How can the IeDEA platform contribute to global efforts on cancer surveillance?

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Cancer and the Health of Populations

- **As much as any other disease/discipline, cancer epidemiology has been a leader in *surveillance in populations***
  - Population-based death from cancer: 1830's (UK)
  - Population-based occurrence of cancer: 1926 (Germany)

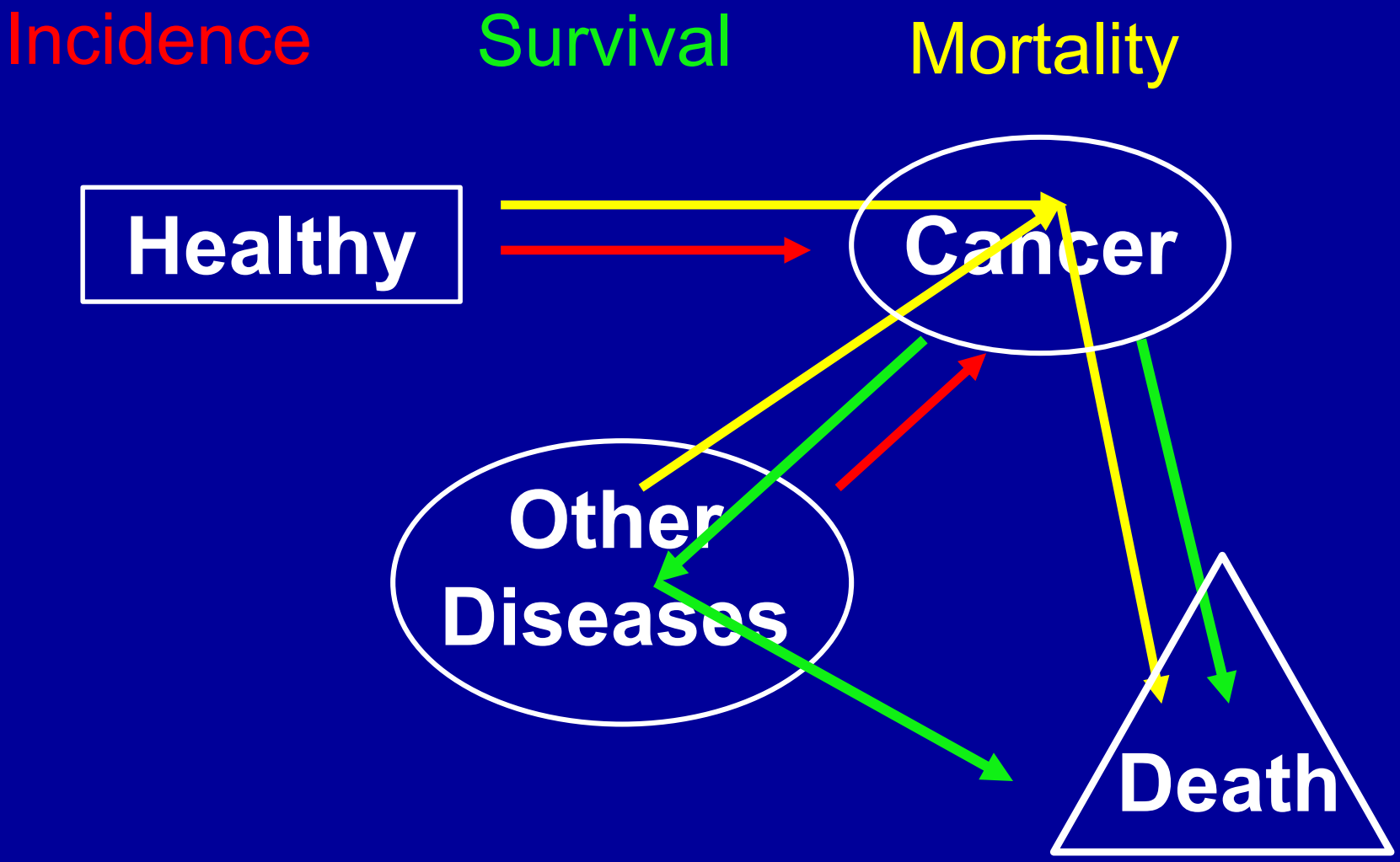
- **Cancer epidemiologists have been leaders in clarifying and estimating indicators of burden of a given cancer in populations**
  - Incidence
  - Survival
  - Mortality

3 Indicators of Population-based Cancer Surveillance

	Incidence	Survival	Mortality
Definition	Occurrence of new cancer diagnoses among everyone in the population	Death after diagnosis of cancer among those with cancer	Death from a particular cancer among everyone in the population
Relevance	• Burden of cancer • Etiologic research	• Clinical impact of cancer among those with the cancer • Monitoring population effects of therapy	• "Integrates" incidence and survival • Overall population-level importance of cancer

All 3 are dynamic and must be followed over time

Relationship between Incidence, Survival, and Mortality



Measurement: Incidence

$$\text{Incidence} = \frac{\text{New cases of cancer}}{\text{Person-time at risk}}$$

New cases of cancer

Pathologic confirmation	Virtually all cases	Variable; clinical only
Source of data	"Registries" via pathology labs	Unclear ascertainment; likely substantial underascertainment for most cancers
Screening for early dx	Common	Rare

Person-time at risk

Source of data	Well funded frequent large area census	True denominator that might be counted if cancer occurred may be underestimated (↑ inc.)

Measurement: Survival

$$\text{Survival} = 1 - \frac{\text{Deaths (any cause) at a given point in time after diagnosis}}{\text{No. of cancer cases newly diagnosed}}$$

Death from any cause

Source of data	Registry-performed individual-level ascertainment	Lack of resou… prohibit re… pe…
Linkage to death registries	Common	

Stymied by high loss to follow-up from clinical care sites

No. of new cancer cases

Source of data	Complete capture of cases in large geographic area	Collection of cases of unclear representativeness

Measurement: Mortality

$$\text{Mortality} = \frac{\text{Deaths attributed to specific cancer}}{\text{Person-time at risk}}$$

Death from cancer

Source of data — Death Registries — De

Only 1 available (South Africa)

Person-time at risk

Source of data — Well funded frequent large area census — Census, but effective "catchment" area unclear because of uneven access to care

Scorecard in Sub-Saharan Africa

	Incidence	Survival	Mortality
No. of countries with potential viable data	4 regional (Malawi, South Africa, Uganda, and Zimbabwe)	3 regional (Gambia, Uganda, Zimbabwe)	1 national (South Africa)
Certified by	Cancer Incidence in 5 Continents (CI5 - IARC)	Cancer survival in Africa, Asia, the Caribbean and Central America (SurvCan - IARC)	Estimated cancer incidence, mortality, and prevalance worldwide (GLOBOCAN - IARC)
Limitations	• ? complete case ascertainment • ? denominator • ? representativeness	• nothing since 1999 • still large % LTFU despite attempts at active tracing	• Complete deaths but "low quality data" (Mathers 2005)

Research

The Royal Society of Medicine

of Medicine; 2015, Vol. 108(2) 57–67
DOI: 10.1177/0141076814554671

This is a resources problem

Appraising the quality of sub-Saharan African cancer registration systems that contributed to GLOBOCAN 2008: a rev praisal

Could IeDEA contribute to the solution to the problems of cancer surveillance in sub-Saharan Africa?

Tim Crocker-Buq
Centre for Primary Car
Corresponding autho

tes are based on
stration systems,
erage. It is essen-
tial the GLOBOCAN 2012 estimates should provide information on the quality of the data collection and explain the limitations of the estimates. Development organisations and the World Health Organization need to take a more cautious approach when using these data to determine priorities and allocating resources.

Advantages of IeDEA for Studying Cancer Surveillance in Resource-Limited Settings

- **IeDEA provides enormous size (10,000's of patients), enumeration, and built-in follow-up (done via the clinical care system)**
  - We are not guessing at the denominator
  - Instead, we have our hands on it

- **If the cancer diagnoses are made, IeDEA provides opportunity for community-based complete ascertainment**
  - By definition allowing for representativeness

Cancer Incidence in IeDEA: Example of KS

$$\text{Incidence} = \frac{\text{New cases of KS}}{\text{Person-time at risk}}$$

- **Historically, diagnosis made mostly on clinical visual grounds (replete with error)**
- **Skin punch biopsy introduced at 3 HIV primary care sites in Uganda & Kenya in East Africa IeDEA**

Laker-Oketta et al. *Oncology* 2015

- **3 HIV primary care sites in East Africa IeDEA**
  - 140,552 HIV-infected adults
  - 319,632 person-years
  - enumerated in electronic medical record systems (OpenMRS)

Semeere et al. *Cancer Medicine* 2016

Incidence of KS in East Africa IeDEA

Incidence =

$$\frac{\text{New cases of KS}}{\text{Person-time at risk among HIV-infected individuals}}$$

Overall incidence:

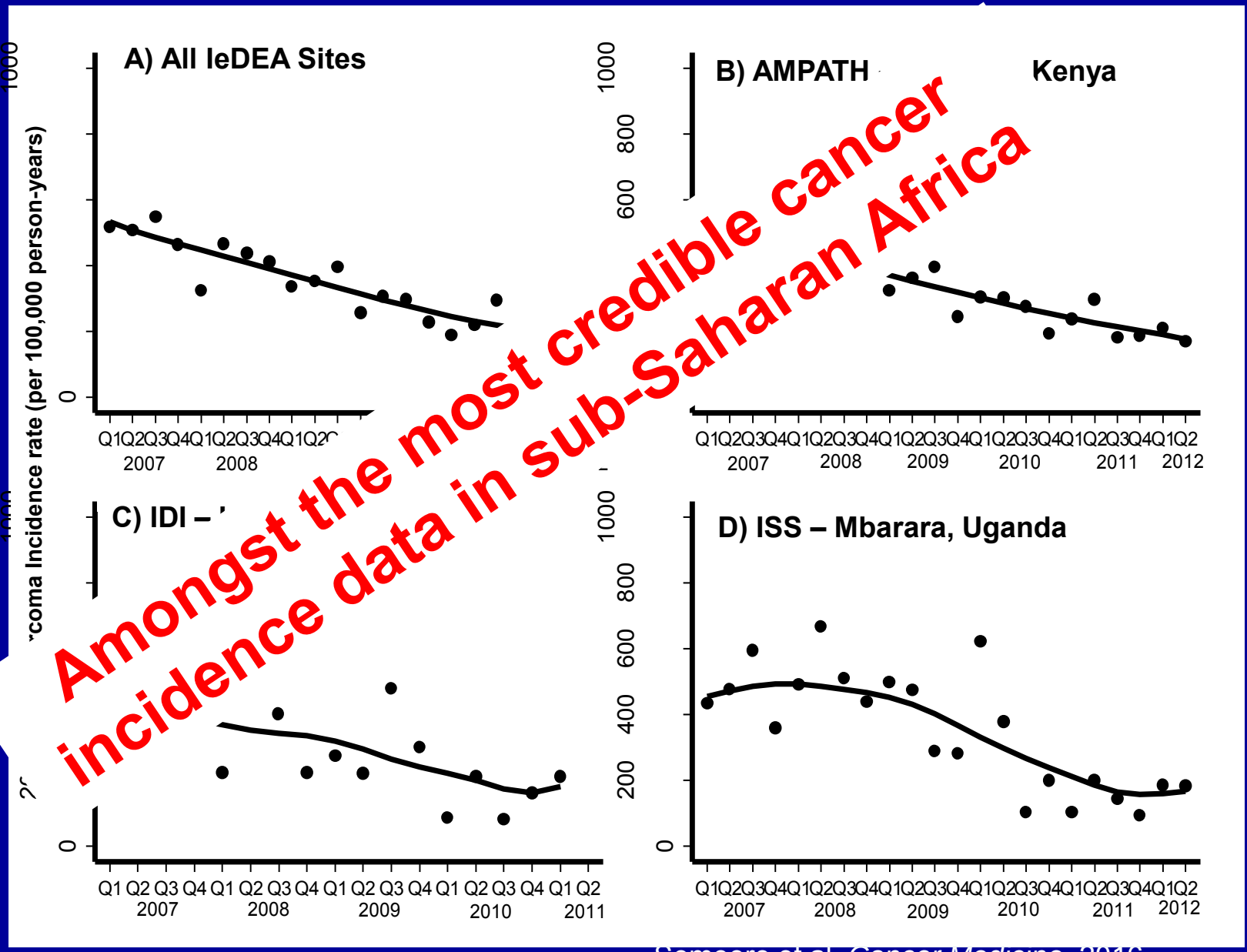
321/100,000 person-years

(95% CI: 302 to 341)

cf:

Prostate cancer (most common in US)

140/100,000 person-years



Amongst the most credible cancer incidence data in sub-Saharan Africa

Semeere et al. *Cancer Medicine* 2016

Advantages of IeDEA for Studying Cancer Surveillance in Resource-Limited Settings

$$\text{Survival} = 1 - \frac{\text{Death (any cause) at a given point in time after diagnosis}}{\text{New cases of cancer}}$$

- **If the cancer diagnoses are made, IeDEA provides opportunity for community-based complete ascertainment**
  - By definition allowing for representativeness
- **Complete ascertainment of all-cause mortality is feasible in IeDEA**
  - (although cause-specific mortality is not)

Cancer Survival in IeDEA: Example of KS

- Tracking the lost in the community by phone & by land ("shoe leather")

$$\text{Survival} = 1 - \frac{\text{Deaths after Dx}}{\text{New cases of KS}}$$

	Number
No. with KS	1222
No. apparently lost to follow-up	440
Vital status updated	349 (79%)

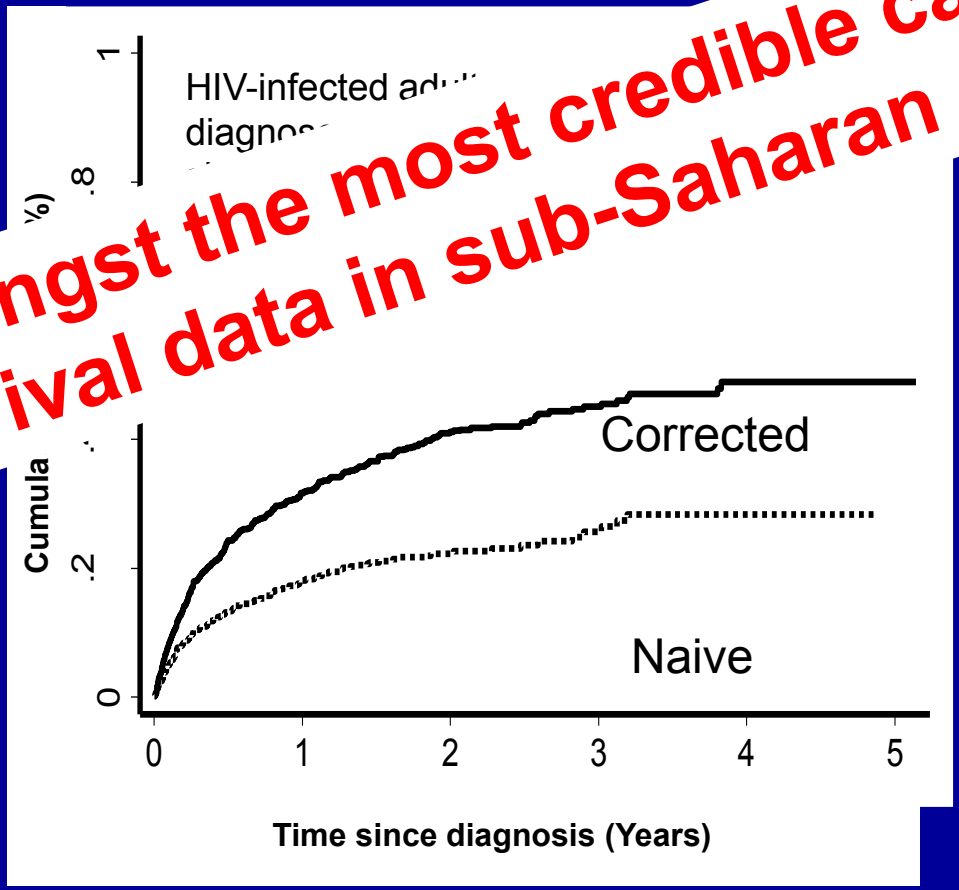
- 1222 cases of KS newly diagnosed during course of primary care (representative community-based ascertainment) at 5 IeDEA sites in West, East, and S. Africa

Freeman et al. ICMAOI 2015; Semeere et al. AORTIC 2015

Cancer Survival in IeDEA: Example of KS

- After updating vital status among the lost, corrected o[illegible]mes much worse than naïve estimate.

Amongst the most credible cancer survival data in sub-Saharan Africa



Semeere et al.
ICMAOI and AORTIC 2015

Advantages of IeDEA for Studying Cancer Surveillance in Resource-Limited Settings

$$\text{Mortality} = \frac{\text{Death attributed to specific cancer}}{\text{Person-time at risk}}$$

- **IeDEA provides enormous size (10,000's of patients), enumeration, and built-in follow-up (done via the clinical care system)**
  - We are not guessing at the denominator
  - Instead, we have our hands on it

- **Problem: IeDEA does not have cause-specific mortality and will not have it in foreseeable future**
  - May be overcome by estimating net survival and some math

Could it work for cancers other than KS?
The key is a systematic process for diagnosis

Cancer	Need
Cervical	Screening Colposcopy Biopsy/Pathology
Breast	Mammography Biopsy/Pathology
Liver	AFP, Ultrasound Biopsy/Pathology
Colon	Screening Colonoscopy Biopsy/Pathology

What if we did no extra work to improve cancer diagnosis but we asked patients about cancer dx & adjudicated answers?

$$\text{Incidence} = \frac{\text{New cases of cancer}}{\text{Person-time at risk}}$$

- Counting the same diagnoses that the registries count
- Seems to be equally (in)accurate as registry approaches
  - Exception: diagnoses never told to patients
- Individual-level enumeration seems more accurate than registry approaches which rely upon national census and unclear catchment

Bottomline: No worse than registries and, because of unambiguous denominator, probably better

A health care system-based, rather than a geographic population-based, approach to cancer surveillance

- **This is fine for inference regarding HIV-infected persons but what is the relevance to the general population?**

1. **To the extent HIV is not causally related to a cancer and HIV-infected persons are representative of the general population**
   - Incidence of cancer in HIV-infected persons should be same as HIV-uninfected and thus relevant

2. **Serves as a model for other emerging health care systems, predominantly serving HIV-uninfected populations**
   - EMRs in health care systems, spurred by HIV care, may likely emerge before accurate cancer registries & geographic censuses

Is this a new I(e)dea?

NIAID RFA AI-05-014 (later supported by NCI)

"… overall objectives … to establish regional data centers for the **compilation of data** to address research questions that are not possible to answer with currently-existing individual cohorts…"

- **But it will take work**
- **We cannot be passive and rely solely upon the typical IeDEA data that is coming via routine clinical care**
- **We need to perform additional measurements/processes and incorporate these into the rich IeDEA epidemiologic framework**

Investigation of Cancer in IeDEA:

Ask not what IeDEA can do for you

Ask what you can do for IeDEA

Modified from U.S. President
John F. Kennedy, 1961

Summary

- **Incidence, survival and mortality are the key indicators of cancer surveillance in any setting**

In sub-Saharan Africa

- **IeDEA, via enumeration of health care system-based populations, can contribute to *if not outdo* geographic registry approaches**

- **At a minimum, systematic questioning of patients for self-reported cancer diagnoses followed by adjudication (= registries)**

- **Better yet: Like the example of KS, establish focused screening and diagnostic processes for "easy to access" cancers**
  - cervical, breast, liver etc.
  - enhances surveillance, research, and clinical care

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- Principal Investigator: Edward Mbidde
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Uganda Cancer Institute

- Jackson Orem & Victoria Walusansa

Makerere University

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Mbarara University

- Mwebesa Bwana & Michael Kanyesigye

Moi University

- Naftali Busakhala, Nathan Buziba, Chite F. Asirwa, and Elyne Rotich

Funding

National Hospital of Abuja

- Kenneth Iregbu

Institute of Human Virology (Nigeria)

- Elima Jedy-Agba & Emmanuel Oga

Lighthouse Trust Clinic

- Sam Phiri

University of Abuja Teaching Hospital

- Vivian Kwaghe

R4D International (Cameroon)

- Habakkuk Azinyui Yumo

University of Bern

- Julia Bohlius & Matthias Egger

INSERM U897 & ISPED, Université Bordeaux

- Francois Dabis & Antoine Jaquet

Regional Alliance for Sustainable Dev. (Rwanda)

- Jean Claude Dusingize

Harvard University

- Esther Freeman

Albert Einstein College of Medicine

- Kathryn Anastos

CDC

- Sheila Dollard

Indiana University

- Bev Musick, Kara Wools-Kaloustian, & Constantin Yiannoutsos

UCSF

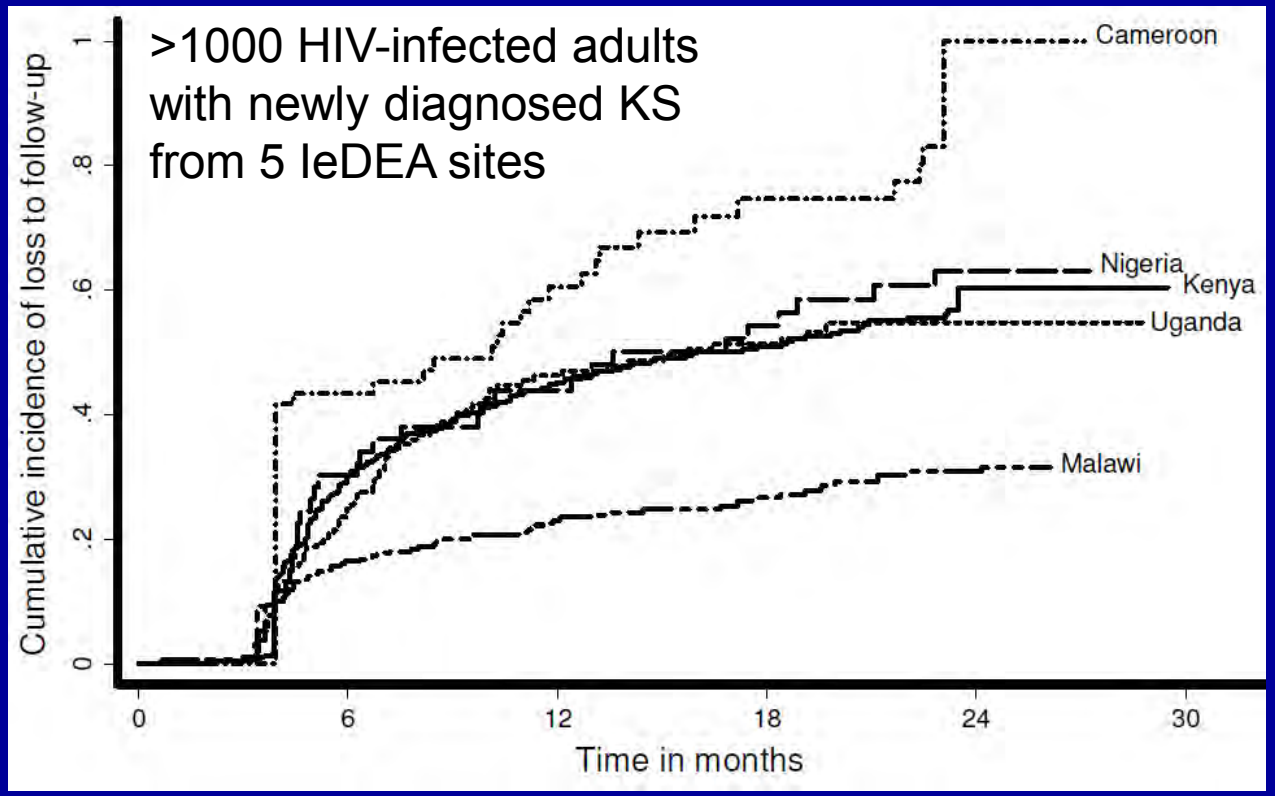
- Donald Abrams, Erin Amerson, Stephen Asiimwe, John Bennett, Lisa Butler, Dana Clutter, Steven Deeks, Debbie Garcia, David Glidden, Warner Greene, Janet Ho, Peter Hunt, David Janka, Melissa Kanchanapoomi, Toby Maurer, Mike McGrath, A. Rain Mocello, Abigail Phillips, Paul Volberding, Megan Wenger, and John Ziegler

Cancer Survival in IeDEA: Example of KS

- **>1000 HIV-infected adults with KS newly diagnosed during course of primary care (representative community-based ascertainment)**
  - 5 IeDEA sites in West, East, Central and Southern Africa

Challenge

- **Enormous incidence of loss to follow-up from routine clinical care**
- **If we did nothing else, precludes any accurate estimate of survival**



Freeman et al. BMC Cancer In press

Advantages of IeDEA for Studying Cancer in Resource-Limited Settings

NIAID RFA AI-05-014 (later supported by NCI)

"… overall objectives … to establish regional data centers for the compilation of data to address research questions in HIV/AIDS that are not possible to answer with currently-existing individual cohorts…"

- **Enormous size (10,000's of patients) and follow-up (done via the clinical care system) of IeDEA potentially facilitates holy grail in cancer epidemiology:**
  - *prospective longitudinal analysis*

- **Community-based cancer diagnosis allows for representativeness not seen in many pathology/hospital-based registries**

Semeere et al.
Cancer Medicine 2016

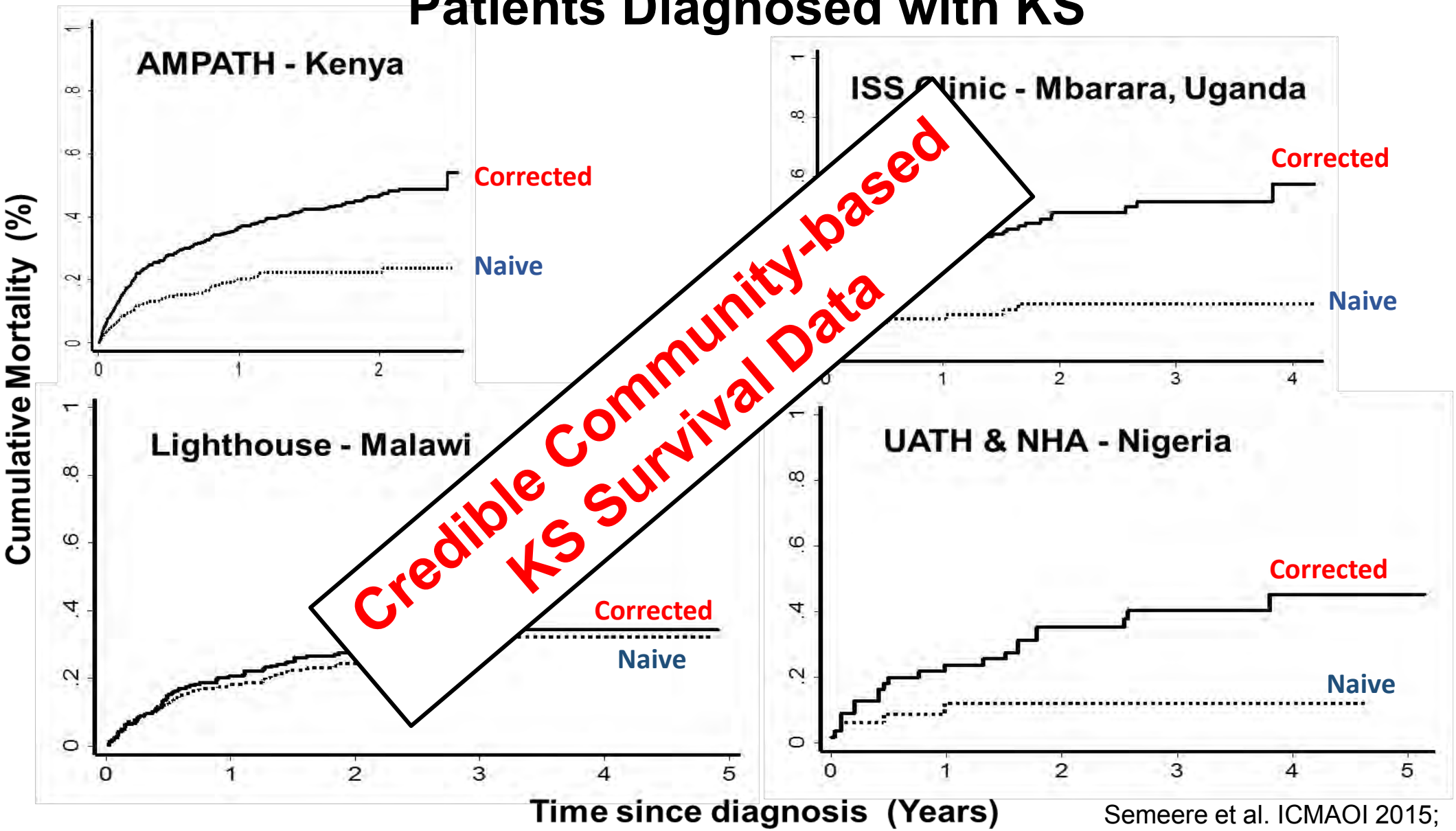
Incidence of KS in East Africa IeDEA

Table 3. Incidence rate of Kaposi sarcoma amongst HIV-infected adults at three health care systems in East Africa.

Group	All Patients			Non-ART Users			ART Users			F	RT Users	
	Female n=94,334	Male n=46,218	Overall n=140,552	Female n=84,552	Male n=43,039	Overall n=127,591	Female n=66,470	Male n=31,440	Overall n=97,910		ale 839	Overall n=75,122
Age, Years												
18-19	479* (249,920)	921 (230,3681)	524 (290,947)	877 (418,1840)	1300 (183,9229)	914 (457,1828)	185 (46,739)	713 (100,5100)				268 (86,829)
20-24	248 (190,323)	1080 (746,1565)	336 (271,417)	340 (231,499)	476 (214,1059)	359 (254,508)	198 (137,287)	1700 (1100.[illegible]			,2986)	356 (261,485)
25-29	233 (190,286)	789 (622,1001)	333 (285,388)	206 (139,305)	939 (660,1335)	363 (279,471)	245 (193,312)				945 (675,1323)	397 (321,491)
30-34	239 (198,288)	711 (590,856)	358 (314,409)	214 (147,312)	1025 (777,1353)	440 (352,550)	248 (20[illegible]			9 ,251,406)	731 (557,960)	424 (354,508)
55-59	269 (160,455)	391 (246,620)	326 (231,462)	435 (195,969)	795 (398,1590)	587 (348,99[illegible]			,385)	230 (96,553)	395 (198,791)	310 (180,533)
60-64	90 (22,359)	456 (245,847)	271 (154,478)	168 (24,1190)	854 (321, 2276)	[illegible]			209 (99,437)	112 (16,793)	637 (286,1418)	381 (182,799)
Age-standardized rates												
New WHO §	249 (227,271)	602 (550,654)	334 (314,354)	347 (295,400)	7[illegible] (6[illegible]			579 (516,642)	270 (249,291)	255 (224,286)	725 (638,812)	340 (311,369)
Old WHO †	254 (232,276)	616 (563,669)	340 (319,361)	361 (306,4[illegible]			4 ,1,237)	593 (528, 658)	271 (250,292)	254 (223,285)	741 (652,830)	341 (312,370)
CD4+ T-cell cells/mm^3 **												
0-50	1392 (749,2587)	1938 (1073,3500)	1633 (1065, 2[illegible]			,3069)	1400 (530,3800)	1300 (416,4000)	1357 (647,2847)	1696 (547,5260)	1304 (326,5213)	1500 (630,3600)
51-100	728 (347,1526)	494 (185,1316)				1357 (706,2607)	172 (24,1200)	190 (27,1300)	180 (45,721)	0¶ (0, 946)	0¶ (0,1025)	0¶ (0,492)
101-200	181 (86,380)	33[illegible] (1[illegible]			754 (314,1811)	391 (186,820)	183 (76,439)	215 (89,516)	197 (106,367)	108 (27,433)	340 (141,816)	211 (101,442)
201-350	125 (73,216)			,376)	940 (557,1587)	406 (259,636)	111 (56,223)	129 (58,286)	118 (70,200)	156 (74,327)	192 (80,462)	169 (96,298)
351-500	74 (35,155)	(12,	[illegible]	135 (51,359)	164 (41,655)	143 (64,319)	46 (15,144)	0¶ (0, 125)	32 (10,99)	81 (26,253)	0¶ (0, 246)	58 (19,179)
>350	66 (39,112)	80 (36,179,	70 (45,109)	141 (76,263)	161 (60,428)	146 (87,247)	29 (11,76)	40 (10,161)	32 (14,70)	40 (13,125)	43 (6.0,302)	41 (15,109)
>500	60 (29,126)	121 (46,323)	74 (41,133)	146 (66,325)	158 (39,630)	149 (74,298)	13 (1.9,95)	99 (25,394)	31 (10,98)	0¶ (0,98)	118 (17,834)	22 (3.1,154)
All Patients	229 (210,250)	526 (483,574)	321 (302,341)	267 (230,311)	762 (663,877)	411 (371,455)	213 (192, 237)	443 (398,494)	286 (265,309)	283 (251,319)	645 (573,728)	394 (362,429)

Amongst the most credible cancer incidence data in sub-Saharan Africa

Naïve and Corrected Estimates of Survival Among Patients Diagnosed with KS



Semeere et al. ICMAOI 2015; AORTIC 2015

Survival after KS Diagnosis: Challenges

- **Population-based registries with data on KS survival (IARC SurvCan)**
  - N = 2 (Uganda and Zimbabwe)
  - 1993-97; not relevant in ART era
  - Pathology/hospitalization-based identification of KS cases makes representativeness very unclear