Maintaining the Third 90

Clinical Research from Rakai

Steven J. Reynolds, M.D., M.P.H., F.R.C.P.(C)

Senior Clinician
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Associate Professor of Medicine Johns Hopkins University

NIH National Institute of Allergy and Infectious Diseases

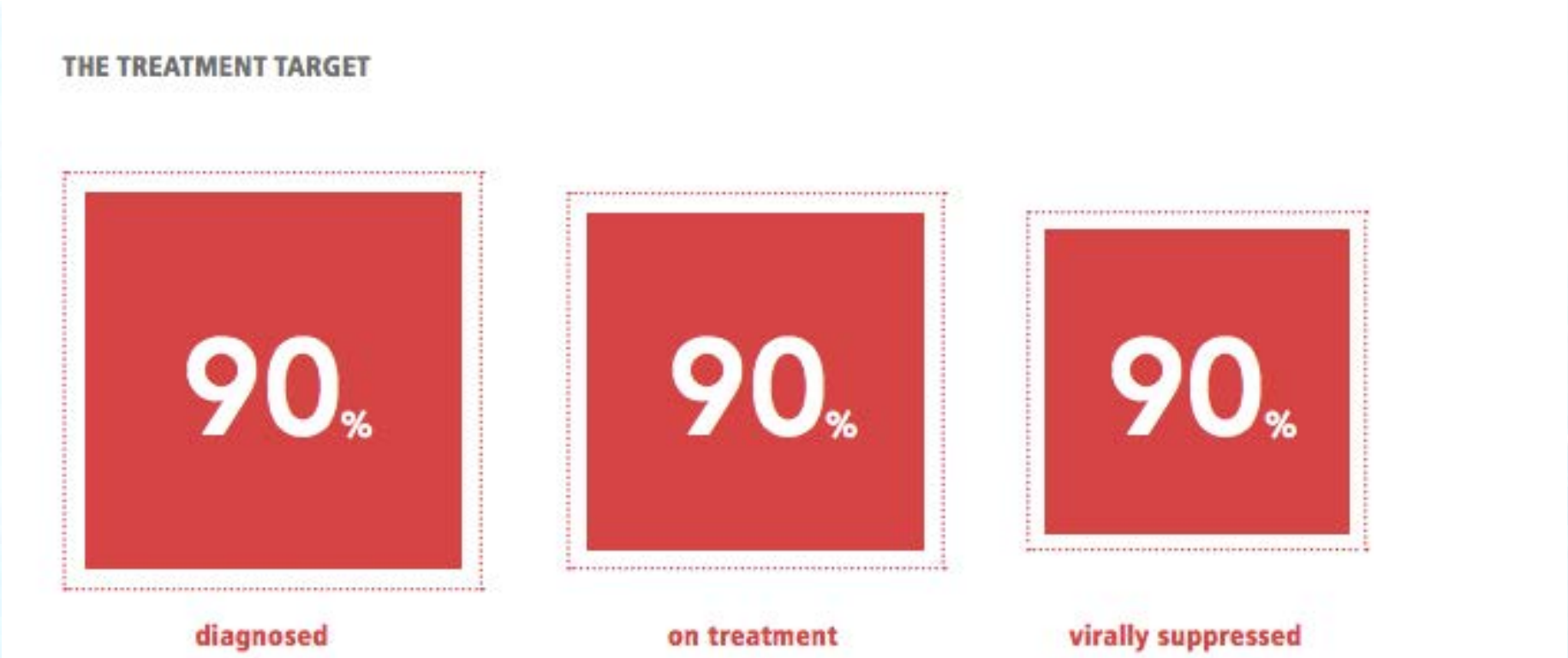
30+ ANNIVERSARY

Rakai Health Sciences Program

JOHNS HOPKINS UNIVERSITY

90-90-90

An ambitious treatment target to help end the AIDS epidemic



UNAIDS 2014

IAPAC
INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE

Outline

- **VL monitoring, evidence from RHSP**
- **Switching to second line ART**
- **Implications on HIV transmission and ultimately maintaining the third 90**

The Slow Death of Immunologic Monitoring

AIDS
Official Journal of the International AIDS Society

Sept. 12, 2008 Vol. 22 No. 14

Evaluation of the WHO Criteria for Antiretroviral Treatment Failure among Adults in South Africa

Mee et al.

AIDS
Official Journal of the International AIDS Society

March 27, 2009 Vol. 23 No. 6

Failure of Immunologic Criteria to Appropriately Identify Antiretroviral Treatment Failure in Uganda

Reynolds et al.

Aug. 1, 2009 Vol. 49 No. 3
Clinical Infectious Diseases

Misclassification of First-Line Antiretroviral Treatment Failure Based on Immunological Monitoring of HIV Infection in Resource-Limited Settings

Kantor et al.

European Journal TM&IH Tropical Medicine & International Health

August 2009 Vol. 14 No. 8

Diagnosis of Antiretroviral Therapy Failure in Malawi: Poor Performance of Clinical and Immunological WHO Criteria

Van Oosterhout et al.

European Journal TM&IH Tropical Medicine & International Health

October 2009 Vol. 14 No. 10

Accuracy of WHO CD4 Cell Count Criteria for Virological Failure of Antiretroviral Therapy

Keiser et al.

PLOS ONE | A peer-reviewed, open access journal

July 6, 2016

Positive Predictive Value of the WHO Clinical and Immunologic Criteria to Predict Viral Load Failure among Adults on First, or Second-Line Antiretroviral Therapy in Kenya

Waruru et al.

WHO HIV Treatment Guidelines 2003-present

2003

1) Clinical monitoring
2) CD4 monitoring if available
3) VL monitoring not recommended due to cost/complexity

2006

1) Clinical monitoring
2) CD4 monitoring needs to be expanded and not seen as a luxury
3) VL monitoring if available

2009

1) Clinical monitoring
2) CD4 monitoring
3) VL monitoring to confirm suspected treatment failure
4) Encourage expansion of viral load monitoring

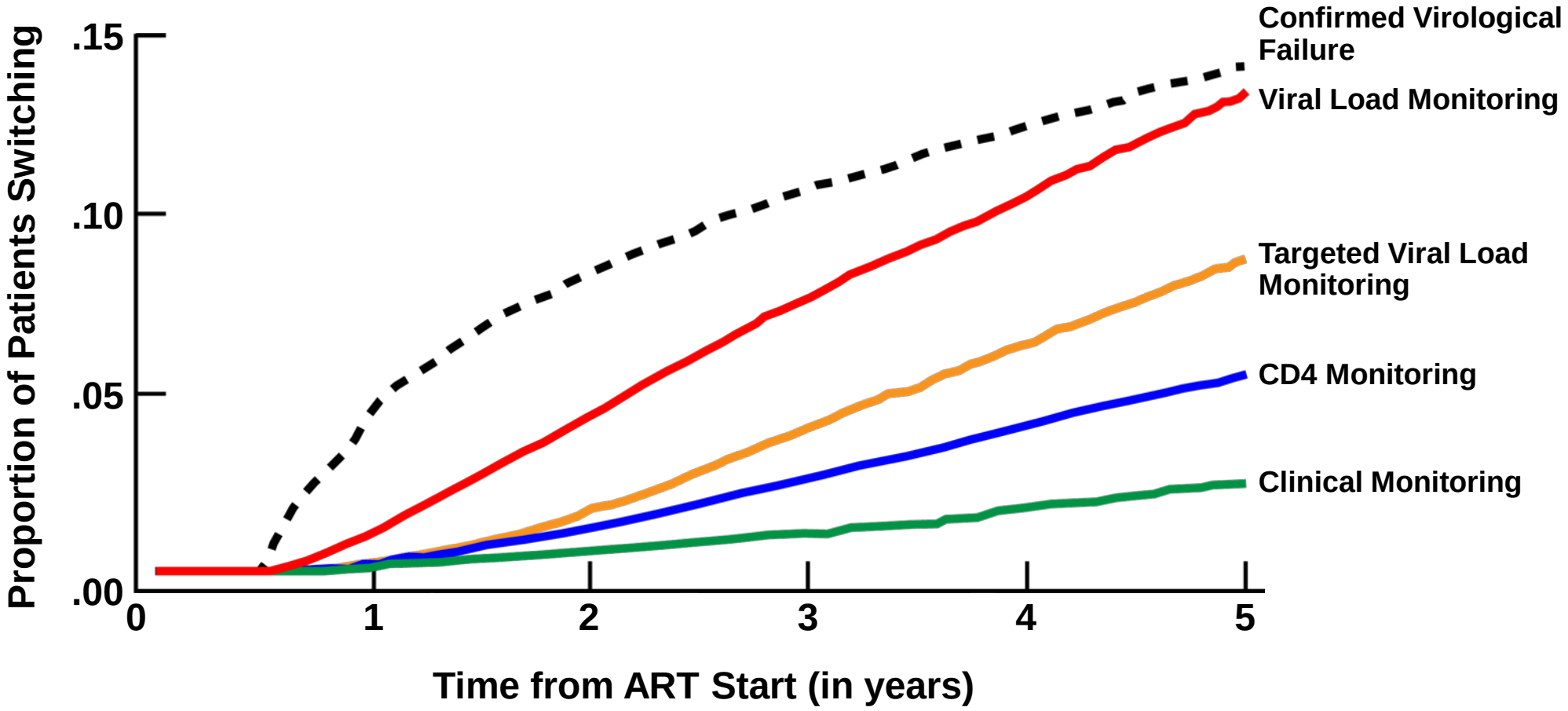
2013

1) Routine VL monitoring recommended as preferred method to identify treatment failure

Switching to Second Line Therapy

Delayed Switching

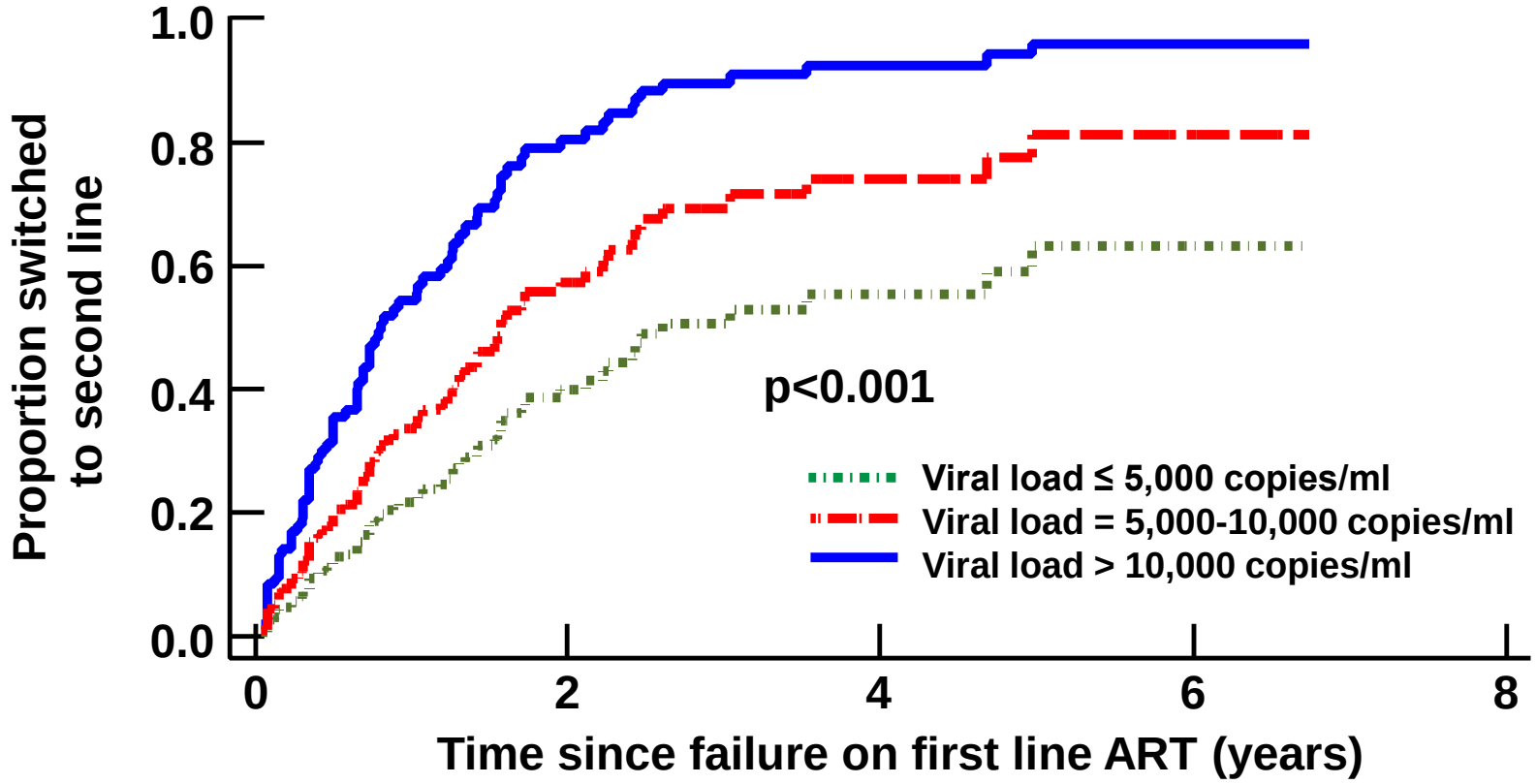
- **Despite the increased availability of viral load monitoring, many programs in sub-Saharan Africa are switching individuals late after first failure detected**



Hass et al., *Lancet HIV* 2015

Delayed Switching Even with Routine VL Monitoring

- **Rakai program results 2004-11 revealed significant delays in switching to second line (median time to switch 8.1 months)**
- **Switching rates influenced by stage of disease**



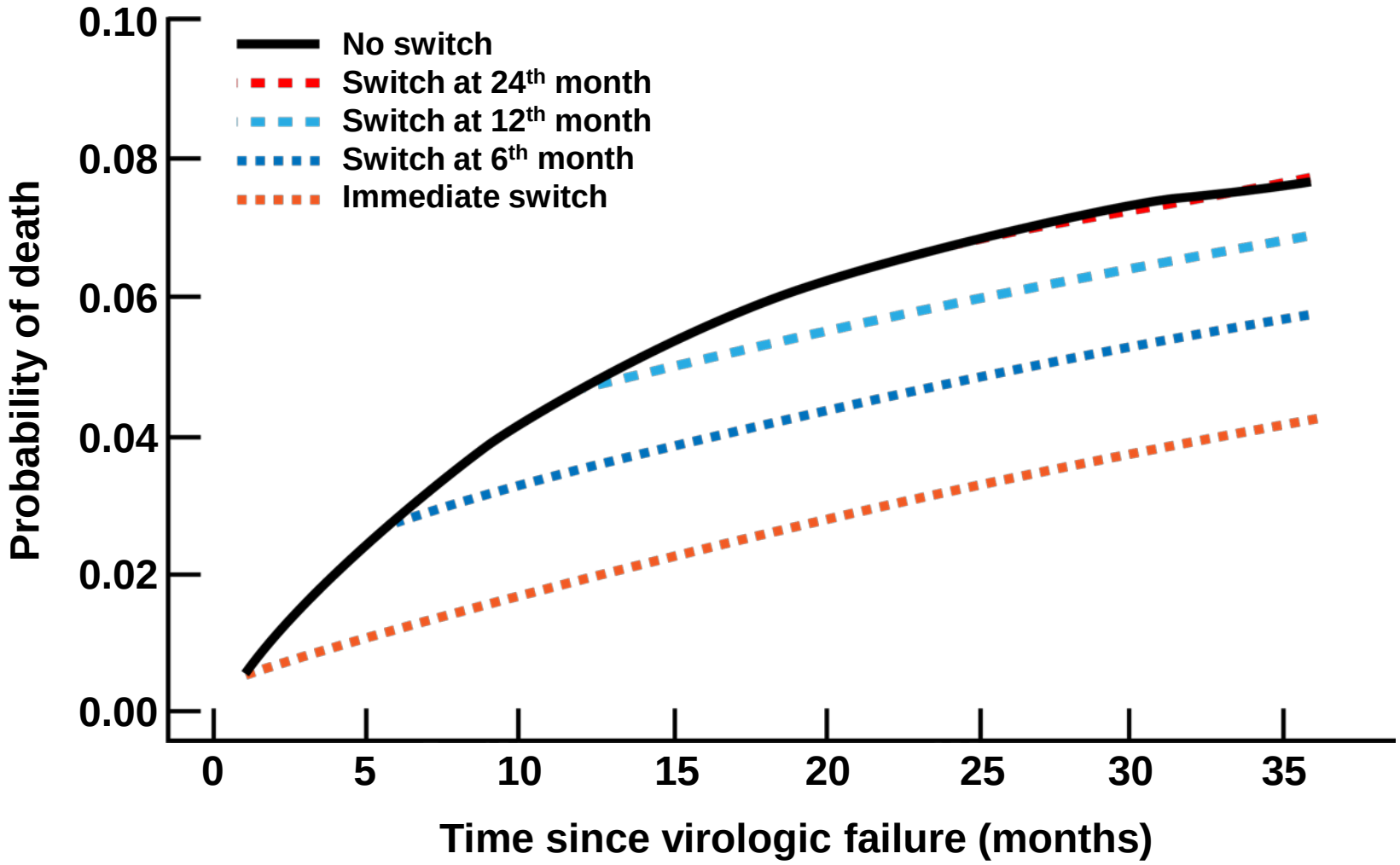
Ssempijja BMC ID 2017

Delayed Switching Even with Routine VL Monitoring: Mortality

Mortality in patients NOT switched to second-line ART was 11.9%, compared to 1.2% among those switched (p = 0.009)

Ssempijja BMC ID 2017

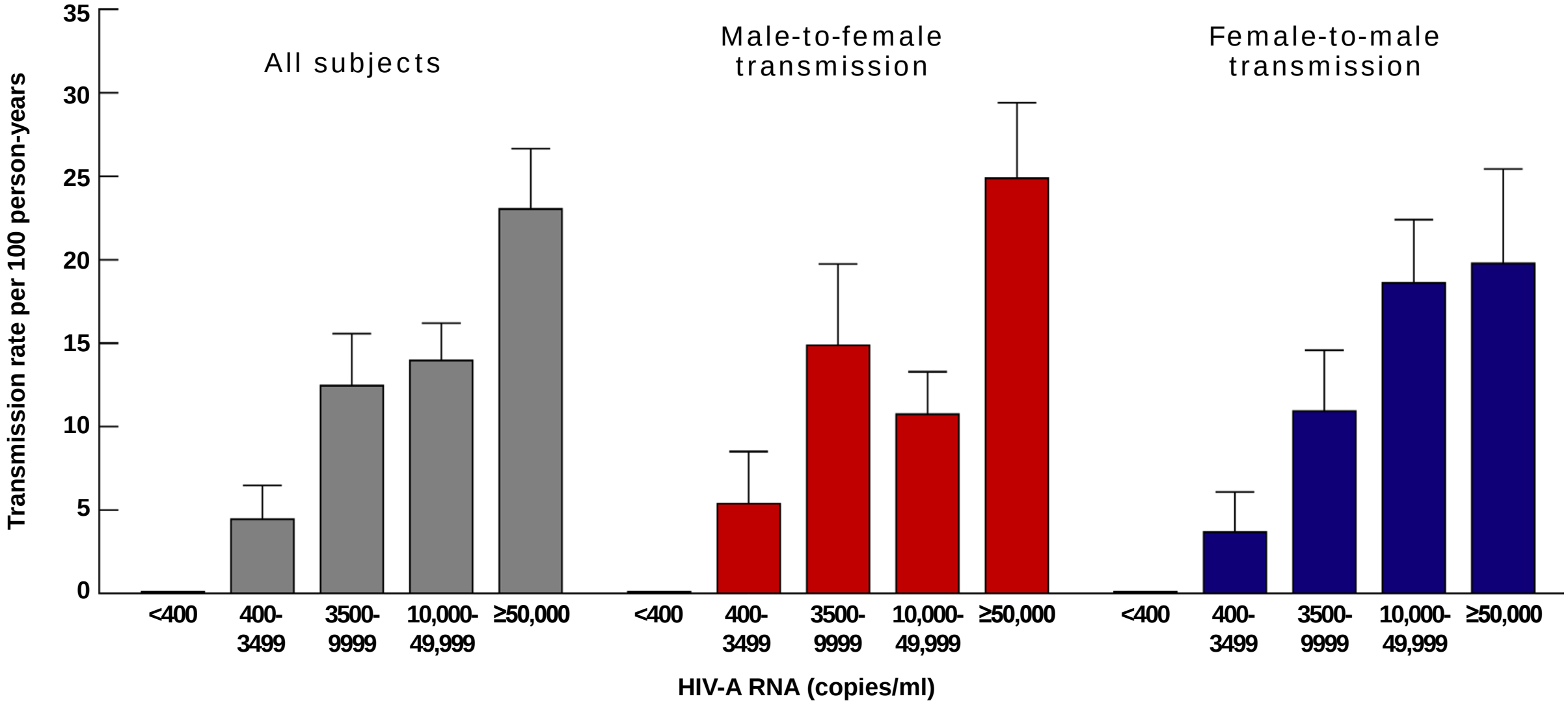
Mortality Increases As Treatment Switch is Delayed



Petersen et al., *AIDS* 2014

HIV Transmission

Viral Load is the Main Driver of Transmission



Quinn et al. *New England Journal of Medicine* 2000

ART and HIV Transmission

HIV-1 transmission among HIV-1 discordant couples before and after the introduction of antiretroviral therapy

Steven J. Reynolds[a,b], Frederick Makumbi[c], Gertrude Nakigozi[d], Joseph Kagaayi[d], Ronald H. Gray[e], Maria Wawer[e], Thomas C. Quinn[a,b] and David Serwadda[c]

- **42 HIV transmissions occurred 459.4 person years among couples not on ART, incidence:**
  - **9.2/100 py (95% CI 6.59-12.36)**

- **No HIV transmissions occurred over 53.6 person years during periods when index partner was on ART**

Reynolds AIDS 2011, 25;473

Antiretroviral therapy works

ART also prevents Hepatitis B Transmission

Hepatitis B incidence and prevention with antiretroviral therapy among HIV-positive individuals in Uganda

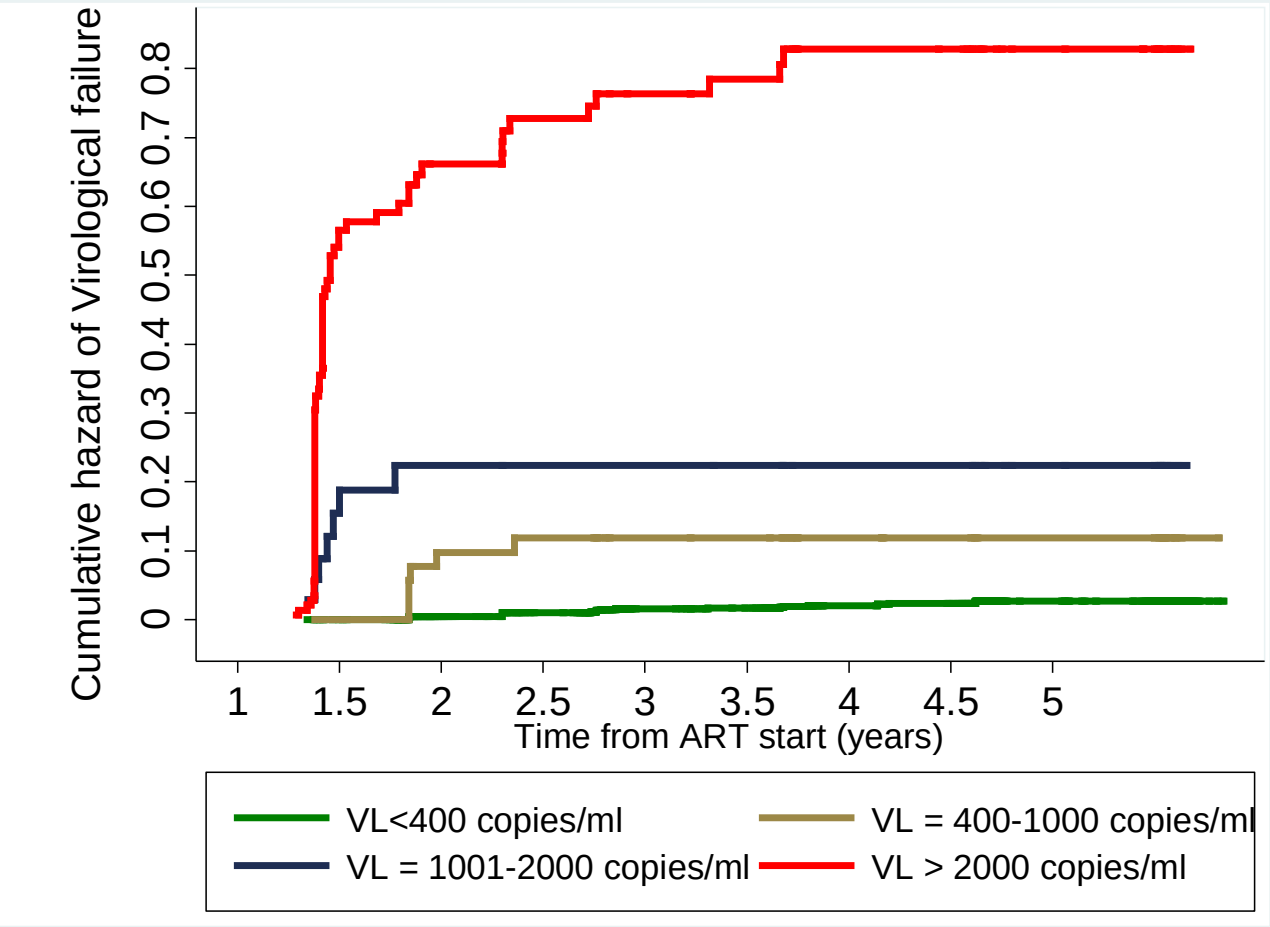
Emmanuel Seremba[a], Victor Ssempijja[b], Sarah Kalibbala[c], Ronald H. Gray[d], Maria J. Wawer[d], Fred Nalugoda[c], Corey Casper[e], Warren Phipps[e], Ponsiano Ocama[a], David Serwadda[c,f], David L. Thomas[g] and Steven J. Reynolds[g,h]

- **39 Hepatitis B transmissions occurred 3342 person years among HIV positive individuals not on ART:**
  - **1.17/100 py (95% CI 6.59-12.36)**

- **Hepatitis B incidence reduce by 75% among those receiving ART; NO incident cases among individuals receiving Tenofovir**

Seremba AIDS 2017, 31; 781

Viral Load Monitoring and Differentiated Care



- **12 months after ART initiation:**
  - **90% had VL<400 copies/ml**
  - **3% 400-1000 had copies/ml**
  - **2% had 1001-2000 copies/ml**
  - **5% had >2000 copies/ml**
- **Viral load measurement at 12 months post-ART initiation predicted patients at high risk of subsequent virological failure.**

Ssempijja OFID 2018

Conclusions

- **VL monitoring can help us maintain the third 90**
- **Implementation challenges need to be addressed to maximize the benefit of VL monitoring**
- **Acting on VL can improve patient care, clinical outcomes and our ability to control the epidemic**

Médecins Sans Frontières, 2016