AFRICOS

The African Cohort Study: Exploring opportunities for collaborative research

Francis Kiweewa, MD, MPH

on behalf of the AFRICOS Study Team

17th July 2016

This research has been supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) through the U.S. Department of Defense. The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army or the Department of Defense.

Global HIV status - December 2015

- 78M people had become infected with HIV since the epidemic started
- 35M AIDS-related death had occurred since the epidemic start
- In 2015, 36.7M people were living with HIV
- 1.1M people died from AIDS-related causes, compared to 2M in 2005 (45% decrease)
- 2.1M people became newly infected with HIV in 2015, down from 2.2M in 2010 (6% decrease)
- 17M were accessing ART, up from 7.5M in 2010

Source: ***UNAIDS (July 2016)***

AFRICOS

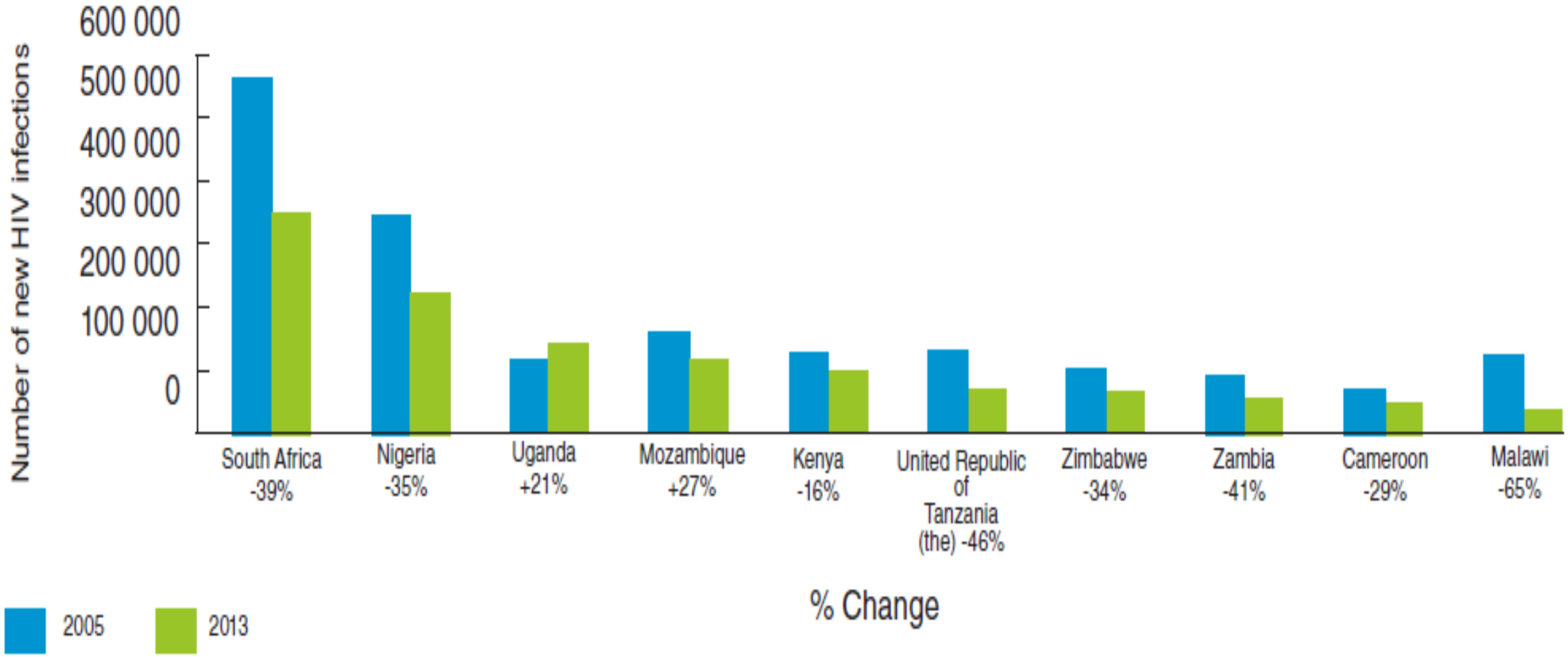
Eastern and Southern Africa- 2015

- **19M people living with HIV**
- 960 000 new HIV infections
  - Accounting for 46% of the global total of new HIV infections
  - New HIV infections declined by 14% between 2010 and 2015
- **470 000 people died of AIDS-related causes in 2015**
  - Representing a 38% decline in AIDS related death since 2010
- 10.3M people were accessing antiretroviral therapy
  - Representing 54% of all people living with HIV in the region
  - Six out of 10 people on ART live in eastern and southern Africa

Source: ***UNAIDS (July 2016)***

AFRICOS

Trends in HIV Incidence – Sub-Saharan Africa

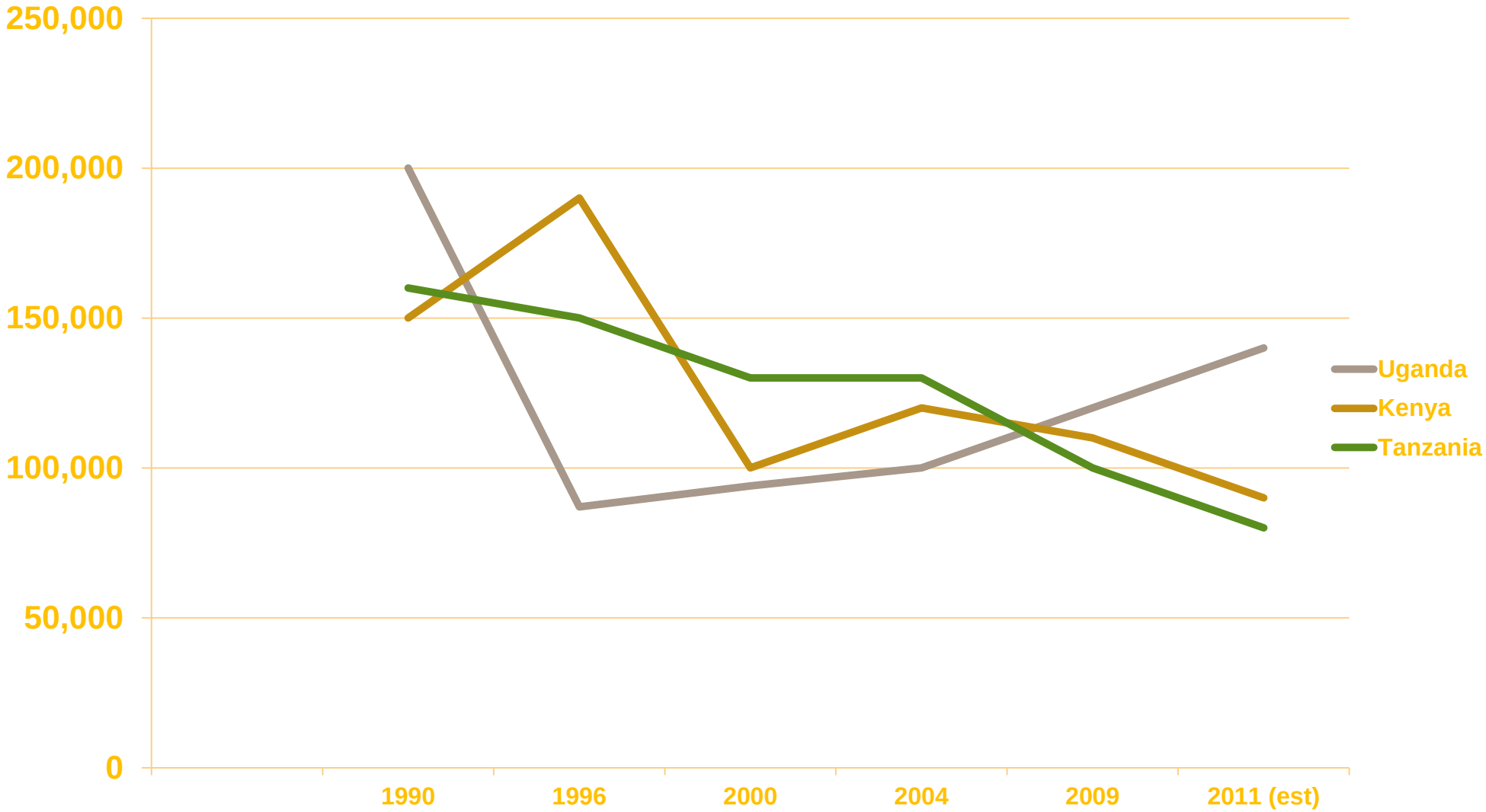


Source: ***UNAIDS (July 2013)***

AFRICOS

Reversal of the epidemic

(Number of New HIV Infections, East Africa, 1990 – 2011)



Source: UNAIDS 2013

AFRICOS

Why prospective cohorts

- Necessary to enable the attainment of robust long term outcome data
- Used to attain longitudinal data to explore and describe a variety of broad objectives
- Facilitate a comprehensive understanding of the epidemic on an individual and programmatic level
- Enhance our understanding of the evolution and pathogenesis of HIV disease, as well as other comorbidities overtime and shape our response

Why prospective cohorts

- Many examples of long-lived western HIV-focused cohorts: Swiss Cohort, Multi-Center AIDS Cohort Study (MACS), Women's Interagency Cohort Study (WHIS). Such studies have described the natural history of the disease and its comorbidities, infectious and noninfectious.
- Few such long lived cohorts exist in Africa
- Many key aspects of HIV disease remain poorly described in the African context
  - will premature cardiovascular disease emerge as a leading comorbidity?
  - Which comorbidities are appropriate for our programmatic focus?
  - Which adherence strategies prevent acquisition of HIV drug resistance in the long run?
  - What is the implication of the apparent evolution of HIV subtypes on treatment outcome?

RV329: African Cohort Study (AFRICOS)

- Prospective observational open cohort focused on global health
- Assess the impact of clinical practices, biological factors and socio-behavioral issues on HIV infection and disease progression in an African context
  - Evaluation tool for MHRP PEPFAR program
  - HIV pathogenesis and impact of comorbidities
  - Measurement of long term outcomes
- Several secondary objectives: Sub-study mechanism to facilitate collaboration

RV329: African Cohort Study (AFRICOS)

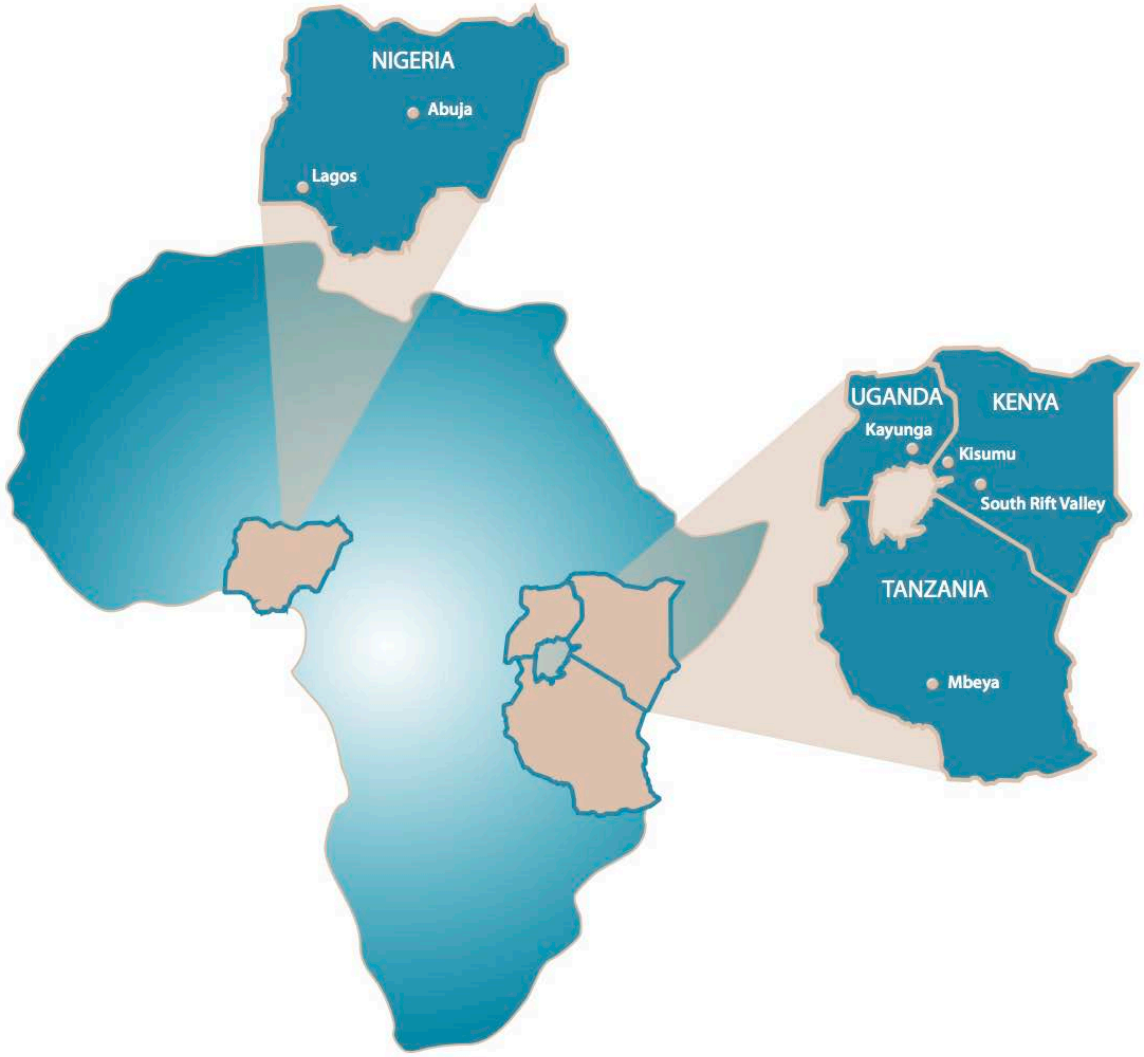
- Secondary objectives grouped under seven domains
  - Social and behavioral
  - HIV prevention and management –programmatic
  - HIV management – subject/clinical outcome
  - Opportunistic infections and other morbidities
  - Maternal-child transmission and management
  - Prevention of horizontal HIV infection
  - Host genetics and pathogenesis

RV 329: African Cohort Study (AFRICOS)

- Enrolling at 11 HIV clinical care and treatment sites across 5 programs in 4 countries:
  - Makerere University – Walter Reed Program, Uganda
    - Kayunga District Hospital
  - KEMRI/Walter Reed Program – Kericho, Kenya
    - District Hospitals: Kericho, Kapkatet, Nandi Hills, Kapsabet
    - Mission Hospitals: AC Litein, Tenwek
  - KEMRI/Walter Reed Program - Kisumu West, Kenya
    - Kisumu West District Hospital
  - Walter Reed Program – Nigeria
    - Defence Headquarters Medical Center, Abuja
    - 68th Nigerian Army Reference Hospital, Lagos
  - Walter Reed Program – Tanzania, Southern Highlands
    - Mbeya Referral Hospital

AFRICOS

AFRICOS Enrollment Sites



RV 329: African Cohort Study (AFRICOS)

- Sample size;
  - 3,000 HIV infected
  - 600 HIV uninfected

Table 1: AFRICOS Sites	Total enrollment target	HIV infected	HIV uninfected
Kenya: South Rift Valley Province	1200	1000	200
Kenya: Kisumu West, Nyanza Province	600	500	100
Uganda: Kayunga and Mukono Districts	600	500	100
Tanzania: Southern Highlands HIV Care Program	600	500	100
Nigeria: Dept of Defense HIV Program	300	250	50
Kenya: Dept of Defense	300	250	50

AFRICOS

Study Procedures

- HIV infected volunteers recruited from HIV clinic lists
  - Existing clients and new referrals
- HIV uninfected volunteers are serodiscordant partners, counselling and testing clients
- Visits: Enrollment, 6 monthly follow up, unscheduled visits for acute illness
- Physical exam, questionnaire, demographic, social, and medical history (including obstetric history)
- HIV outcomes: Clinical staging, CD4+, viral load, GRT
- HIV uninfected volunteers: routine HIV testing
- PBMC, plasma, serum stored at each visit

Study Procedures - Comorbidities

All

- Malaria (Ke, Ug, Nig)
  - Dried blood spot
  - Thin and thick film slides
- Syphilis, HBV, HCV screening
- Cervical cancer screening (VIA +/- Pap)
- Neurocognitive battery
- Functional assessment
- Depression screen

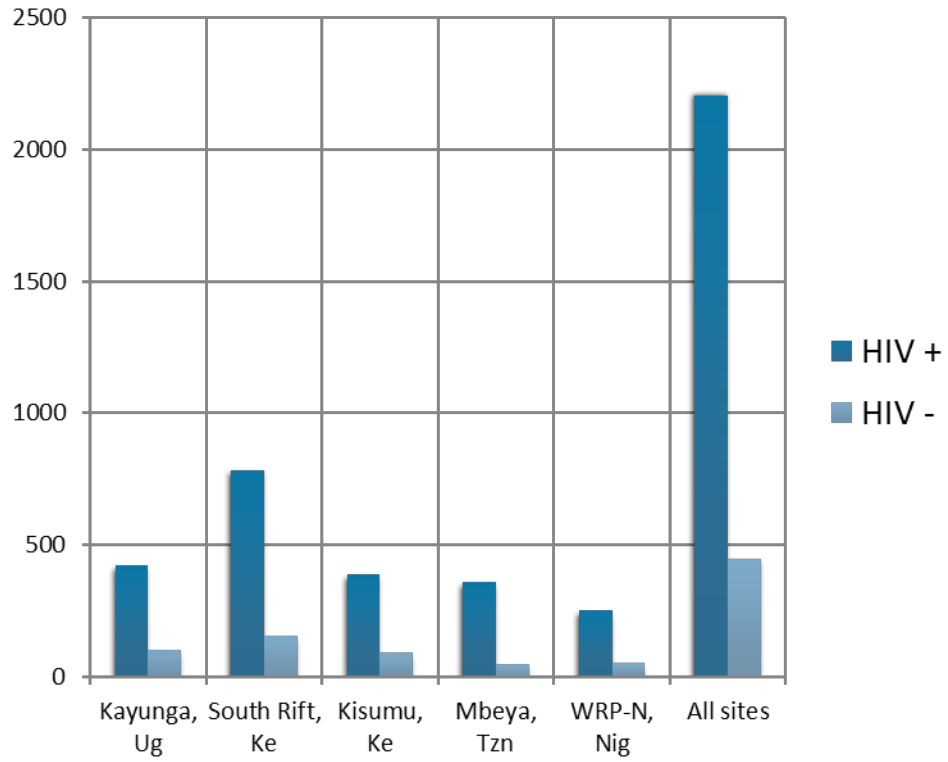
HIV+

- Tuberculosis
  - Sputum for Xpert® MTB/RIF
  - Interferon gamma release assay in ART naïve
- Cryptococcal Ag screening (CD4+ ≤ 200)
- Fasting glucose, lipids

AFRICOS

Enrollment through June 2016

	UG	KSRV	KKW	TZN	NIG	All sites
Total	536	992	480	426	300	2734
HIV+	435	830	388	367	250	2270
HIV-	101	162	92	59	50	464

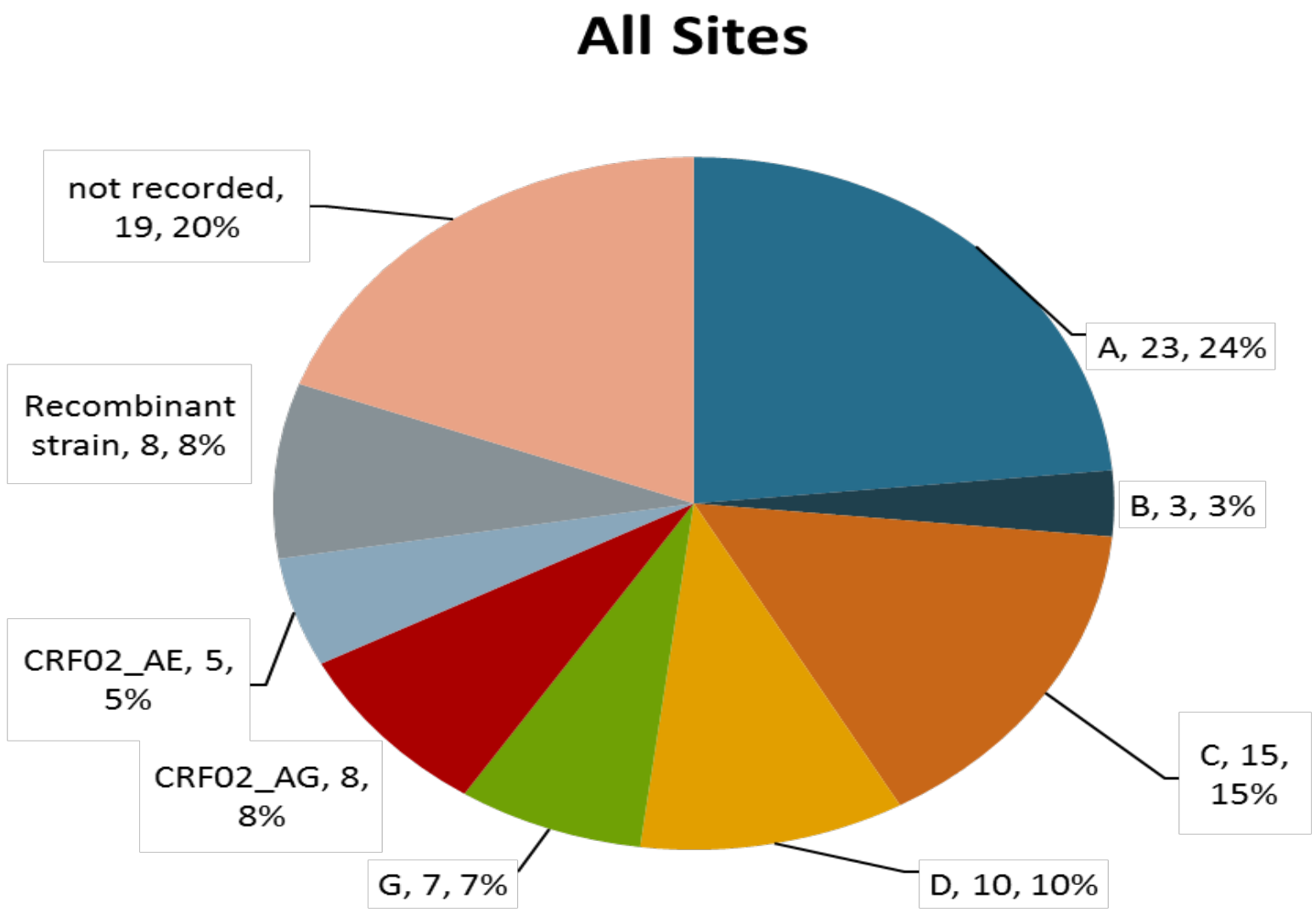


Basic Characteristics:

- Median age: 38.4 y
- 58.3% female
- 56% had only primary or no education
- Median CD4: 384
- 66.1% on ART

AFRICOS

HIV Subtype – All Sites



AFRICOS

Rates of CTX Uptake, ART Uptake, & Viral Suppression by CD_4 Strata at Enrollment Visit, HIV-Infected Participants

	BY CD4 GROUP AT ENROLLMENT VISIT (Color code: Dark Green = 90%+; Light green = 80-89%; yellow = 60-79%; Red = <60%				
CHARACTERISTIC	**CD4 <200 (N= 371)**	**CD4 200-349 (N=483)**	**CD4 350-499 (N=433)**	**CD4 >=500 (N=623)**	**All (N=1920)**
Female - n(%)	190 (51.2%)	229 (47.4%)	257 (59.3%)	452 (72.5%)	1128 (59.0%)
Age - Median (Q1 - Q3)	38.6 (32.5 - 45.7)	39.6 (32.9 - 48.6)	38.8 (32.7 - 45.6)	38.5 (31.4 - 46.8)	39 (32.2 - 46.8)
On CTX - n(%)	316 (85.1%)	420 (86.9%)	353 (81.5%)	513 (82.3%)	1602 (83.8%)
On ART - n(%)	187 (50.4%)	346 (71.6%)	304 (70.2%)	424 (68.0%)	1261 (66.0%)
VL <1000, On ART - n(%)	116 (62.0%)	283 (81.7%)	277 (91.1%)	404 (95.2%)	1080 (85.6%)
VL <50, On ART - n(%)	84 (44.9%)	226 (65.3%)	236 (77.6%)	359 (84.6%)	905 (71.7%)
VL <1000, ALL - n(%)	124 (33.4%)	293 (60.6%)	290 (66.9%)	444 (71.2%)	1151 (60.2%)
VL <50, ALL - n(%)	87 (23.4%)	232 (48.0%)	241 (55.6%)	371 (59.5%)	931 (48.7%)

Data as of: 3/31/2016

AFRICOS

Rates of CTX Uptake, ART Uptake, & Viral Suppression by CD_4 Strata at Most Recent Visit, HIV-Infected Participants

	BY CD4 GROUP AT ENROLLMENT VISIT (Color code: Dark Green = 90%+; Light green = 80-89%; yellow = 60-79%; Red = <60%				
CHARACTERISTIC	**CD4 <200 (N= 371)**	**CD4 200-349 (N=483)**	**CD4 350-499 (N=433)**	**CD4 >=500 (N=623)**	**All (N=1920)**
Female - n(%)	112 (46.4%)	198 (50.3%)	252 (59.8%)	465 (69.8%)	1027 (59.6%)
Age - Median (Q1 - Q3)	39.4 (32.5 - 46.7)	40.7 (33.6 - 49.8)	40.5 (33.5 - 46.9)	39.3 (32 - 46.7)	39.9 (32.9 - 47.5)
On CTX - n(%)	207 (85.8%)	347 (88.3%)	343 (81.4%)	546 (81.9%)	1443 (83.8%)
On ART - n(%)	180 (74.6%)	338 (86.0%)	365 (86.7%)	561 (84.2%)	1444 (83.9%)
VL <1000, On ART - n(%)	116 (64.4%)	295 (87.2%)	331 (90.6%)	536 (95.5%)	1278 (88.5%)
VL <50, On ART - n(%)	89 (49.4%)	257 (76.0%)	290 (79.4%)	473 (84.3%)	1109 (76.8%)
VL <1000, ALL - n(%)	117 (48.5%)	307 (78.1%)	340 (80.7%)	567 (85.1%)	1331 (77.3%)
VL <50, ALL - n(%)	90 (37.3%)	265 (67.4%)	295 (70.0%)	488 (73.2%)	1138 (66.1%)

Data as of: 3/31/2016

AFRICOS

Rates of CTX Uptake, ART Uptake, & Viral Suppression by Age Strata at Enrollment Visit, HIV-Infected Participants

	BY AGE AT ENROLLMENT VISIT (Color code: Dark Green = 90%+; Light green = 80-89%; yellow = 60-79%; Red = <60%**)**				
	Age 18-19 (N=28)	**Age 20-24 (N=116)**	**Age 25-49 (N=1474)**	**Age 50+ (N=335)**	**All (N=1953)**
Female - n(%)	20 (71.4%)	87 (75.0%)	900 (61.0%)	148 (44.1%)	1155 (59.1%)
On CTX - n(%)*	21 (75.0%)	86 (74.1%)	1245 (84.4%)	283 (84.4%)	1635 (83.7%)
On ART - n(%)*	19 (67.8%)	60 (51.7%)	947 (64.2%)	271 (80.9%)	1297 (66.4%)
VL <1000, On ART - n(%)*	13 (68.4%)	44 (73.3%)	808 (85.3%)	244 (90.0%)	1109 (85.5%)
VL <50, On ART - n(%)*	9 (47.3%)	35 (58.3%)	676 (71.3%)	209 (77.1%)	929 (71.6%)
VL <1000, ALL - n(%)*	13 (46.4%)	49 (42.2%)	864 (58.6%)	255 (76.1%)	1181 (60.4%)
VL <50, ALL - n(%)*	9 (32.1%)	36 (31.0%)	694 (47.0%)	216 (64.4%)	955 (48.9%)

**** Statistically significant difference (p < 0.05)***

Data as of: 3/31/2016

AFRICOS

Rates of CTX Uptake, ART Uptake, & Viral Suppression by Age Strata at Most Recent Visit, HIV-Infected Participants

	BY AGE AT MOST RECENT VISIT (Color code: Dark Green = 90%+; Light green = 80-89%; yellow = 60-79%; Red = <60%)				
CHARACTERISTIC	**Age 18-19 (N=14)**	**Age 20-24 (N=105)**	**Age 25-49 (N=1348)**	**Age 50+ (N=353)**	**All (N=1820)**
Female - n(%)	9 (64.2%)	79 (75.2%)	839 (62.2%)	157 (44.4%)	1084 (59.5%)
On CTX - n(%)*	11 (78.5%)	73 (69.5%)	1129 (83.7%)	302 (85.5%)	1515 (83.2%)
On ART - n(%)*	8 (57.1%)	78 (74.2%)	1131 (83.9%)	314 (88.9%)	1531 (84.1%)
VL <1000, On ART - n(%)*	4 (50.0%)	60 (76.9%)	1005 (88.8%)	285 (90.7%)	1354 (88.4%)
VL <50, On ART - n(%)*	3 (37.5%)	47 (60.2%)	869 (76.8%)	255 (81.2%)	1174 (76.6%)
VL <1000, ALL - n(%)*	4 (28.5%)	64 (60.9%)	1042 (77.3%)	299 (84.7%)	1409 (77.4%)
VL <50, ALL - n(%)*	3 (21.4%)	48 (45.7%)	889 (65.9%)	264 (74.7%)	1204 (66.1%)

**** Statistically significant difference (p < 0.05)***

Data as of: 3/31/2016

AFRICOS

CD4 at ART initiation vs Timing*

Timing of ART initiation	Stat	Kayunga, Ug (n=162)	SRV, Ke (n=313)	KSM, Ke (n=102)	Mbeya, Tz (n=102)	Abuja, Nig (n=106)	Total (n=785)
All times	Median (range)	293 (157-398)	160 (67-269)	219 (112-285)	174 (64-242)	199 (107-314)	195 (87-307)
Those starting ART *before 2011*	Median (range)	154 127(79-207)	91 (37-185)	179 (97-238)	71 (6-174)	146 (85-198)	114 (51-195)
Those starting ART *after 2011*	Median (range)	309 (199-407)	196 (95-322)	243 (162-343)	183 (79-259)	262 (138-358)	238 (112-350)

*only for HIV treatment indication (vs. PMTCT, PEP)

AFRICOS

Most frequently prescribed regimens

Characteristic	Kayunga, Ug (n=277)	SRV, Ke (n=590)	KSM, Ke (n=264)	Mbeya,Tz (n=215)	Abuja,Ng (n=188)	Total (n=1534)
First line regimens						
NVP-based	78(28.2)	171(29.0)	194(73.5)	8(3.7)	59(31.4)	510(33.3)
EFV-based	192(69.3)	359(60.9)	68(24.8)	45(20.9)	114(60.6)	778(50.7)
TDF based	172(62.1)	385(65.3)	131(49.6)	0(0.0)	116(61.7)	804(52.4)
AZT-based	105(37.9)	187(31.7)	45(17.1)	0(0.0)	61(32.5)	398(26.0)

AFRICOS

HIV – Hepatitis Co-infection

HEP B	Stat	Kayunga UG (n=458)	SRV KE (n=708)	KSM, KE (n=316)	Mbeya, TZ (n=261)	Abuja, NIG (n=242)	Total (n=1985)
All HIV+, +Hep B SAg	N	36(7.9)	11(1.6)	3(1.0)	15(5.8)	29(12.0)	94(4.7)
- On ART	N	19(4.2)	5(0.7)	2(0.6)	9(3.5)	23(9.5)	58(2.9)
- Not on ART	N	10(2.2)	0(0.0)	1(0.3)	3(1.2)	5(2.1)	19(1.0)

Potential areas of collaborative research

Sub-study mechanisms exists to facilitate collaboration between internal and external investigators

This research has been supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) through the U.S. Department of Defense. The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army or the Department of Defense.

Areas for possible collaborative research

- **HIV management domain**
  - Utility of alternative field expedient HIV diagnostic, viral load and lymphocyte measurement testing platforms to gold standard assays
  - HIV disease outcomes, including, but not limited to, mortality, progression to AIDS, event-free survival, and prevalence/incidence of HIV related sequelae
  - HIV treatment monitoring practices and impact on disease outcomes
  - Frequency and amplitude of transient viremia (viral load “blips”) and relation to disease outcomes
  - Frequency and character of HIV resistance mutations and impact on disease outcomes
  - Frequency and character of HIV resistance mutations as associated with viral subtype and prior exposure to anti-retrovirals

AFRICOS

Areas for possible collaborative research

- Opportunistic infections and other morbidities
  - Endemic infections and evaluate their interplay with HIV disease
    - Tuberculosis
      - Incidence of active TB and rifampicin resistance
      - Predictive value of a positive interferon gamma release assay in HIV

      Human papillomavirus and other STIs
      - Effectiveness of cervical cancer screening strategies in national ART programs (visual inspection with acetic acid, histopathology based screening (PAP smear, qualitative rapid HPV tests)
    - Viral hepatitis
      - Hepatitis B, hepatitis C
    - Malaria
    - Stools pathogens

Areas for possible collaborative research

- Host genetics and pathogenesis
  - HLA and other key host genetic markers known to associate with HIV disease acquisition, progression or response to therapy
  - Studies on immunologic and viral factors which are associated with HIV acquisition, disease progression, or response to therapy
  - Markers of systemic inflammation and immune activation as they relate to HIV disease and its progression

AFRICOS

Areas for possible collaborative research

- **Social and behavioral domain**
  - Qualitative and quantitative studies on stigmatizing events and social and economic harms attendant to HIV care and treatment;
  - Studies on the cultural barriers and facilitators of HIV prevention, care and treatment
  - Studies on the impact of behavioral treatment strategies (status disclosure, treatment partners and support groups) on HIV clinical outcomes
  - Substance use and HIV infection and disease outcomes
  - Impact of incarceration and/or institutionalization on HIV treatment and outcomes

Acknowledgements

MHRP

Clinical Research Directorate:
Christina Polyak
Trevor Crowell
Leigh Anne Eller
Deline Glover
Ajay Parikh
Kavitha Ganesan
Gail Smith

Global Health Program:
Peter Coakley
Tiffany Hamm
Lindsay Hughes
Ali Taylor

HDRL:
Sheila Peel
Jennifer Malia
Brook Postek

DCAC:
Heather Liu
Cindy Zhang
Rory Deshano
Ying Fan
Michelle Liu

MHRP Leadership:
Nelson Michael
Merlin Robb

Activation substudy: Mike Eller

AFRICOS Uganda
Hannah Kibuuka
Francis Kiweewa
Fatim Jallow

AFRICOS Kenya

South Rift Valley:
Jonah Maswai
Raphael Langat
Rither Langat

Kisumu West:
John Owouth
Solomon Otieno
Jew Ochola

USAMRU-K Malaria substudy:
Jessica Cowden
Edwin Kamau

AFRICOS Tanzania
Lucas Maganga
Samoel Khamadi
Emmanuel Bahemana

AFRICOS Nigeria
Babajide Keshinro
Senate Amusu

UCSF
Victor Valcour
Kyra Hansson

University of Munich
Michael Hoelscher
Arne Kroidl
Christof Geldmacher
Inge Kroidl