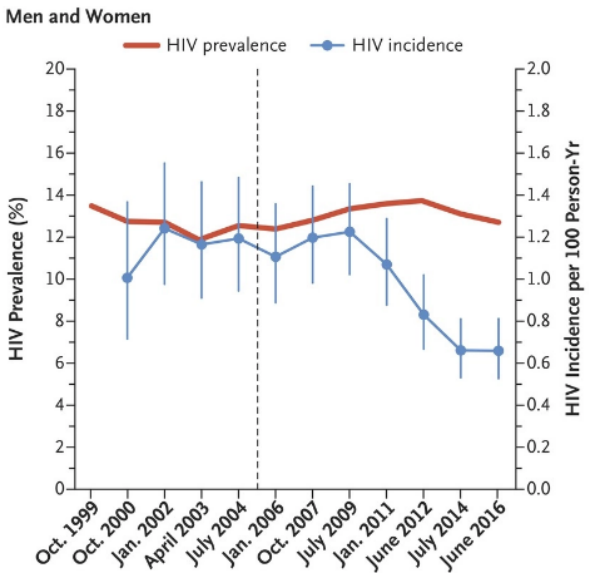
Epidemiology and Viral Dynamics of HIV in the Rakai Community Cohort Study Informing Policy and Programs

Ronald Gray on behalf of Kate Grabowski

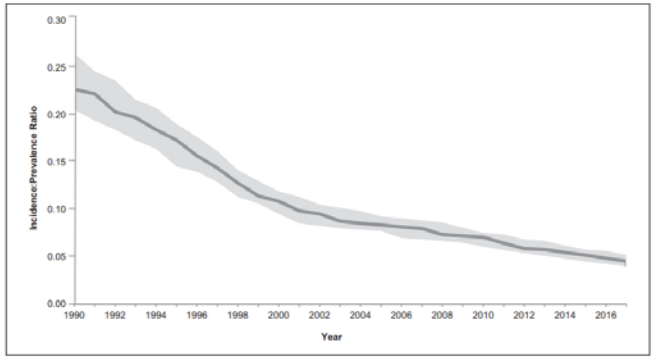
(and Adam)

The African HIV epidemic: the good news

- HIV incidence is declining in Rakai and other African countries.
- **However, no country is on track to reach epidemic control by 2030**
- The future course of the epidemic and ultimate control of HIV depend on identifying and targeting populations with ongoing transmission



Grabowski, *NEJM*, 2019



HIV incidence in sub-Saharan Africa, 1997-2018
UNAIDS, 2018

What is needed for epidemic control?

We need to understand HIV epidemic dynamics during declining incidence and as new and existing interventions are rolled out.

- Who is getting infected?
- Who is infecting whom?
- What is the role of migration?
- What is the role of priority/key populations (e.g., fishing communities)?
- Changes in viral infectivity/virulence?
- Viral suppression on ART/drug resistance?

Where do new HIV infections in Rakai come from?

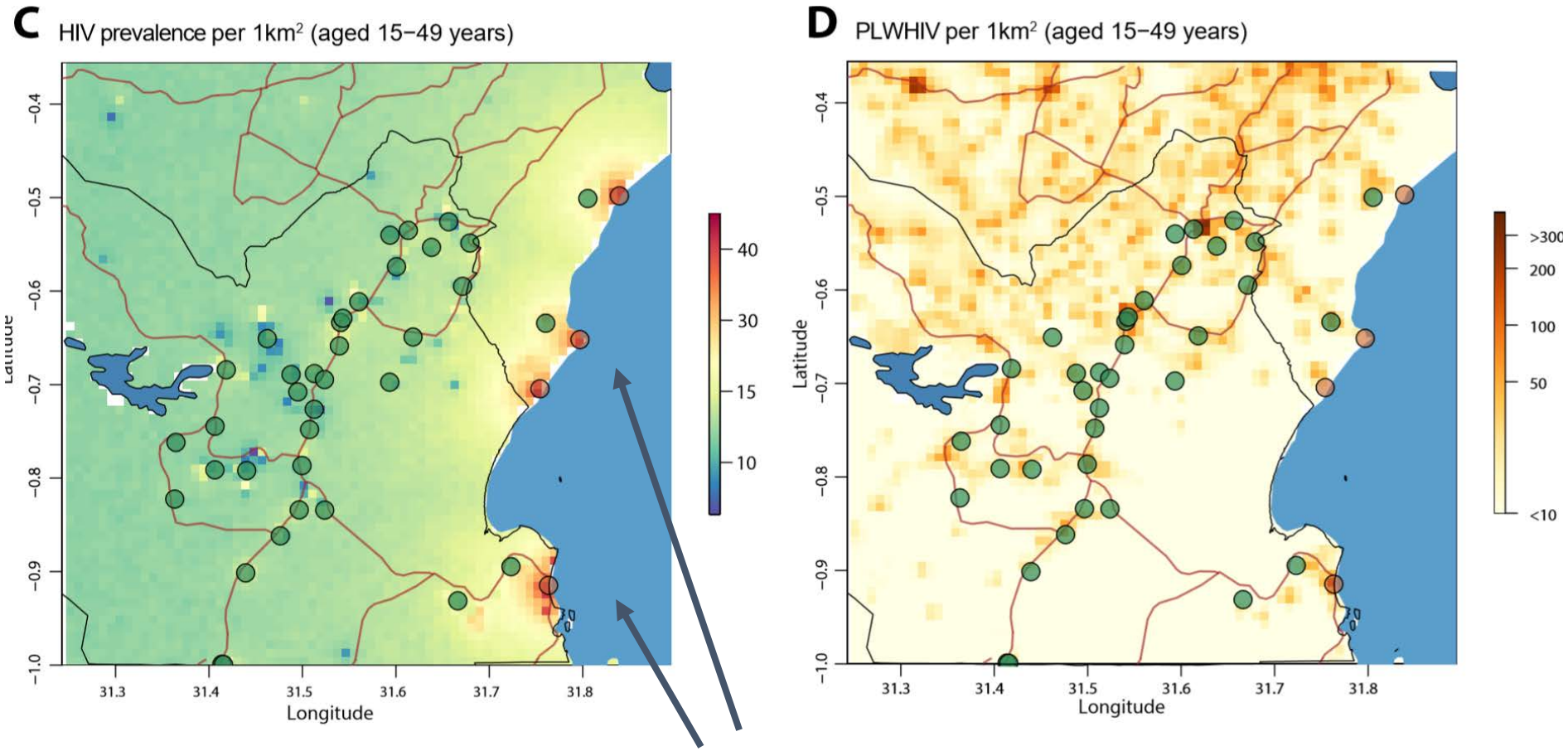
- **39%** of transmissions occurred within **households**
- **40%** of transmissions were from **extra-household** partners of whom **62%** had partners from outside the community.
- There were no transmissions if the partner was on ART

Grabowski et al. *PLoS Med.* 2014

Do high prevalence/incidence fishing communities spread infection to larger inland populations?

NIAID: R01AI110324

HIV prevalence and HIV case burden in RCCS



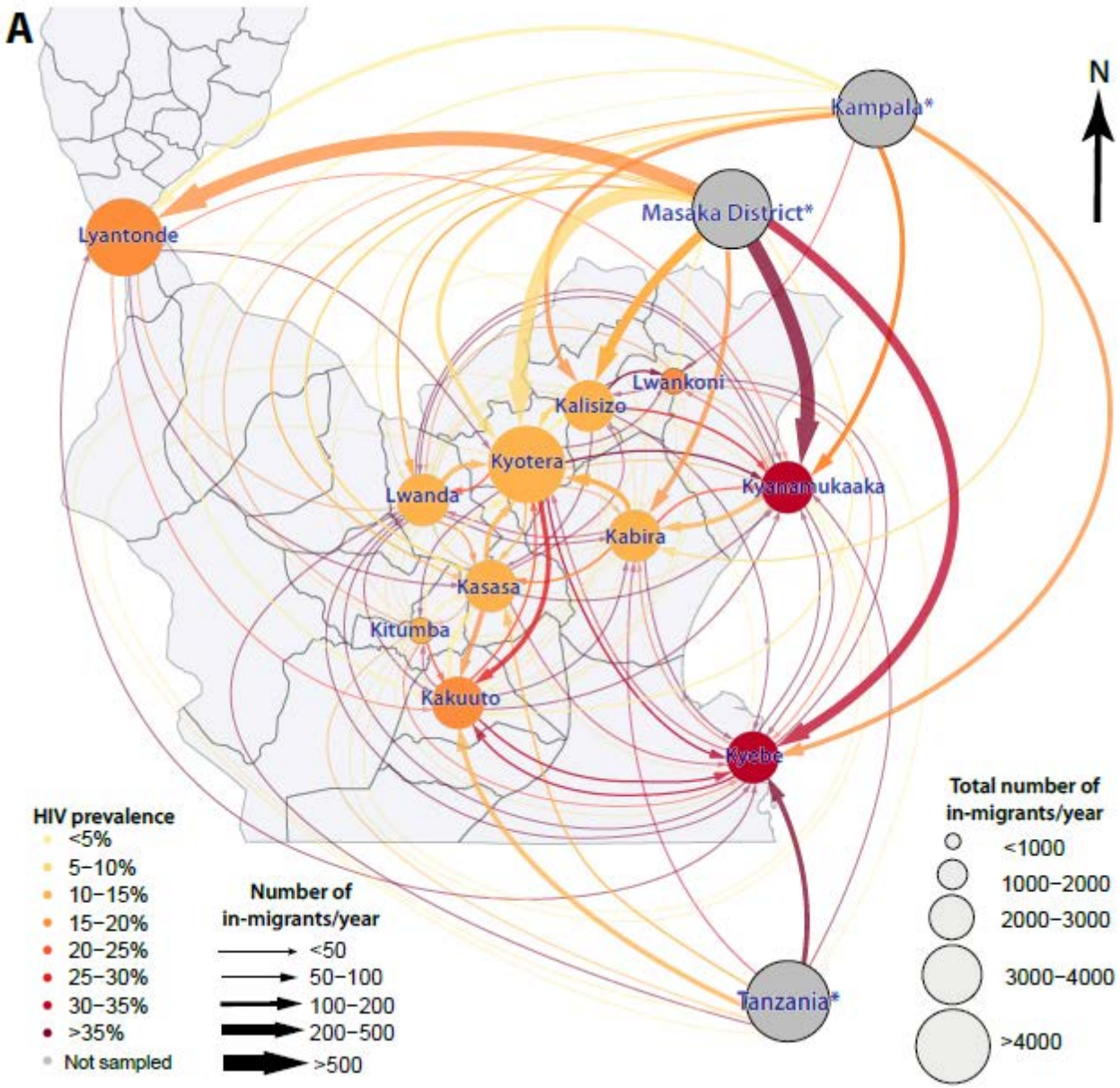
Fishing communities

- Fishing communities have highest prevalence, but smaller populations
- Most infections are in larger inland populations

Chang et al. *Lancet HIV.* 2016

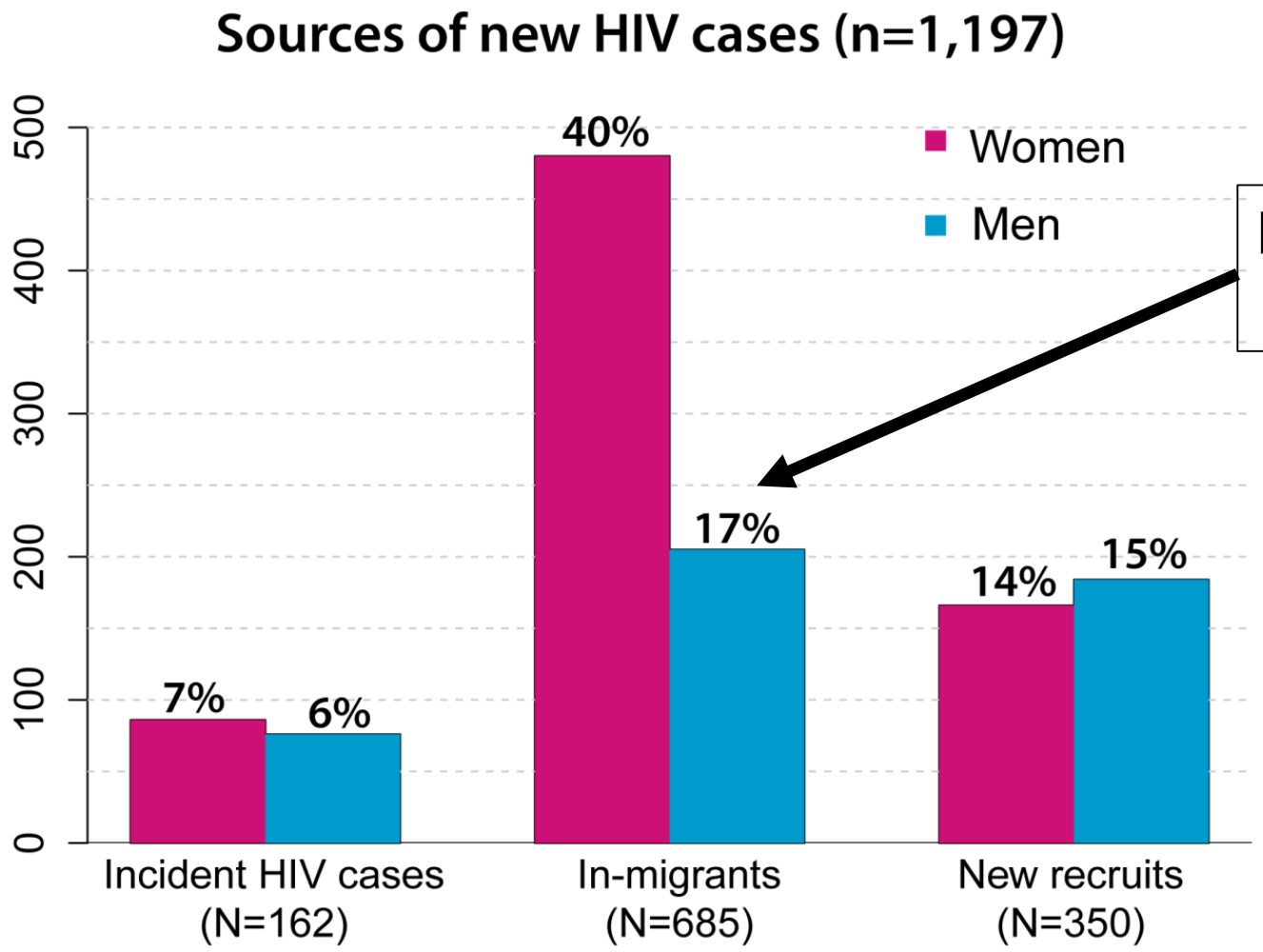
HIV+ and Migration in RCCS communities

- High migration of HIV positive persons into fishing communities
- Diffuse and low prevalence out-migration from fishing to inland



Akullian et al. *HIV Dynamics Evol.* 2018

Migrants contribute most newly detected HIV infections in RCCS; 2011-2015



Most newly identified HIV infections in RCCS are among in-migrants

Olawore et al. *Lancet HIV.* 2018

Recent migrants have high HIV incidence <2 years after arrival

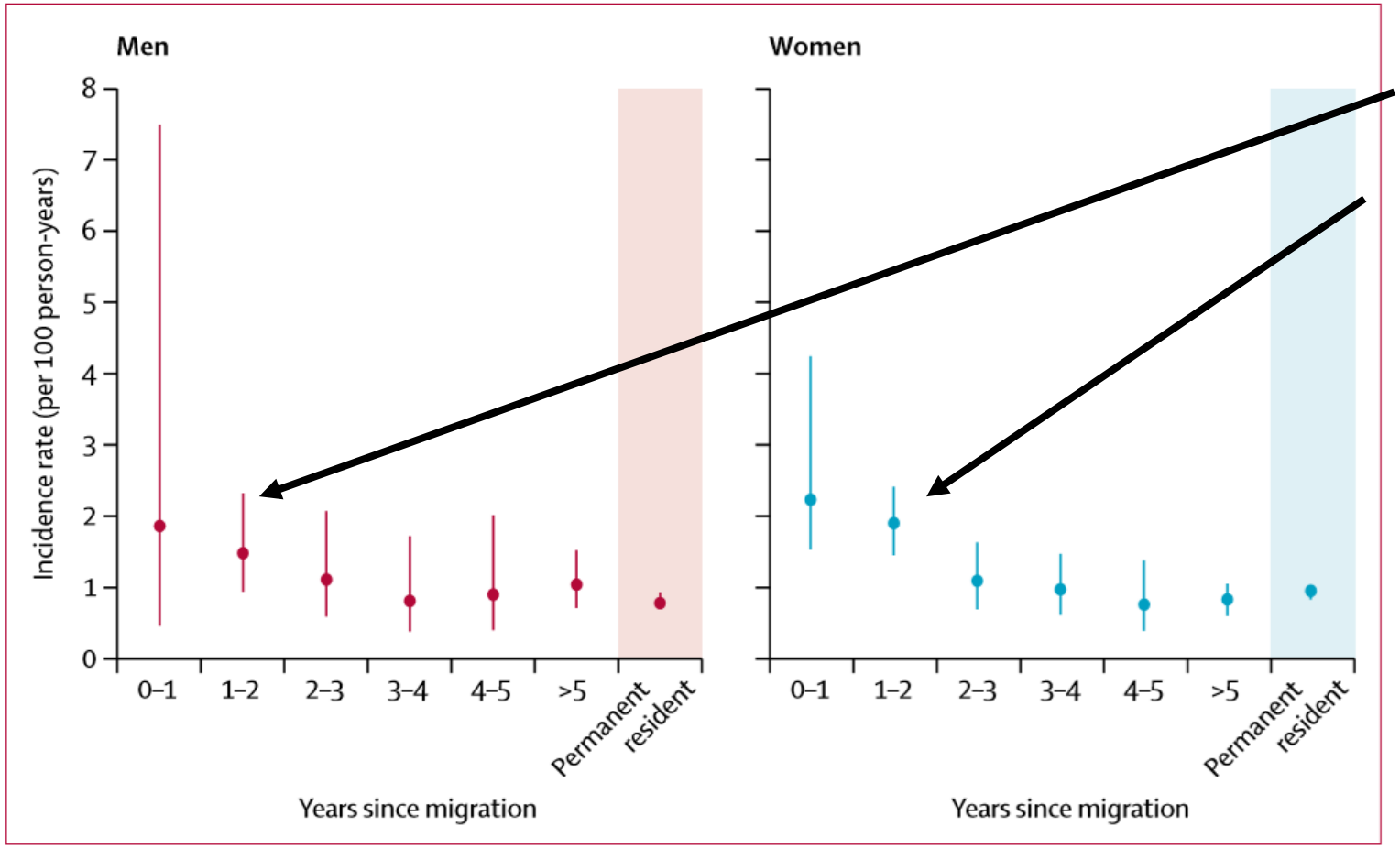


Figure 1: **HIV incidence by year since migration**
Bars are 95% CIs.

- High incidence in recent migrants
- ART use is lower in migrants than residents
- **There is need to rapidly enroll new migrants into treatment and prevention services**

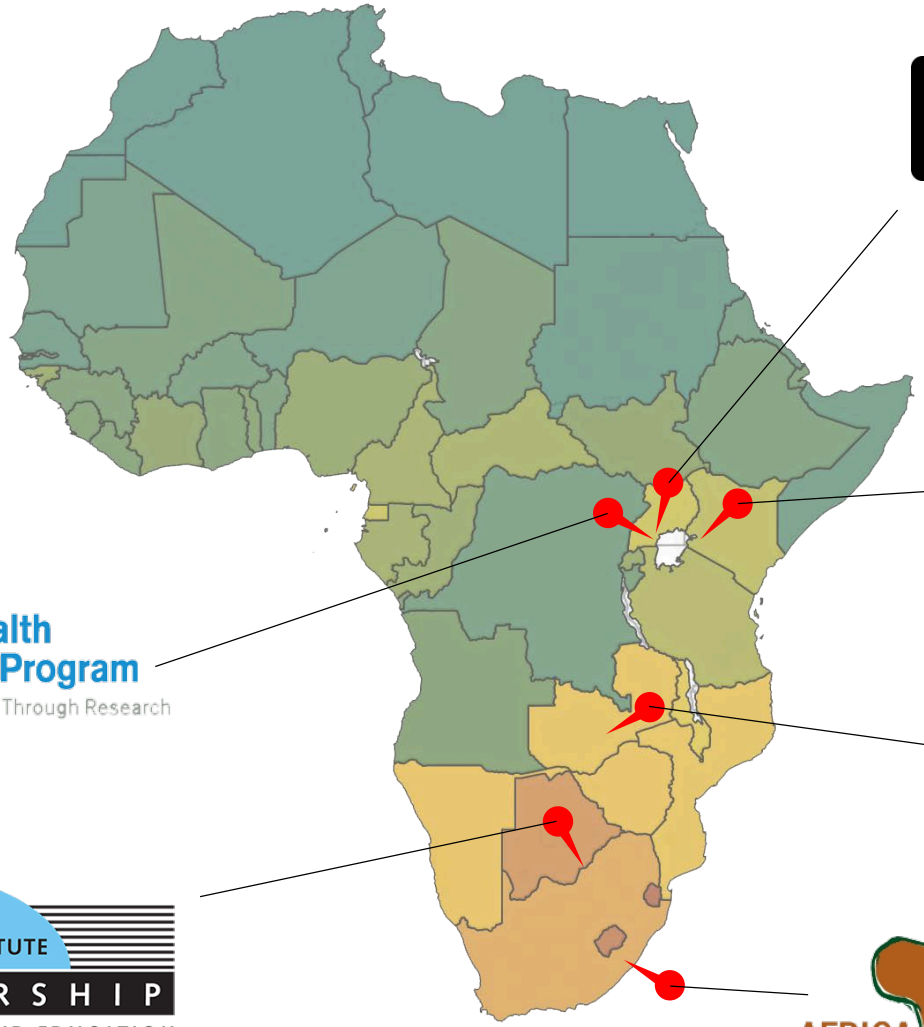
Olawore et al. *Lancet HIV.* 2018

Viral Phylogenetics – PANGEA-HIV collaboration

Phylogenetics **a**nd **N**etworks for **G**eneralised **E**pidemics in **A**frica (**PANGEA**)

% HIV prevalence (UN AIDS 2016)

- <0.1
- 5
- 10
- 15
- 20
- 25



MRC | MRC/UVRI Uganda Research Unit on AIDS

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

INTERNATIONAL CLINICAL RESEARCH CENTER
UNIVERSITY of WASHINGTON

Rakai Health Sciences Program
Improved Health Through Research

Zambart

BOTSWANA HARVARD AIDS INSTITUTE PARTNERSHIP FOR HIV RESEARCH AND EDUCATION

AFRICA CENTRE FOR HEALTH AND POPULATION STUDIES

AHRI

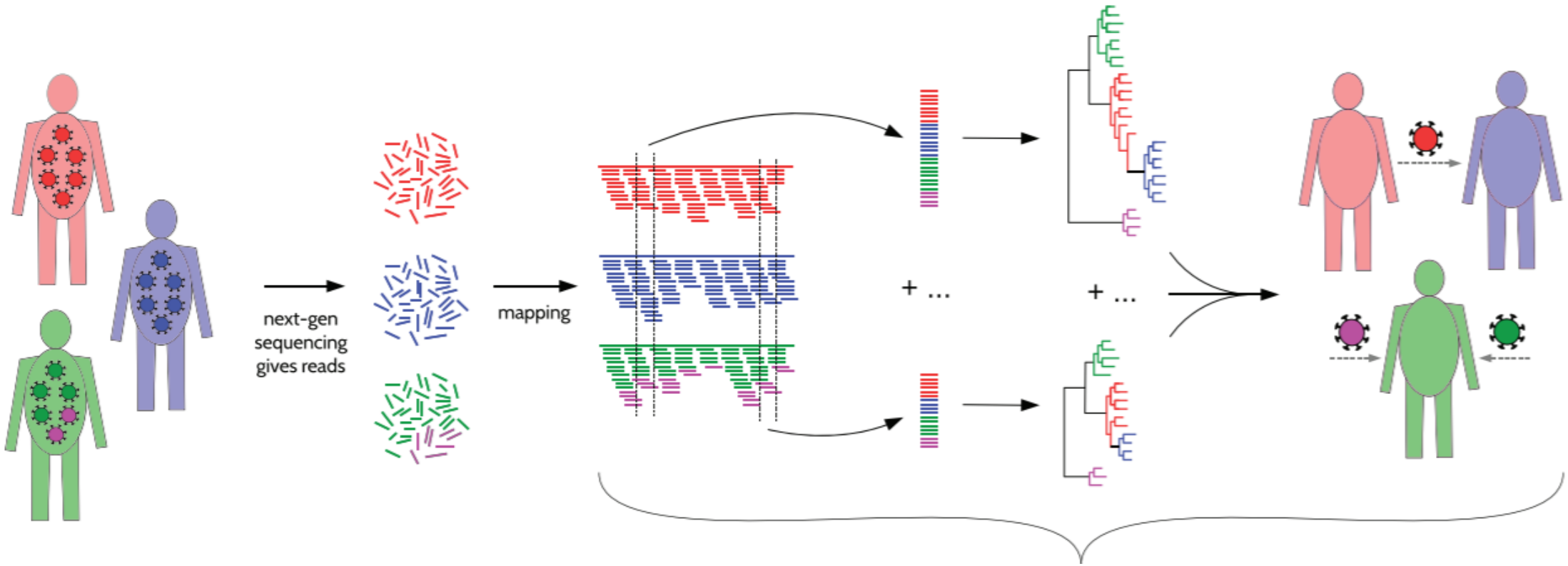
PANGEA HIV

Inferring the direction of HIV transmission between communities

- Used blood samples from HIV-infected participants not on ART with detectable viral loads
- Viral RNA deep sequenced using Next Generation Sequencing.
- Phylogenetic analysis used to infer partial HIV transmission networks and probability of direction of transmission.

Wymant et al. *Virus Evol*. 2017; Ratmann et al. *Nature Comm*. 2019

Reconstruction of HIV transmission networks and direction of transmission with viral deep sequence phylogenetic data



Wymant et al. *Virus Evol*. 2017; Ratmann et al. *Nature Comm*. 2019

Conclusion: Do fishing communities drive the epidemic in the general inland populations of Rakai?

- High prevalence/incidence fishing communities have lower numbers of HIV+ persons than larger inland populations
- Fishing communities attract HIV+ in-migrants, but account for only a small proportion of transmissions to inland communities
- **Targeting HIV services to fishing communities is important, but is unlikely to affect incidence in the larger inland populations in Rakai**

Viral load suppression for HIV positives

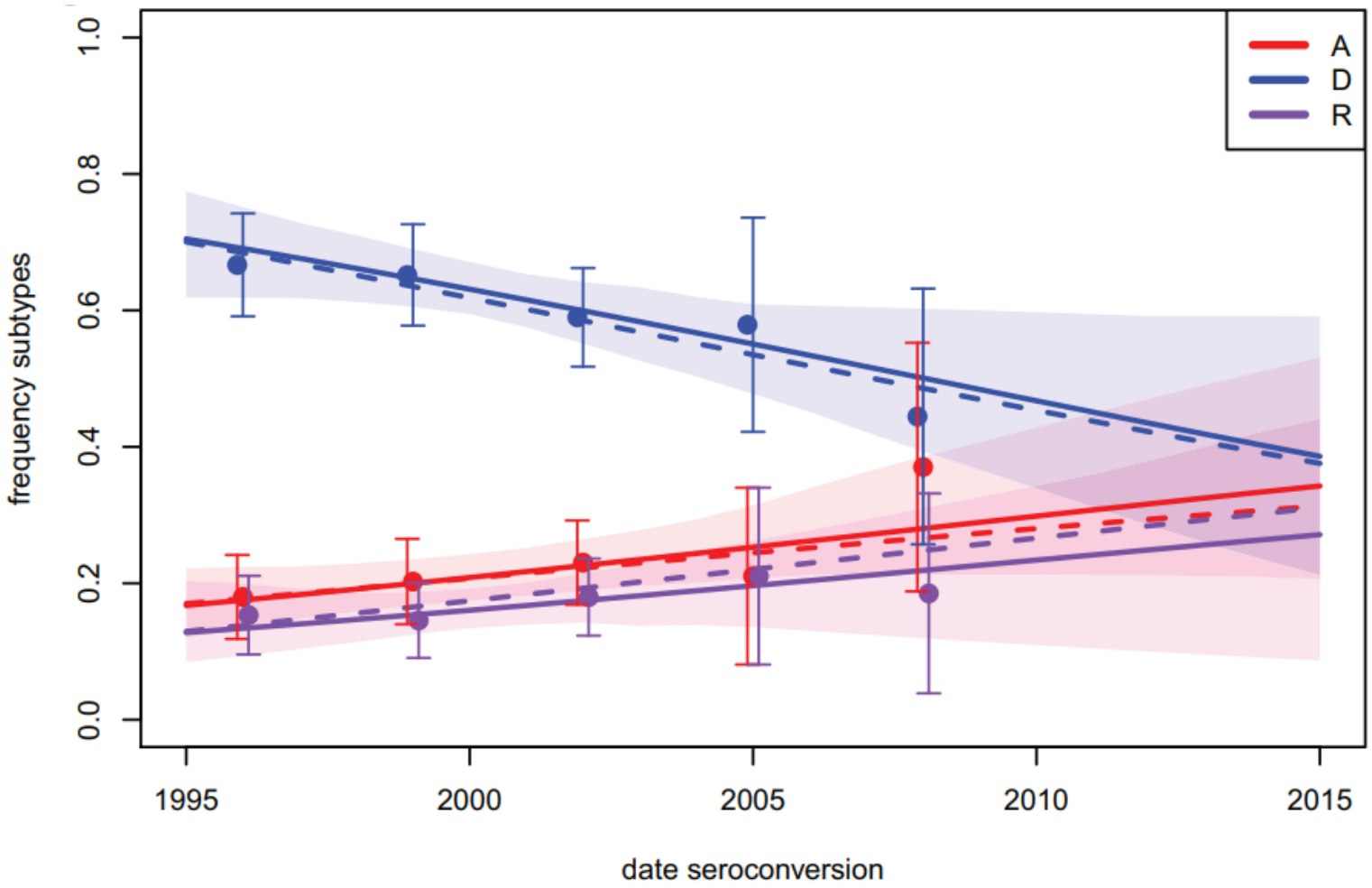
Category of Suppression VL <400	%
Suppressed viral load	**80**
Loss of suppression	3
Persistent Viremia	**16**

- Viral load suppression for HIV+ increases with duration of treatment
- **Persistent viremia is higher in young men, who need extra targeting**
- No transmitted resistance detected yet in Rakai

Patel et al CROI 2019

HIV subtypes are evolving and diversifying in Rakai

- HIV Subtype D is declining in frequency; Viral recombinants and Subtype A are increasing.



- Disease progression faster with subtype D, infectivity greater with subtype A
- A is displacing D

Blanquart et al. *Elife*. 2016

Summary of results

- HIV incidence is declining due to ART and VMMC.
- HIV incidence remains high in fishing communities and mobile/migratory populations.
- Fishing communities do not appear to drive transmission in low prevalence areas
- Durable viral load suppression is increased with ART; but a minority, particularly young men remain unsuppressed (“hard-to-reach/engage”) and have the highest viral loads.
- The HIV epidemic is diversifying
- **Epidemic control remains a major challenge**

Blanquart et al. *Elife*. 2016