IeDEA

International epidemiologic Databases to Evaluate AIDS

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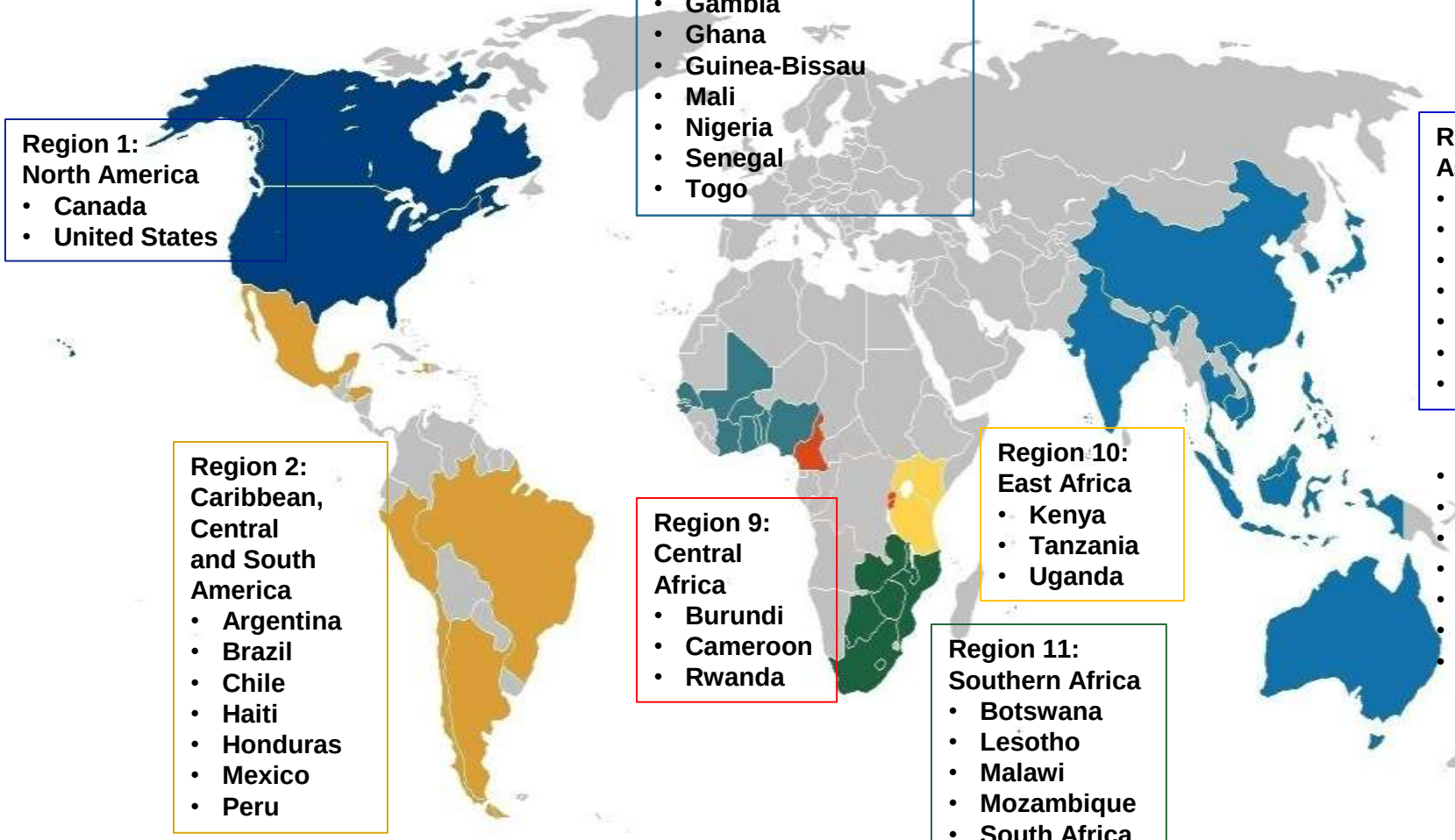


Region 1:
North America
- Canada
- United States

Region 2:
Caribbean, Central and South America
- Argentina
- Brazil
- Chile
- Haiti
- Honduras
- Mexico
- Peru

Region 8:
West Africa
- Benin
- Burkina Faso
- Côte d'Ivoire
- Gambia
- Ghana
- Guinea-Bissau
- Mali
- Nigeria
- Senegal
- Togo

Region 9:
Central Africa
- Burundi
- Cameroon
- Rwanda

Region 10:
East Africa
- Kenya
- Tanzania
- Uganda

Region 11:
Southern Africa
- Botswana
- Lesotho
- Malawi
- Mozambique
- South Africa
- Zambia
- Zimbabwe

Region 5:
Asia and Australia
- Australia
- Cambodia
- China
- Hong Kong SAR
- India
- Indonesia
- Japan
- Malaysia
- Philippines
- Singapore
- South Korea
- Taiwan
- Thailand
- Vietnam

Global
Executive Committee
Chair (2 yr term)
PIs each region
Program Staff

7
IeDEA Regions

WGs

Data

Sites

Analytics

Strategic
Data
Working
group

Distributed to regions

publications

concepts

website

Coordination & Communication

meetings

Data harmonization

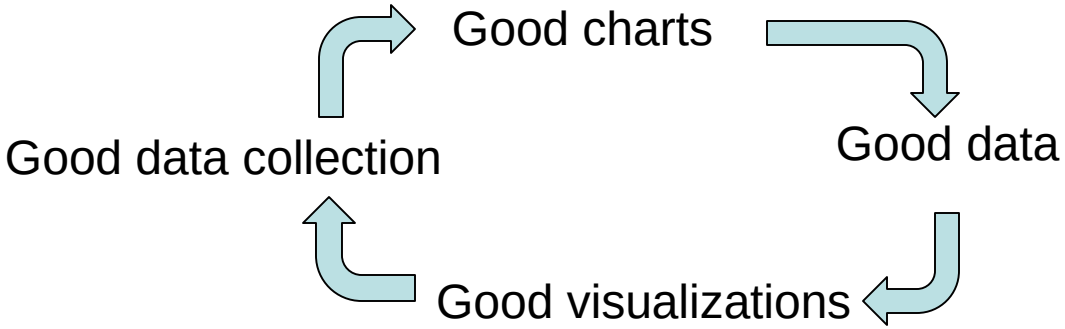
BD2K

Harmonist

Working Groups

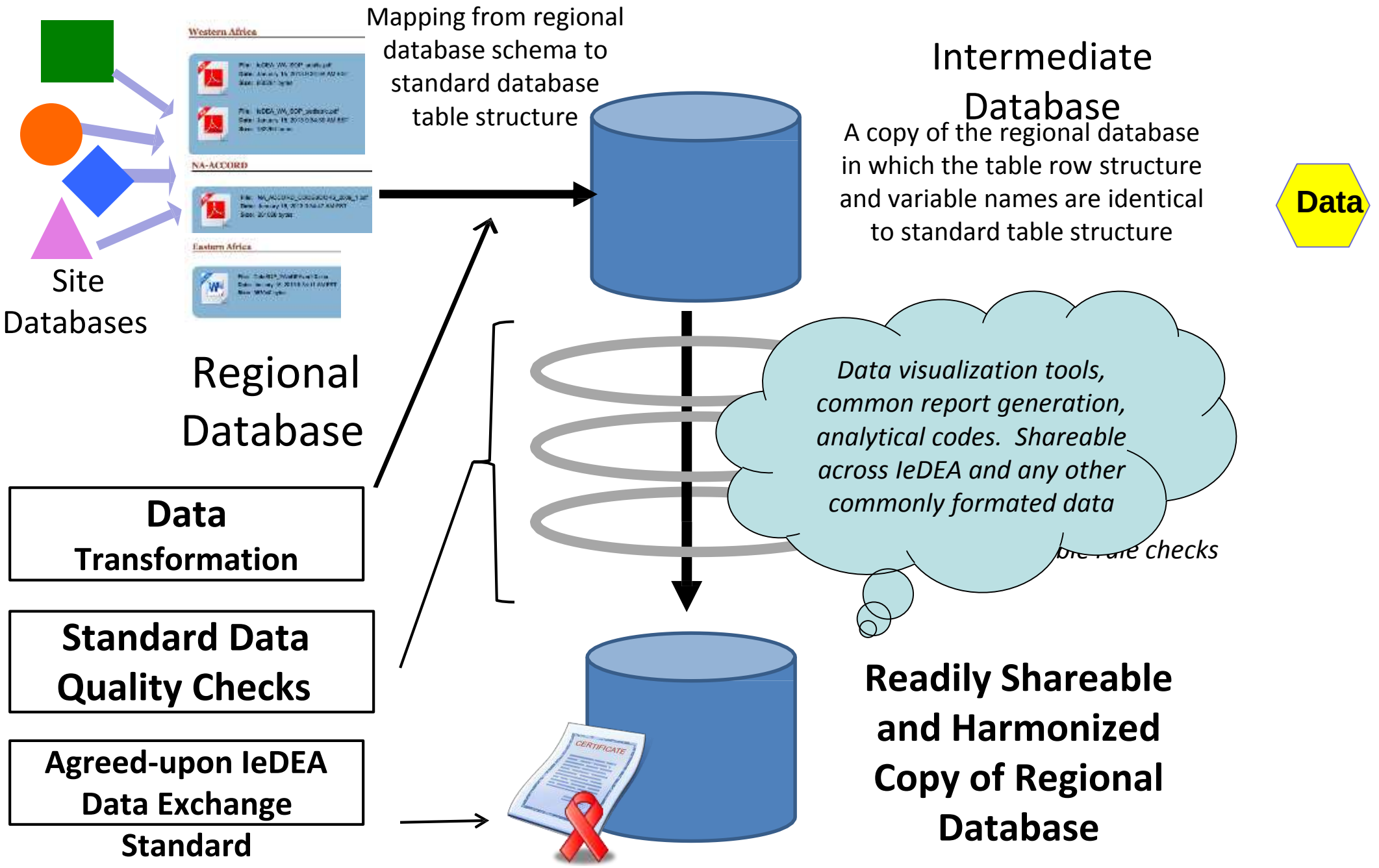
Enhance for the Future

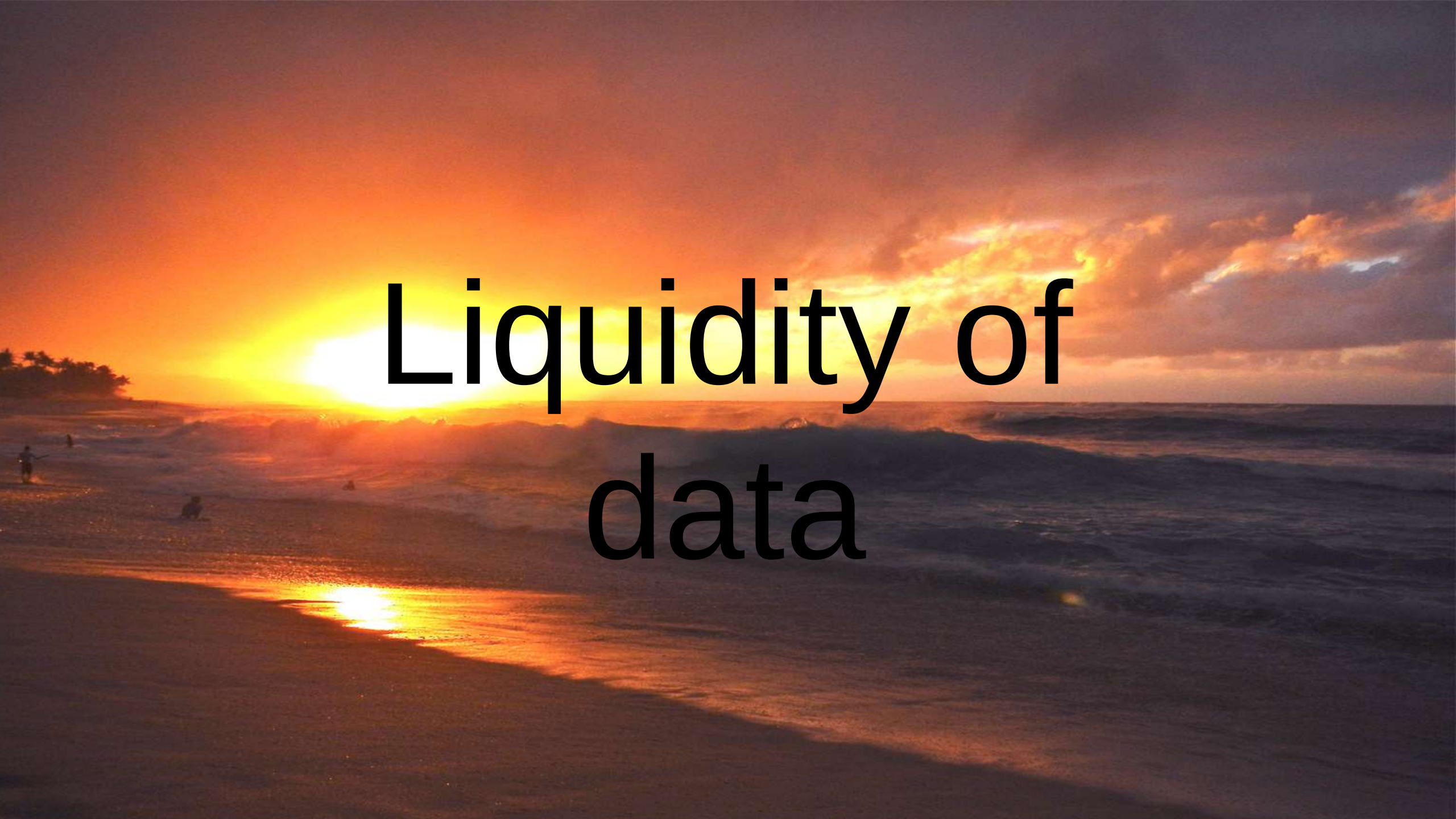
- **Build Infrastructure**
  - Establish quality data at the clinic level
  - Foster regionally relevant research by giving in-country investigators access to data
  - Improved data leads to a higher level of care



- **Train In-Country Investigators**

Data


Site Databases
Western Africa
NA-ACCORD
Eastern Africa
Mapping from regional database schema to standard database table structure
Intermediate Database
A copy of the regional database in which the table row structure and variable names are identical to standard table structure
Data
Regional Database
Data visualization tools, common report generation, analytical codes. Shareable across IeDEA and any other commonly formated data
Data Transformation
Standard Data Quality Checks
Agreed-upon IeDEA Data Exchange Standard
CERTIFICATE
Readily Shareable and Harmonized Copy of Regional Database



Liquidity of data

IeDEA Enrollment

July 17, 2015

Region	# Adults	# Children	Total Adults & Children
East Africa	255,443	51,897	307,340
Southern Africa	877,385	60,000	930,385
West Africa	88,578 (4,979 HIV-2)	12,533	101,111
Central Africa	46,658	5,936	52,594
CCASAnet	26,688	1,861	28,549
NA-ACCORD	149,359		149,359
Asia Pacific	110,610	11,626	122,236

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TOTAL	1,568,479	143,853	1,705,332

10% of adults
15% of children
~14,000’ peaks
Filled with Glacial scree to 7,000
Teton Valley 31,000 feet deep

Big Data

We must organize the body of knowledge, to do science.

- We are generating so much data. *(Big Data)*
- That we are losing the “organization of knowledge”. *(The problem that Big Data causes)*
- Take the morass of data back into systematically organized knowledge. *(How to address the problem that Big Data causes)*

The Challenge to IeDEA

- Secure and validate data. (data)
- Map the generalizability of data (organize)
- Answer meaningful questions (knowledge)

CCASAnet

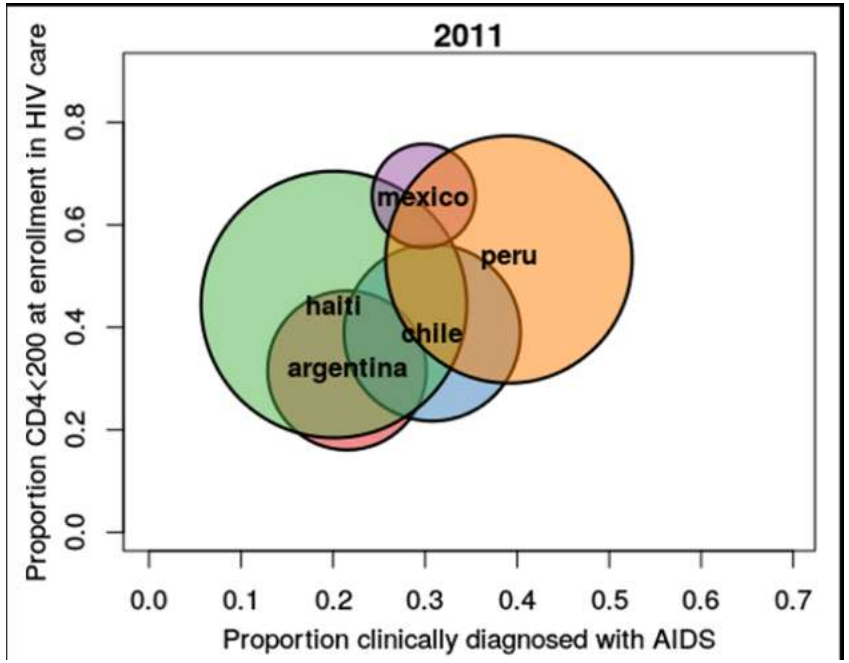
- Better data and analytical capacity of global IeDEA through efforts on data quality and harmonization

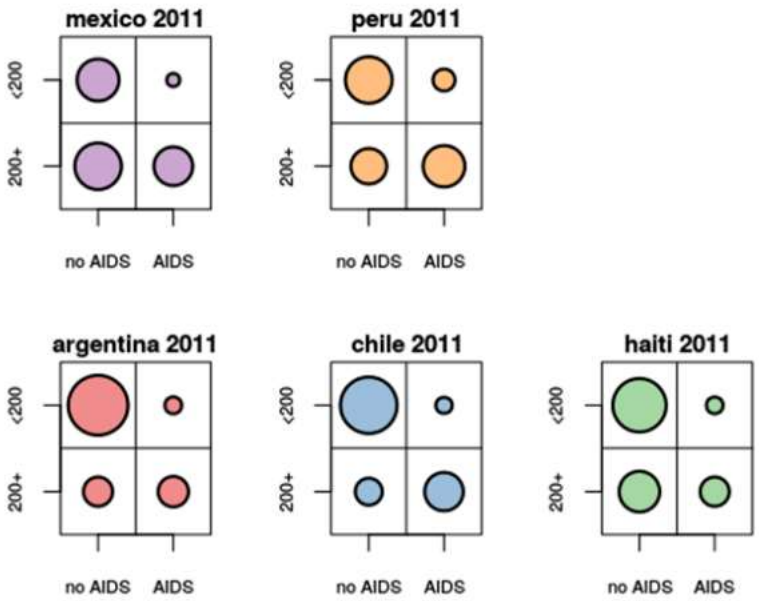
Duda, et al: Measuring the Quality of Observational Study Data in an International HIV Research Network. PLoS ONE 7(4): e33908. doi:10.1371/ journal.pone.0033908

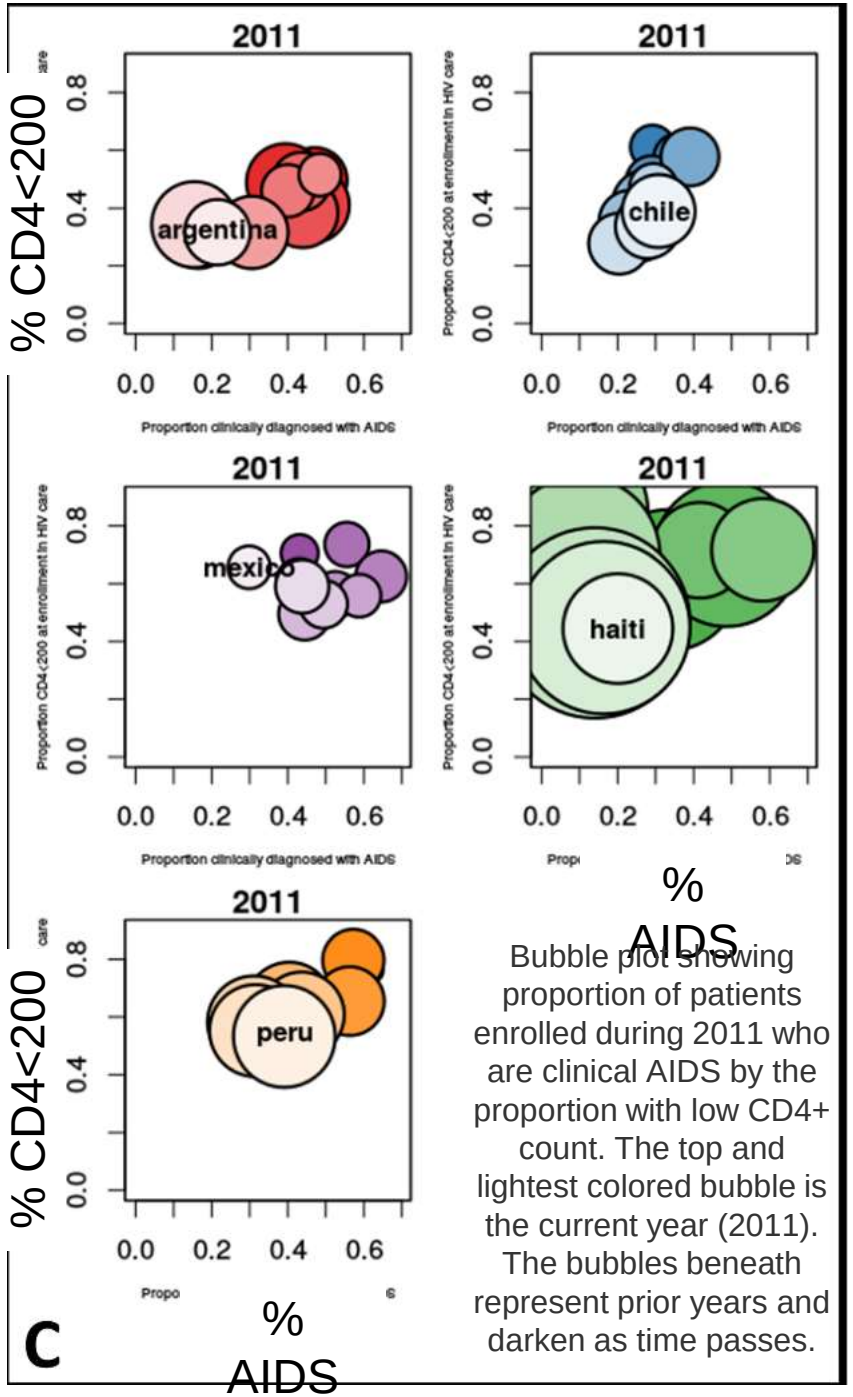
- Inclusion of context through development of IeDEA Site Assessments

Duda, et al: Characteristics and comprehensiveness of adult HIV care and treatment programmes in Asia-Pacific, sub-Saharan Africa and the Americas: results of a site assessment conducted by the International epidemiologic Databases to Evaluate AIDS (IeDEA). Journal of the International AIDS Society 2014, 17:19045

Enhanced data sharing through development of HIV cohort visualization tools







Bubble plot showing proportion of patients enrolled during 2011 who are clinical AIDS by the proportion with low CD4+ count. The top and lightest colored bubble is the current year (2011). The bubbles beneath represent prior years and darken as time passes.

Blevin, et al: Interactive Data Visualization for HIV Cohorts: Leveraging Data Exchange Standards to Share and Reuse Research Tools. PLOS ONE | DOI:10.1371/journal.pone.0151201 March 10, 2016

Treatment: Its Delivery & Outcomes

- **ART: adults, adolescents & children**
  - HIV morbidity and mortality globally
  - Treated HIV: long term & trends in regimen durability/tolerability
  - Evaluation of implementation – reaching goals

- **Cancer – AIDS and non-AIDS**
  - Assessment of diagnosis & treatment
  - Epidemiology of cancer outcomes
  - Registry matches

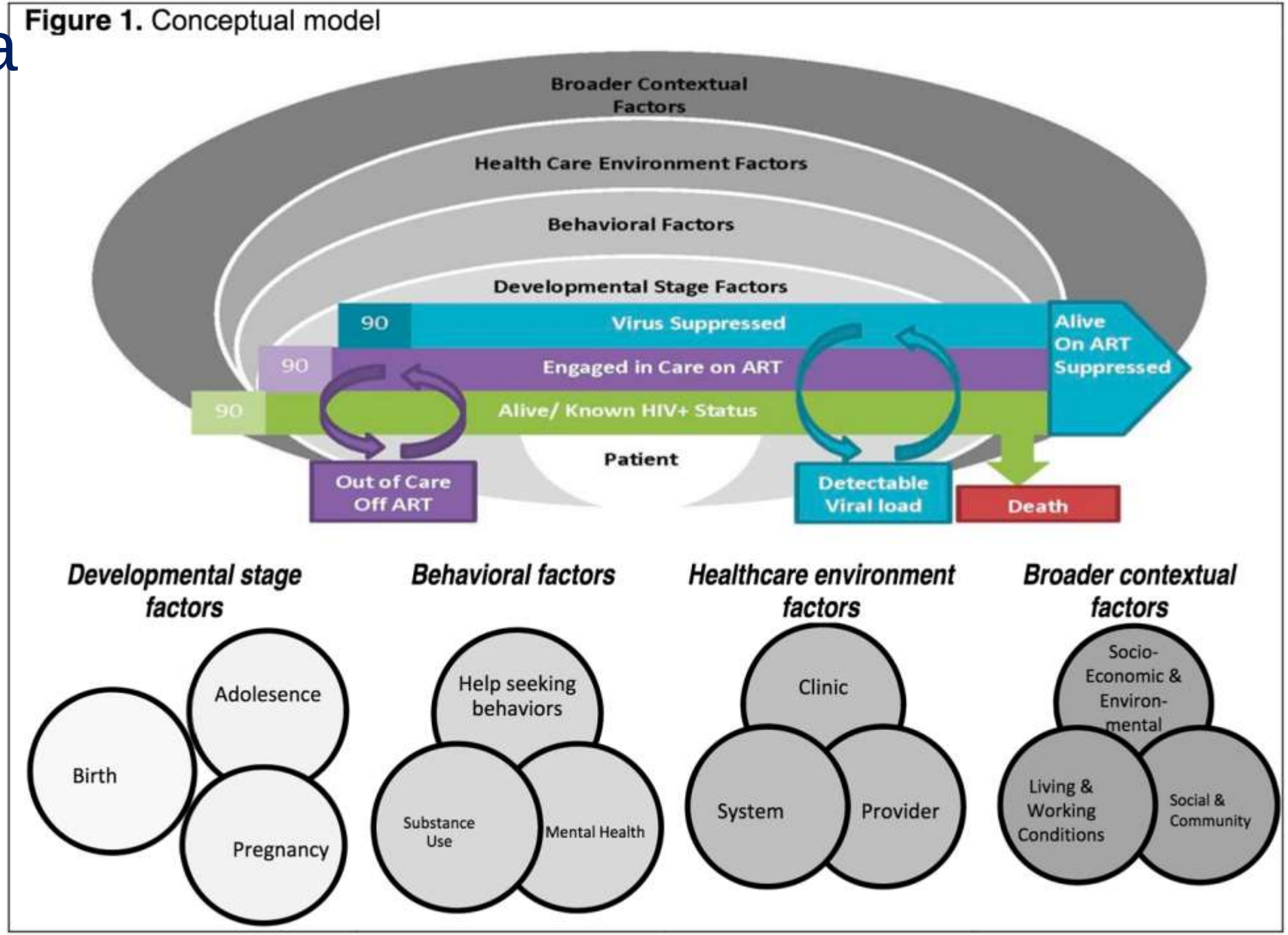
- **Co-morbidities and co-infections**
  - Tuberculosis, co-treatment, resistance
  - Significant co-morbidities: hypertension, diabetes
  - Aging with HIV across regions

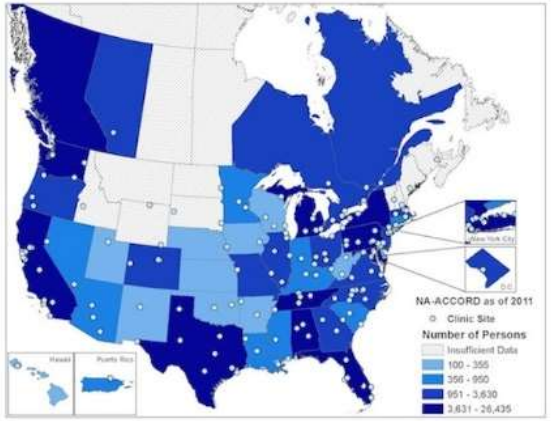
- **Mental Health and Neurologic disease**

- **Substance use and its impact on HIV**
  - Pathogenesis of HIV
  - Therapeutic outcomes

East Africa IeDEA

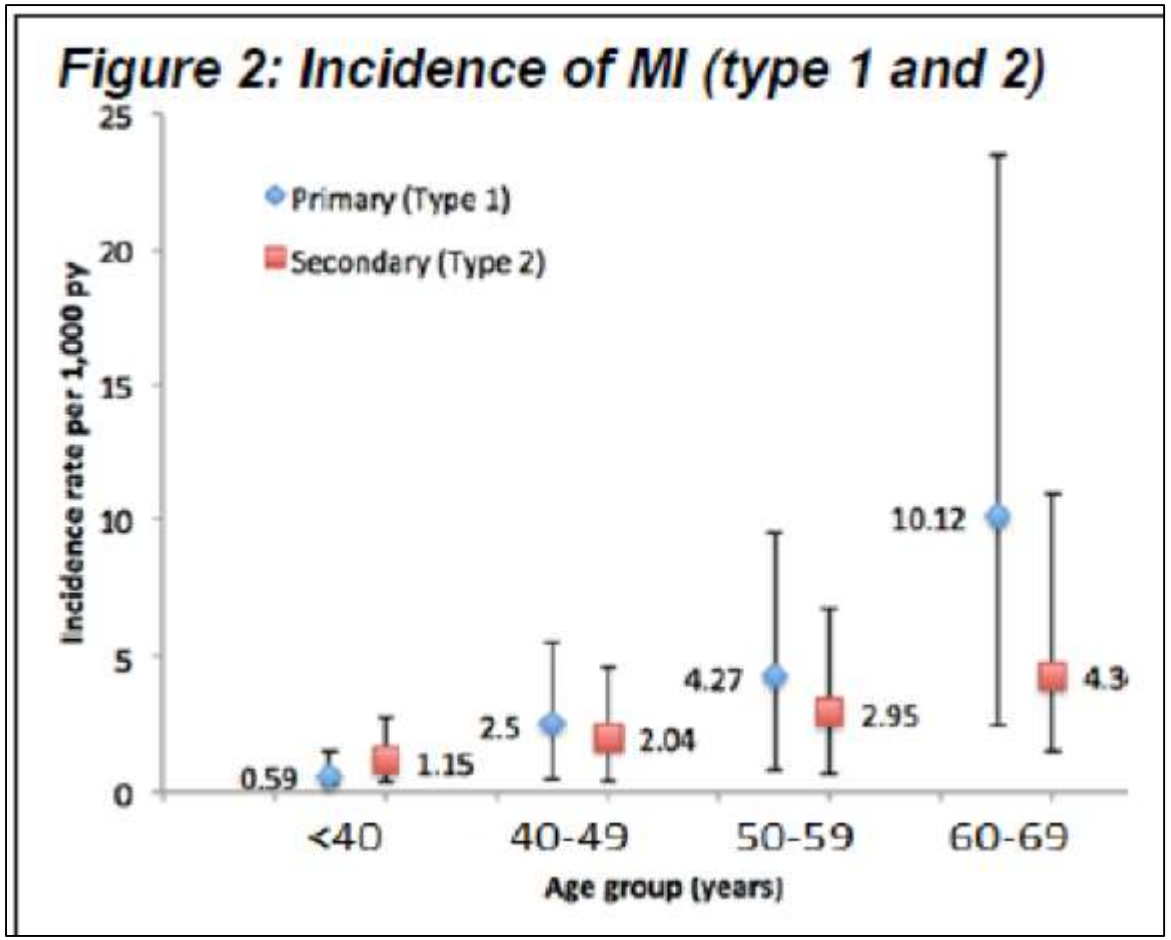
Focusing beyond the clinic to community & societal data

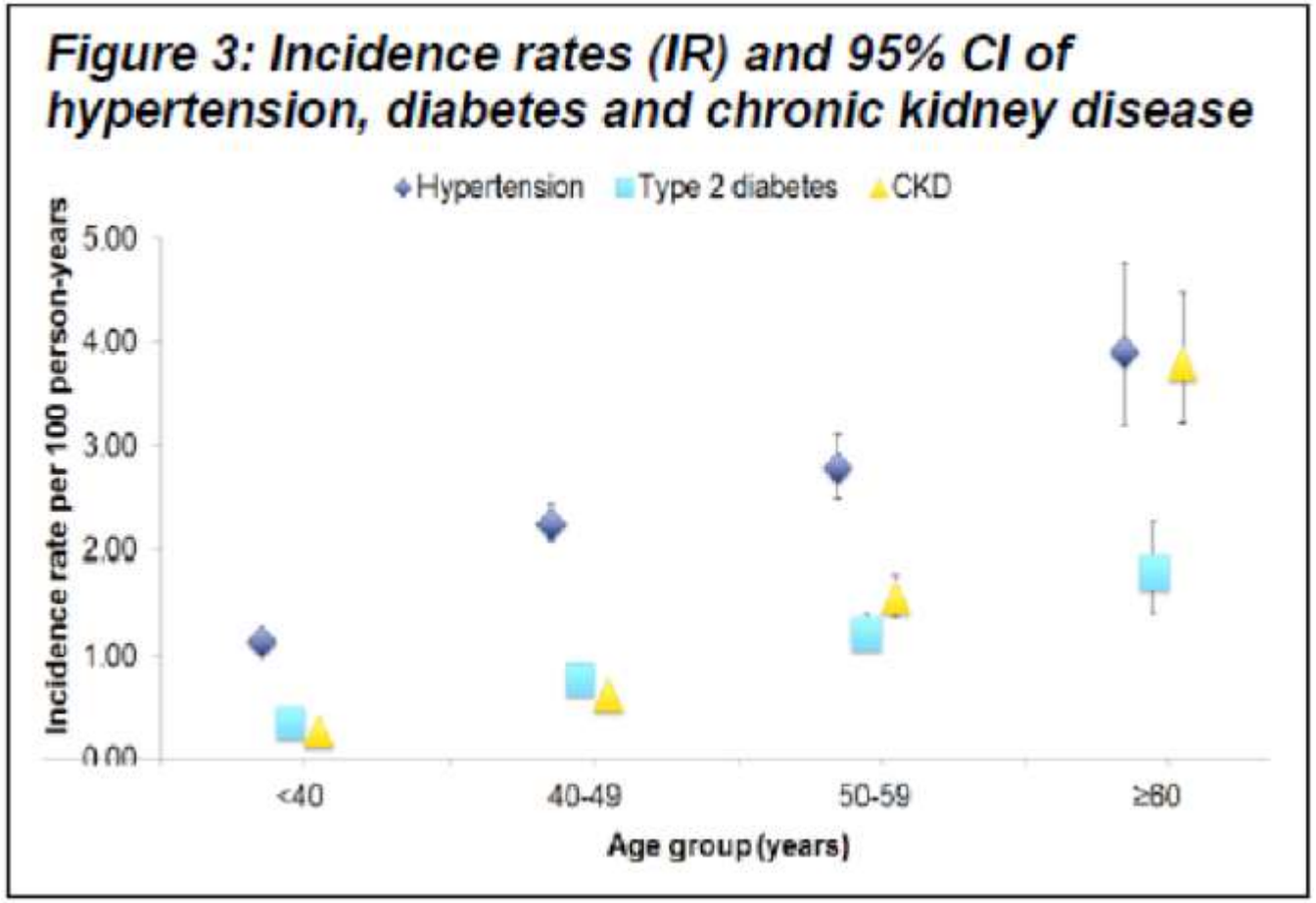




NA-ACCORD

Characterize the clinical course of HIV infection in North America with a focus on aging, major non-AIDS comorbidities and life-expectancy.





HIV infection, viral hepatitis and liver fibrosis among prison inmates in West Africa.

Jacquet et. al. West Africa IeDEA

Prevalence

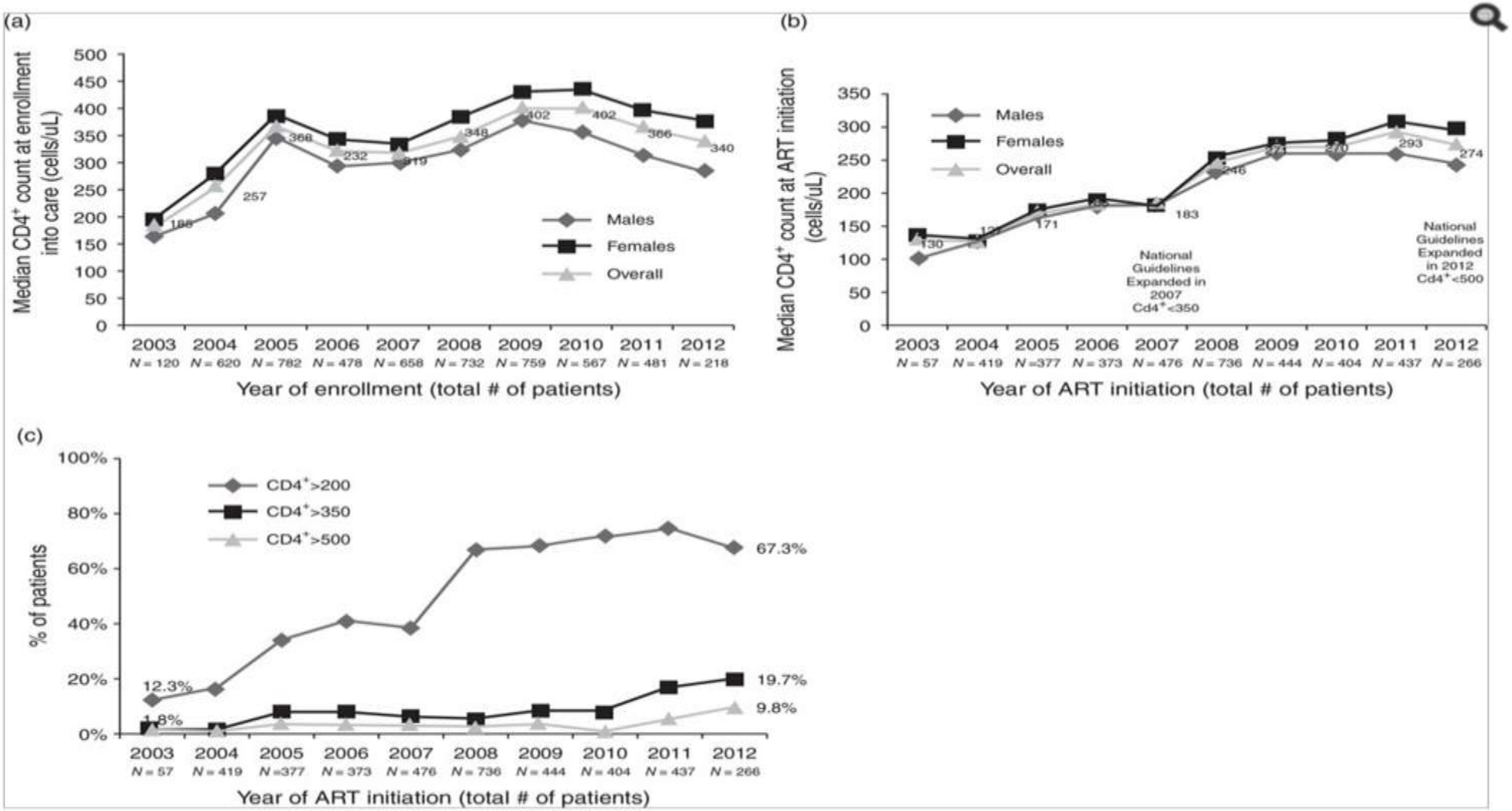
HIV 2.6%
HBV 12.5%
HCV 0.5%
Severe Liver Fibrosis 3.1%

Liver Fibrosis - OR

HIV	7.6	1.8 – 32.1
HBV	4.8	1.8 – 12.8
HCV	52.6	4.10 – 673.8
Traditional med	3.7	1.4 – 10.1
Lome vs Dakar	3.3	1.1 – 9.8

Antoine Jaquet, Gilles Wandeler, Judicaël Tine, Claver A. Dagnra, Alain Attia, Akouda Patassi, Abdoulaye Ndiaye, Victor de Ledinghen, Didier K. Ekouevi, Moussa Seydi, François Dabis BMC Infect Dis. 2016; 16: 249.

Trends in and correlates of CD4+ cell count at antiretroviral therapy initiation after changes in national ART guidelines in Rwanda



Median CD4+ cell count by sex among (a) all patients at enrollment and (b) antiretroviral therapy (ART) patients at ART initiation between 2003 and 2012. (c) The proportion of patients with a CD4+ cell count at more than 200, 350, and 500 cells/μl between 2003 and 2012.

Eugene Mutimura,[a] Diane Addison,[b] Kathryn Anastos,[c] Donald Hoover,[d] Jean Claude Dusingize,[a] Ben Karenzie,[e] Isabelle Izimukwiye,[f] Leo Mutesa,[g] Sabin Nsanzimana,[h] Denis Nashi,[i] and for the IeDEA Central Africa Collaboration AIDS. 2015 Jan 2; 29(1): 67–76.

Treatment Cascade

- Uptake of care
- Initiation of therapy
- Time to suppression
- Durability of 1st line/time on failing regimen
- Durability of subsequent regimens, assessment of need for third, later regimens
- Dynamics of care engagement – churn.

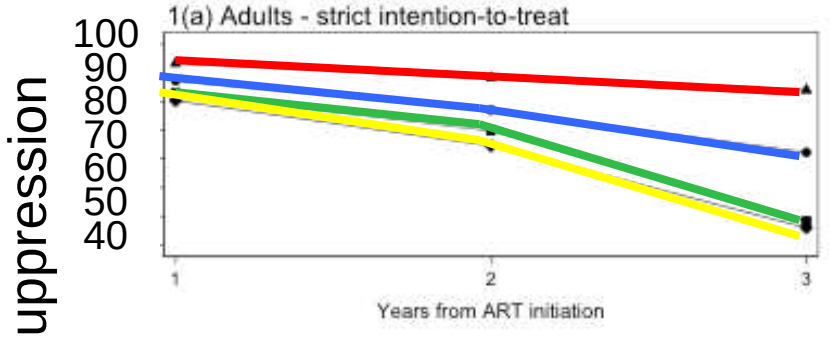
HIV viral load suppression in adults and children receiving antiretroviral therapy – results from the IeDEA collaboration

35,561 adults
38 sites/16 countries

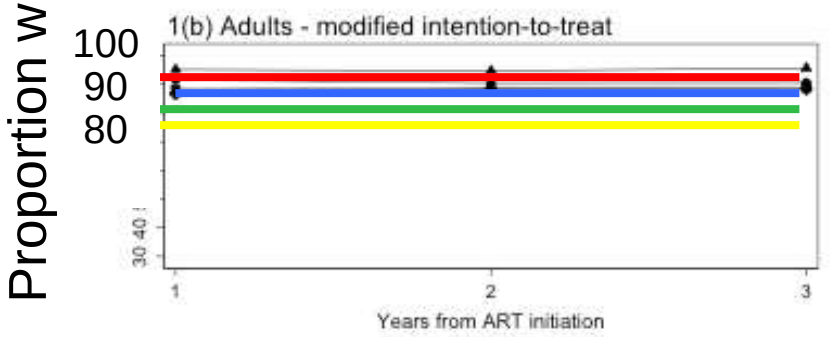
older age,
higher CD4 pre-ART
homosexual/bisexual

2,601 children
18 sites/6 countries

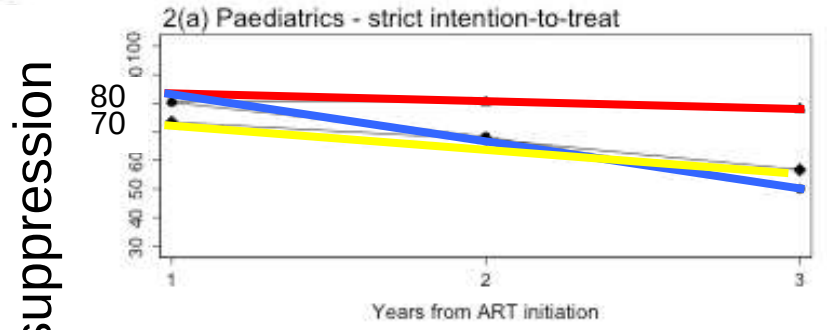
older age
higher CD4% pre-ART



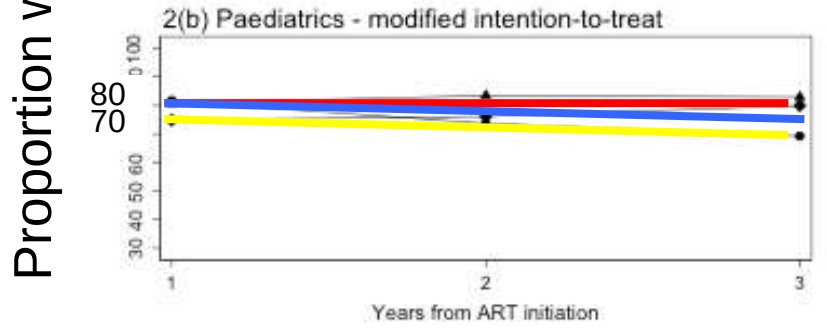
	1842	1358	920
	2918	2097	1240
a	11677	6884	3223
	11441	7041	3872



Asia-Pacific	1806	1266	808
CCASAnet	2777	1784	852
North America	10970	5410	1392
South Africa	10600	5142	1577



	229	194	137
	61	41	18
	1714	1070	556



Total patients			
Asia-Pacific	229	187	129
CCASAnet	60	38	13
South Africa	1679	948	394

Asia **CCASA** **North America** **Southern Africa**

East Africa IeDEA: Kenya, Uganda, Tanzania

17% were lost to follow-up → 17% of those lost were traced

"After adjustment for measured biological drivers, mortality differs substantially across settings despite delivery of a similar clinical package of treatment. Implementation research to understand the systems, community, and patients' behaviours driving these differences is urgently needed."

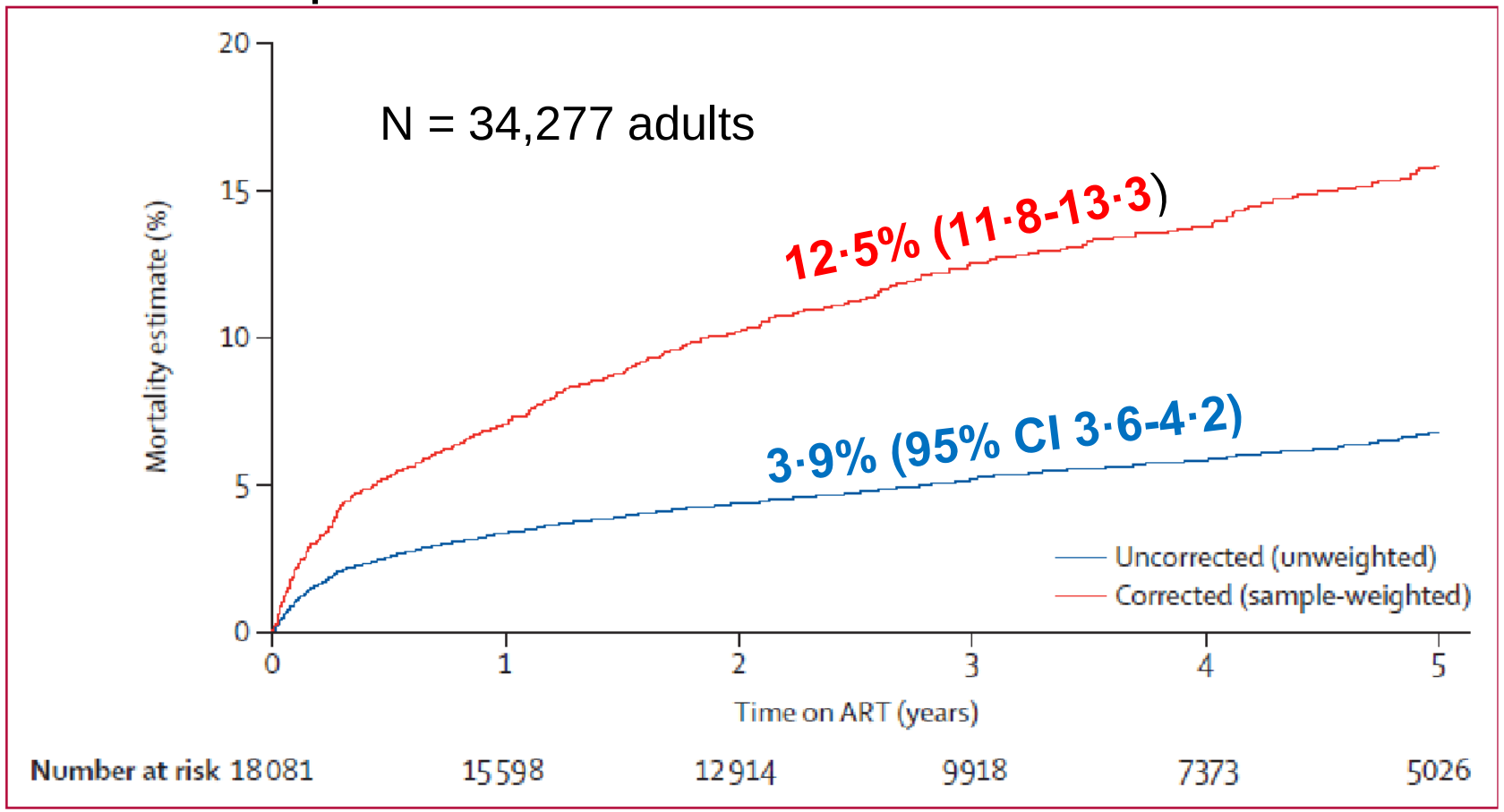


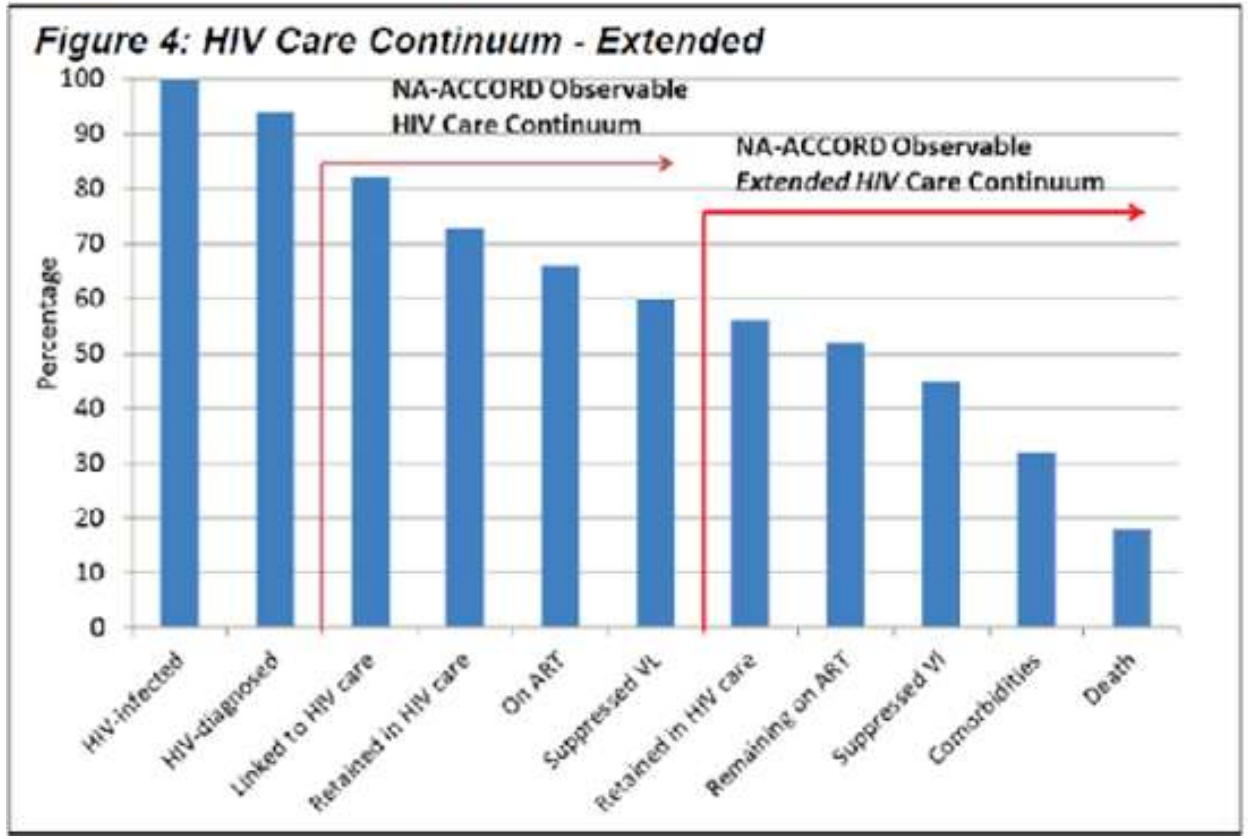
Figure 3: Overall mortality estimates

Geng, et al: Estimation of mortality among HIV-infected people on antiretroviral treatment in East Africa: a sampling based approach in an observational, multisite, cohort study. Lancet HIV. 2015 Mar;2(3):e107-16.

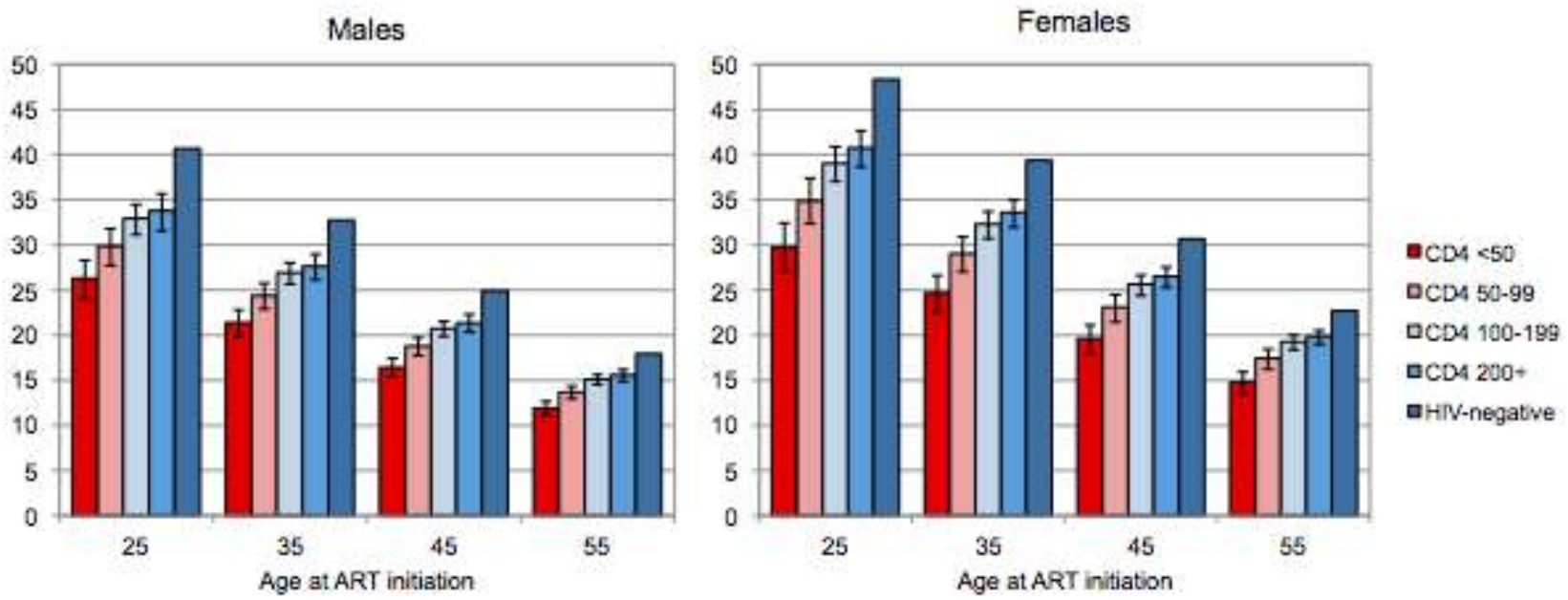
SPECIFIC AIMS

2. Characterize the *HIV Care Continuum* in North America and extend it beyond the current terminus of viral suppression to include clinical outcomes and life expectancy.

- Extend beyond viral suppression to include long-term retention, ART utilization, viral suppression and failure.
- Evaluate the impact of social and geographic disparities and other associated contextual factors on the extended Continuum.



Life expectancies of adults starting ART in South Africa

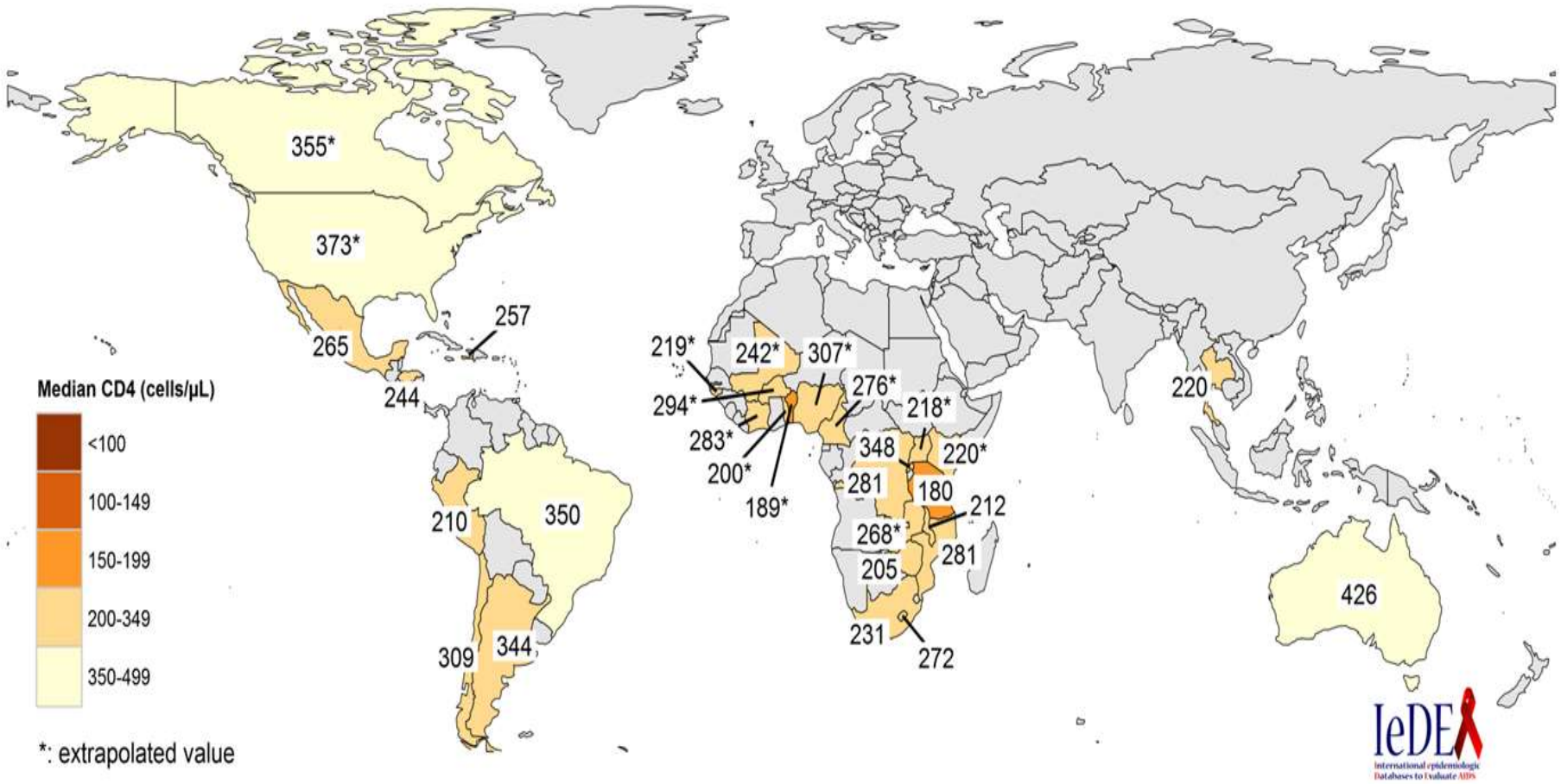


Near-normal expectancy for adults starting ART above 200 cells/µL

Johnson et al, PLoS Med 2013

Median CD4 count at ART start in 2013

(data for some countries extrapolated)

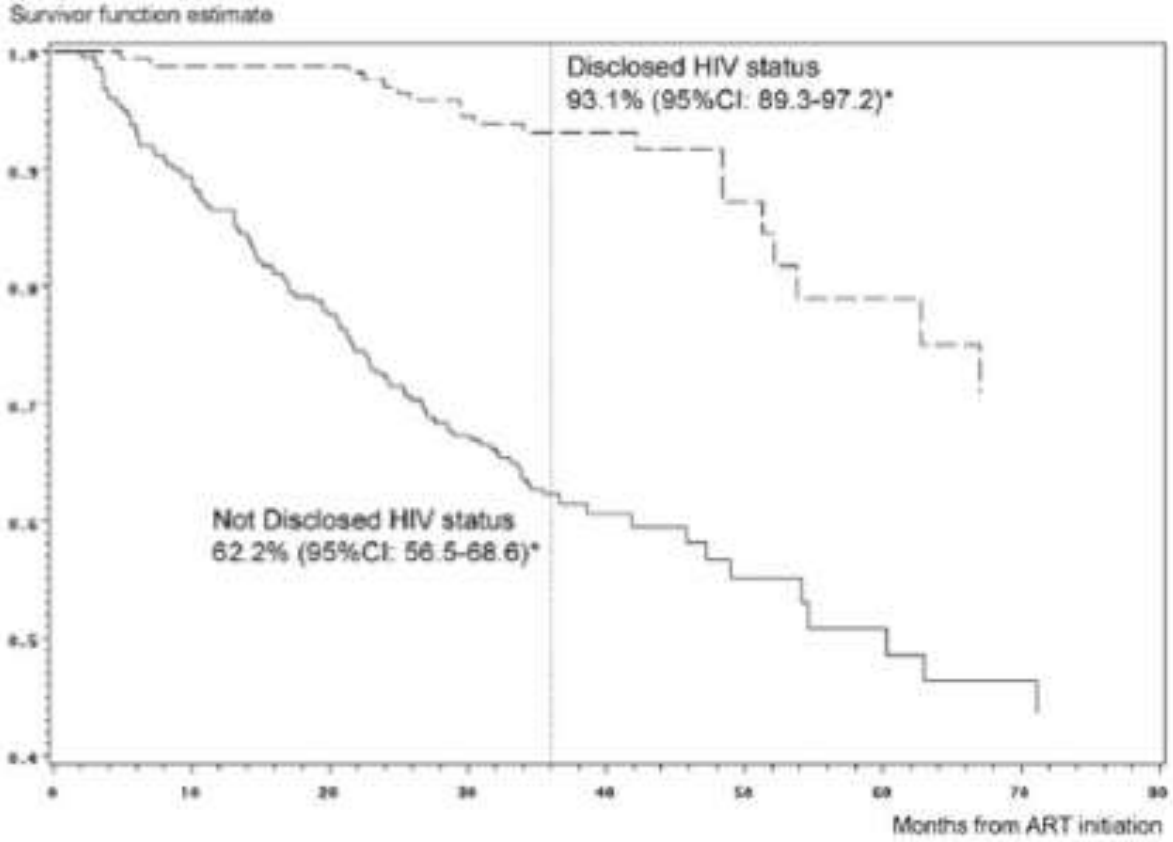


Pediatrics

- Significant opportunities from the large pediatric database allows for stratified analysis
    - By age
    - By weight and height
    - Immune suppression at start
    - By regimen
- Comparison of survival across treatment programs
- Durability of regimens and toxicities
- Impact of contextual factors
  - Adolescent disclosure and stigma
  - Orphan-hood

HIV status disclosure and retention in care in HIV-infected adolescents on antiretroviral therapy (ART) in West Africa.

Arrivé et al. PLoS One. 2012;7(3):e33690.



Probability of retention in HIV care while on antiretroviral therapy (ART) for 650 adolescents according to disclosed HIV status taking into account the delayed entry at age of 10 years. Pediatric IeDEA West Africa Collaboration. * Estimation at 36 months from ART initiation.

Global Contributions of IeDEA

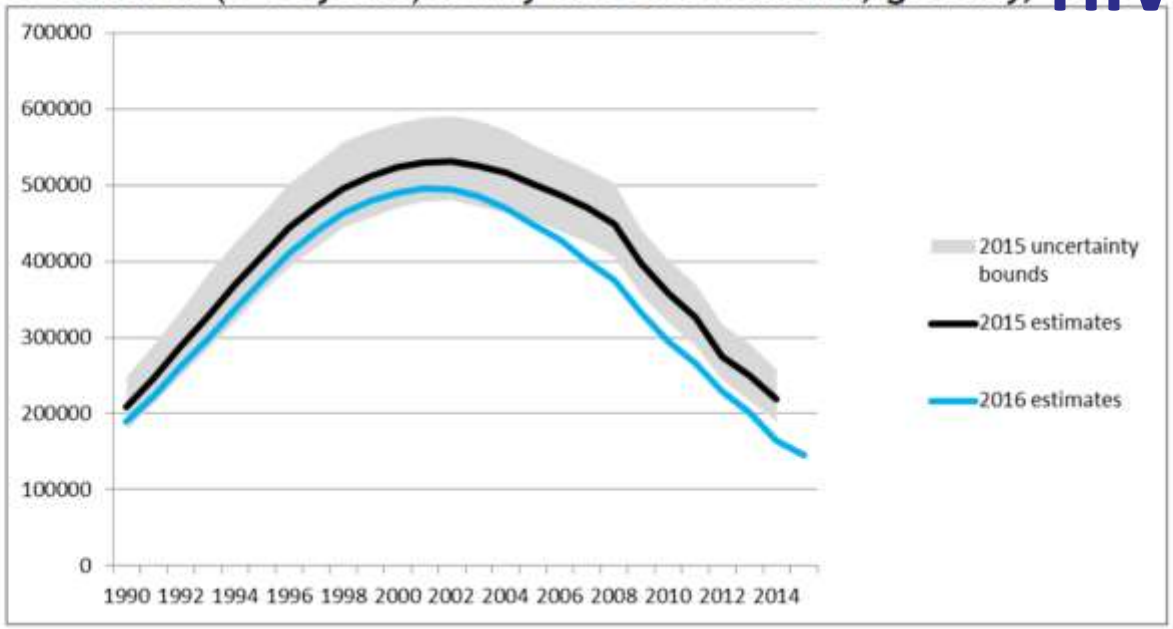
- NA-ACCORD contributed to treatment guidelines on when-to-start ARVs
- East and Southern Africa described the importance of, and created solutions for evaluating program effectiveness in the face of high loss to follow-up
- UNAIDS reduces estimates of children living with HIV from 2.6M to 1.8M
- IeDEA contributed to WHO treatment guideline deliberations 2014.
  - Modifications to GRADE for use of observational data
  - Importance of effectiveness data in adult guideline development.
  - Pediatric guideline participant - PMTCT/Option B+

IeDEA-WHO Collaboration 2016

- Global analysis of retention in care in initial HIV care and treatment program.
- Global analysis of the pre-ART cascade and delay from diagnosis to start of antiretroviral therapy in HIV-infected children aged 0-19 years.
- Global analysis of delays from ART eligibility to antiretroviral treatment initiation among adults.
- Adolescent treatment outcomes in the IeDEA global consortium

Based on IeDEA: UNAIDS Decreases Number of Children Living with HIV

: Number of children (0-14 years) newly infected with HIV, globally, 1990-2015



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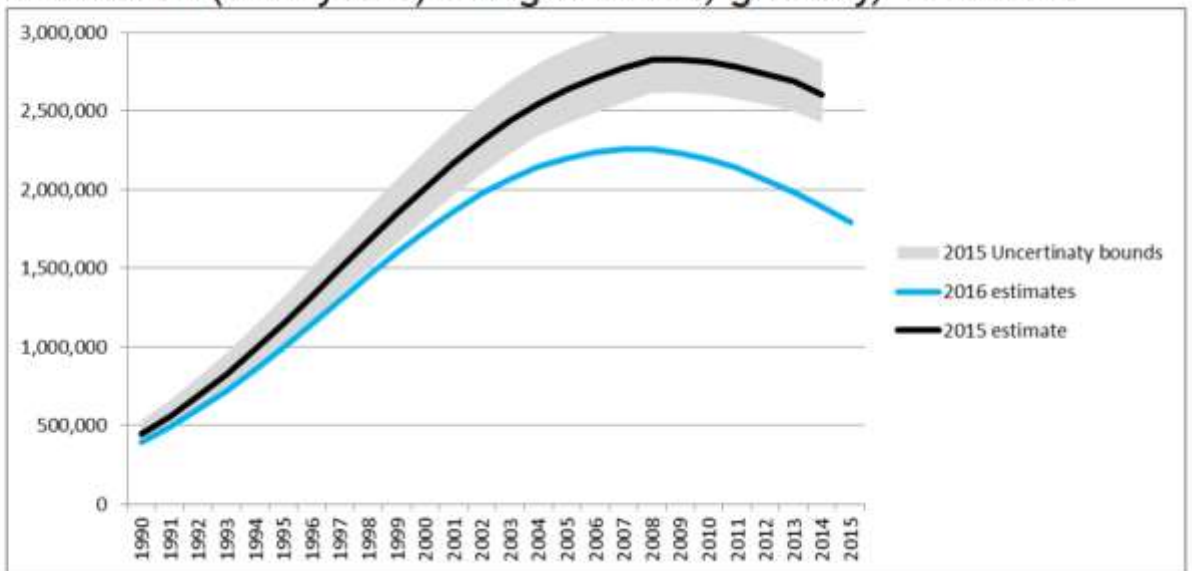
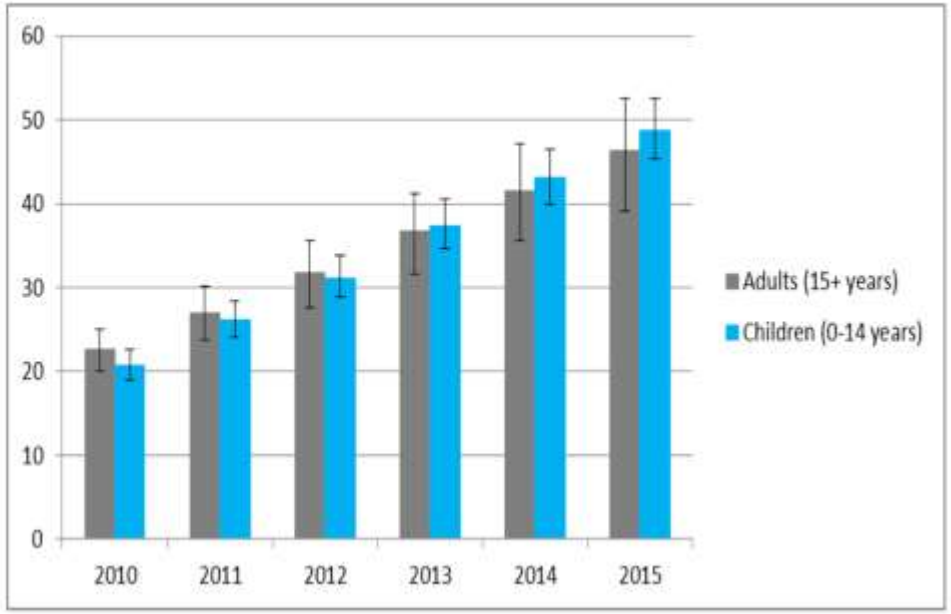


Antiretroviral coverage among adults and children, globally, 2010-2015



Questions?

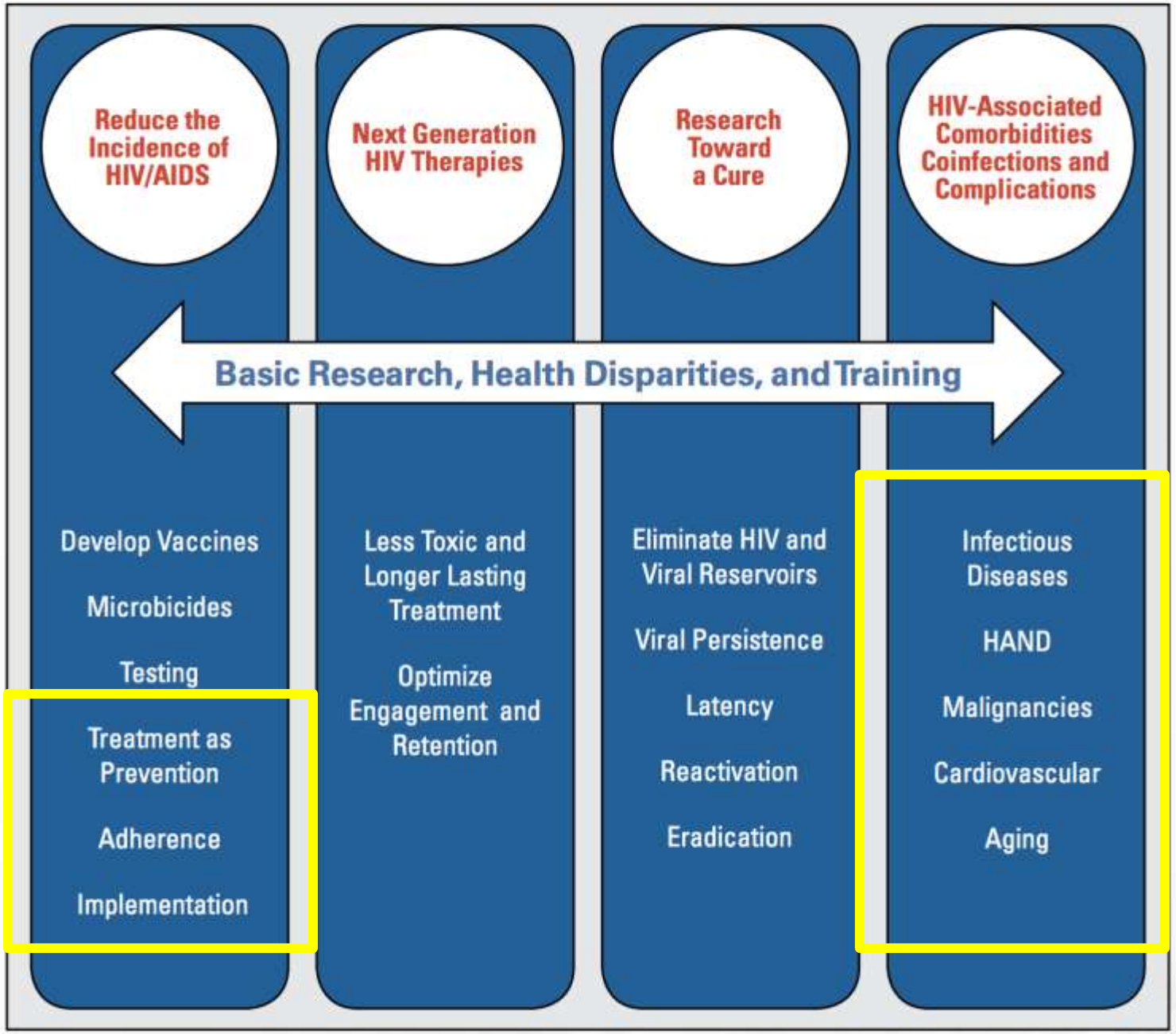
NIH

National Institute of Allergy and Infectious Diseases

IeDEA

International epidemiologic Databases to Evaluate AIDS

Overarching HIV/AIDS Research Priorities



High-priority research opportunities focused on reducing the incidence of HIV/AIDS include:

- Examining the relationship between the genital/rectal-anal tract microenvironment, host factors, immune function, microbiome, and HIV risk, transmission, and acquisition.
- Evaluating the role of immunity (including, but not limited to T cells, B cells, antigen-presenting cells, innate responses and host factors), particularly at mucosal sites, for protection in the context of studies on vaccines, microbicides, and long-acting antiretroviral agents.
- Conducting clinical trials for vaccines, microbicides, MPTs, PrEP, and other biomedical prevention modalities.
- Developing and testing standardized assays to better understand the mechanisms of infection and transmission that inform vaccine, microbicides, and PrEP efficacy.
- Developing models to study the contributions and interactions of behavioral, social, structural, and environmental factors in at-risk communities, as well as models for community engagement to reduce HIV/AIDS in different populations and cultural settings.
- Identifying strategies to overcome barriers to the adoption, adaptation, integration, scale-up and sustainability of evidence-based interventions and tools, as well as clinical guidelines (standards of care) while accounting for racial, ethnic, cultural, gender, sex, and age differences in diverse settings.

High-priority research opportunities focused on HIV-associated co-infections, comorbidities, and other complications include:

- Accelerating the discovery, testing, and validation of therapeutic strategies to prevent and treat HIV-associated comorbidities across the lifespan of HIV-infected individuals.
- Elucidating the mechanisms responsible for the pathogenesis of comorbid conditions of various organ systems, including the contribution of the immune system, inflammation, and long-term antiretroviral therapy on the development of these comorbidities.
- Defining the mechanisms that increase the risk of acquiring HIV-associated coinfections in diverse populations, and evaluating the interaction of coinfecting pathogens on HIV disease progression and vice versa.
- Examining the prevalent comorbidities such as substance use and abuse, mental disorders, and malnutrition within the context of HIV/AIDS.