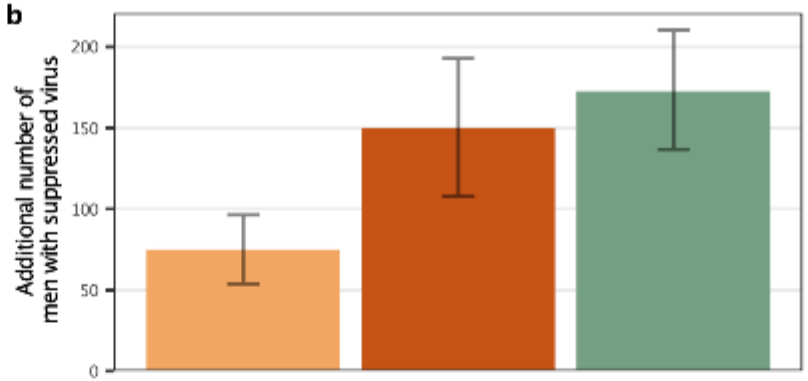


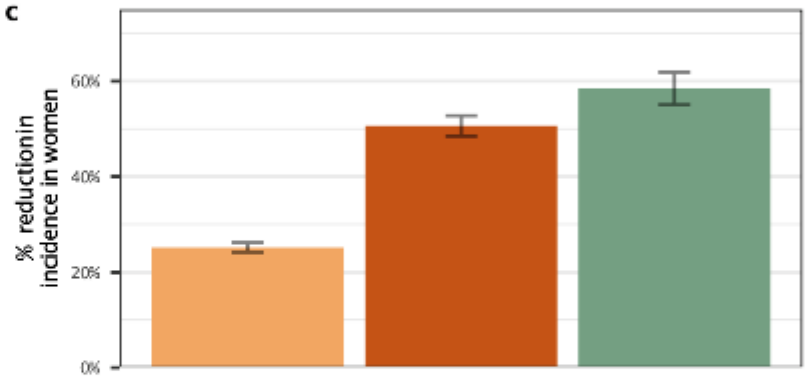


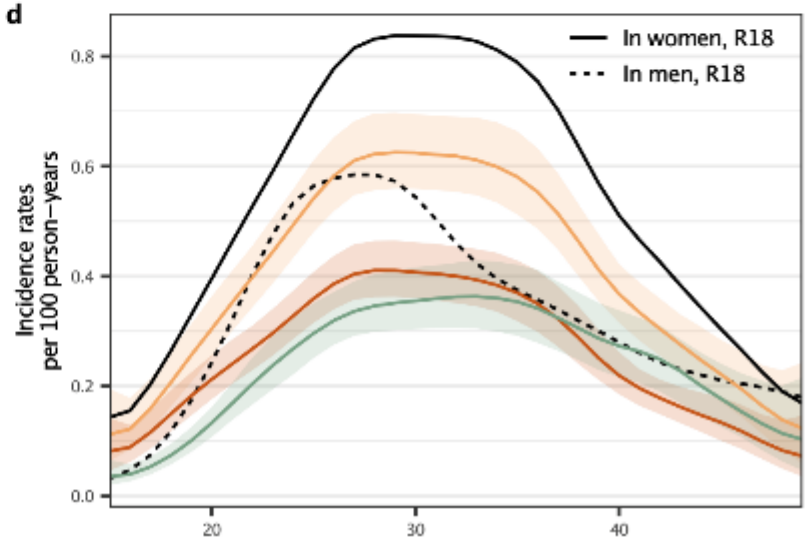


- Having closed the viral load suppression gap between men and women, would have reduced HIV incidence by 50% in women over the last decade.
- Only a small number of men needed to treat to achieve substantial reductions in female HIV incidence.









Conclusion

- HIV incidence has declined faster among men than women.
- Average age of infection is increasing among women; and avg. age of transmission is increasing among men.
- While viral load suppression has increased in both genders, the viral load suppression gap has increased between men and women.
- Men are accounting for an increasing proportion of transmissions.
- Having closed the viral load suppression gap between men in women, would have reduced female HIV incidence by 50%.

Acknowledgments

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University of Oxford
Johns Hopkins Bloomberg School of Public Health
Center for AIDS Research Johns Hopkins University