All Africa 2017: Review of priorities and progress to date

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Disclosures and conflicts of interest

• I have no financial or other conflicts of interest to disclose
Outline of talk

• Research Priorities from the all Africa meeting, Kigali 2017
• Progress to date on these priorities and insights
• What’s in the IeDEA pipeline
The evolution of WHO ART Guidelines and their global implementation in 2016-17

**2006**
Treat CD4<200

**2009**
Treat CD4<350

**2013**
Treat CD4<500

**2015**
Treat all

Implementation of the "treat all" recommendation among adults and adolescents living with HIV, October 2016

30% of all LMIC and 63% of fast track countries have implemented "treat all"

'Treat all' as a national policy, mid 2017

July 2017, Source: WHO
IeDEA All-Africa Meeting, Kigali, Rwanda, November 5-6, 2017
Now is the time to identify and articulate ‘Treat all’ research priorities for SSA

• Rigorous research on outcomes of early ‘Treat all’ implementation efforts in SSA is critically needed, including:
  • Assessing the uptake and impact of ‘Treat all’ implementation
  • Identifying and addressing major bottlenecks impeding effective implementation of ‘Treat all’
  • Identifying evidence-based strategies that best and most efficiently promote uptake of ‘Treat all’

• Such research can help ensure that data from the early implementation and scale-up experience of ‘Treat all’ are rapidly examined, disseminated and translated
  • Optimal strategies can be identified sooner rather than later.
HIV care continuum and number of people with untreated HIV in sub-Saharan Africa, 2017

>10M with HIV as yet unreached in SSA

10.3M plus an estimated 1.2M people newly infected with HIV each year

Adapted from UNAIDS 2018 estimates

UNAIDS and Nash et al. J Virus Erad 2018
Undertaking a consensus-building process to identify ‘Treat all’ research priorities for SSA

• IeDEA Consortium includes 140 clinics in 23 countries in SSA, many of which have adopted ‘Treat all’ policy.

• In 2017, a group of about 200 researchers, expert clinicians, and program specialists involved in IeDEA Consortium undertook a multi-step process to identify a set of research priorities that can inform and guide ‘treat all’ implementation in SSA.

• **Overall goal:** Guide study design, collection and analysis of data on ‘Treat all’ implementation in order to identify optimal strategies for rapidly realizing individual and public health benefits of ‘Treat all’.
Results: Participants in Consensus Process

• More than 200 individuals participated in one or more rounds of the process
• 60% of respondents based in SSA
  • Burundi, Cameroon, Democratic Republic of Congo, Kenya, Republic of Congo, Rwanda, Senegal, South Africa, Tanzania and Uganda
• ~20% of respondents completed the survey in French
• 12% of respondents based in Europe (France, Switzerland)
• 28% based in USA
Results: Participants (continued)

10 mean years’ experience in HIV/AIDS, across diverse backgrounds
Research priorities to inform “Treat All” policy implementation for people living with HIV in sub-Saharan Africa: a consensus statement from the International epidemiology Databases to Evaluate AIDS (IeDEA)

Marcel Yotebieng1,* id, Ellen Braizer2,3,* id, Diane Addison2,3,* id, April D Kimmel4, Morna Cornell5, Olivia Keiser6, Angela M Parcesepe7 id, Amobi Onovo7 id, Kathryn E Lancaster1 id, Barbara Castelnuovo8, Pamela M Murnane9, Craig R Cohen10, Rachel C Vreeman11 id, Mary-Ann Davies12 id, Stephany N Duda13, Constantin T Yiannoutsos14, Rose S Bono4, Robert Agler1, Charlotte Bernard15, Jennifer L Syvertsen16, Jean d’Amour Sinayobye17, Radhika Wikramanayake2,3, Annette H Sohn18 id, Per M von Groote19, Gilles Wandeler19 id, Valeriane Leroy20, Carolyn F Williams21, Kara Wools-Kaloustian22, Denis Nash2,3,8,23 id, and for the IeDEA Treat All in sub-Saharan Africa Consensus Statement Working Group

Downloadable PDFs at: http://cunyisph.org/iedea-treat-all-jve/

- Deploying research priorities within the IeDEA network’s 4 SSA regions
- Each region will present plans for two multi-country projects at 2019 All-Africa meeting
Research Priority 2: Characterize and understand critical facilitators of and barriers to timely diagnosis, care linkage, ART initiation, and sustained care engagement and ART adherence, particularly for key populations and underserved groups, including infants, adolescents, and men.

- What factors (individual, cultural, and structural/systems) influence timely diagnosis of HIV (i.e. at higher CD4 counts) and timely linkage to HIV care? How does this vary by sociodemographics and for key and underserved populations (e.g. MSM, SW, PWID, infants, adolescents, men)?

- Mixed methods approaches with PLWH, providers, and policy makers; implementation science/intervention studies; studies exploring new settings for HIV testing.

Research Priority 4: Develop and apply metrics that reflect the timeliness with which short-term and long-term HIV care continuum outcomes are achieved (i.e. early diagnosis, rapid linkage to care following diagnosis, rapid ART initiation following linkage, viral suppression within 4 weeks of ART initiation, and rapid achievement of sustained viral suppression)

- What is the most appropriate care cascade metric for Treat All and what metrics should be used to monitor it? Is it possible to develop a metric of time from infection to ART initiation?

- What is the optimal timing of ART initiation after diagnosis confirmation (e.g. immediately after diagnosis, after initial adherence counselling, etc.) for maximizing retention in care, adherence, and clinical outcomes, and how does this vary by population subgroup and co-morbidities (e.g. patients with TB co-infection, substance use and mental health disorders)?

- RCT or cluster RCT in real world implementation setting (vs. research setting).

Research Priority 5: Estimate the incidence and prevalence of HIV drug resistance, as well as switch to second- and third-line regimens at national and subnational levels

- What is the prevalence of acquired and developed HIV drug resistance, and how does this vary across national, subnational and patient populations?

- What is the rate of switching to second- and third-line regimens, and how does this vary by setting and by patient characteristics?

- Routine monitoring data; surveys; targeted studies at sentinel HIV care sites.
Overview of Treat All Research Priorities from IeDEA Consensus Statement

Research priorities reflect consensus around:

- The importance of **generating critical metrics and estimates** to inform policies, planning, monitoring and evaluation of Treat All implementation.

- The need for focused **intervention effectiveness trials and economic evaluations** to improve rollout of Treat All.

- The importance of focusing on **key populations and groups who remain underserved** along each element of the HIV care cascade to better understand and meet their preferences through evidence-informed strategies and models of care.

Yotebieng et al. JIAS 2018
Uptake of ’Treat all’ policy among adults and adolescents, July 2018

Source: WHO
What has been IeDEA’s progress to date on addressing these research priorities?
Treat all has become national policy, globally. Have IeDEA participating sites begun to implement it? What do the outcomes look like?

- In 2015, the World Health Organization recommended treating all persons with HIV as soon as possible after diagnosis — also known as ‘Treat All’.

- The adoption of WHO treatment guidelines often lags at national levels, contributing to suboptimal rates of ART initiation.

- Little is known about the timing and nature of site-level implementation of ‘Treat all’ vis-à-vis national-level adoption, across world regions and countries.

- IeDEA (International epidemiology Databases to Evaluate AIDS), an international research consortium established in 2005, provides a rich resource for monitoring trends in HIV care and outcomes across countries in six world regions.
Status of ‘Treat all’ implementation at IeDEA sites

- By mid/end of 2017, 214/234 (91%) sites reported implementation of ‘Treat all’ (i.e., initiating all patients on ART regardless of CD4 count or clinical criteria).
- Site-level implementation of ‘Treat all’ nearly universal across sites in most IeDEA regions, but lower among the Asia-Pacific and West Africa IeDEA sites.

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Implementation of “Treat-all” at adult HIV care and treatment sites in the Global IeDEA Consortium: results from the Site Assessment Survey

Ellen Brazier¹,², Fernanda Maruri³, Stephany N Duda⁴, Olga Tymejczyk¹,², C William Wester³,⁵, Geoffrey Somi⁶, Jeremy Ross⁷, Aimee Freeman⁸, Morna Cornell⁹, Armel Poda¹⁰,¹¹, Beverly S Musick¹², Fujie Zhang¹³, Keri N Althoff⁸, Catrina Mugglin¹⁴, April D Kimmel¹⁵, Marcel Yotebieng¹⁶, and Denis Nash¹,² for the IeDEA Consortium


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RESEARCH ARTICLE
Has ‘Treat all’ increased rapid ART initiation among adults?

Changes in rapid HIV treatment initiation after national “treat all” policy adoption in 6 sub-Saharan African countries: Regression discontinuity analysis

Timing of ART initiation
- 59% on day of enrollment
- 75% within 14 days
- 81.6% by 30 days

No evidence that “Treat all’ implementation has ‘crowded out’ sicker patients
Has ‘Treat all’ increased rapid ART initiation among adolescents and young adults?

Trends in rapid ART initiation before and after Treat All introduction among young adolescents. by year of Treat All introduction.

O Tymejczyk et al. J Infect Dis (in press)
Aims
• To estimate effect of Treat All on 30-day ART initiation and 6-month retention in care
• To identify patient- and site-level predictors of 30-day ART initiation and retention in care

Data
• Cohort of 2885 PWLH newly enrolling at 10 sites (July 2014 – Jul 2017)
• Site characteristics (location, adherence counseling, ancillary services)

Methods
• Interrupted time series analysis of ART initiation and 6-month retention in care
• Predictors of ART initiation and retention in care modeled using Poisson regression

Results
After implementation of Treat All in Rwanda:
• Immediate 31% increase in predicted probability of starting ART within 30 days
• Median time to ART initiation decreased from 31 to 7 days
• No statistically significant change in 6-month retention in care

Selected predictors of 6-month retention in care

Is retention after ART initiation impacted by treat all?

Early outcomes after implementation of treat all in Rwanda: an interrupted time series study

Jonathan Ross1§, Jean d’Amour Sinayobye2, Marcel Yotebieng3, Donald R Hoover4, Qiuhu Shi5, Muhayimpundu Ribakare6, Eric Remera6, Marcus A Bachhuber1, Gad Murenzi2, Vincent Sugira2, Denis Nash7 and Kathryn Anastos1, for Central Africa IeDEA

• No statistically significant change in 6-month retention in care

J Ross et al. JIAS (2019)
Is viral suppression on ART impacted by rapid ART?

J Ross et al. Association between time to ART and loss to care among newly-diagnosed PLWH in Rwanda (Submitted to CROI 2020)

CONCEPT SHEET: MULTIREGIONAL ANALYSIS

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<tr>
<td>Concept Lead:</td>
<td>Jonathan Ross MD MS; Albert Einstein College of Medicine, Bronx, NY, USA</td>
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<td>Email:</td>
<td><a href="mailto:joross@montefiore.org">joross@montefiore.org</a></td>
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Median CD4 count at ART initiation in landmark controlled trials, and at diagnosis or ART initiation in the real world

Need better strategies on how to target, identify and link persons with undiagnosed HIV earlier
Need better metrics and targets to focus implementation on prioritizing and achieving earlier diagnosis e.g., 90% of persons initiating ART with CD4>500 cells/uL

Nash and Robertson, Current HIV/AIDS Reports (2019)
What are some insights that we have gained?
Insights around ‘treat all’ (1)

• National treat all policies are increasing timely uptake of ART following diagnosis and enrollment in care
  • Same day ART initiation is increasingly the norm
  • Marked improvements in ART uptake among younger persons
  • Sometimes the increase is quick and sometimes there is a long delay of years (USA, Haiti).
  • Little or no impact appears to be the exception (Brazil)
  • Likelihood of rapid ART initiation improves with time after national policy change, suggesting sustainability.
  • Room for improvement everywhere
    • Inequities in rapid ART initiation for men and younger persons were noted, and should be addressed.

• No apparent negative effects on ART initiation (i.e., “crowding out”) for patients eligible under prior treatment guidelines.
Insights around ‘treat all’ (2)

• Suboptimal CD4 counts at enrollment in care underscore the need to address delays in diagnosis and/or linkage, which greatly limit the potential impact of ‘Treat all’ on individual and population health
  • Decreases in CD4 and VL monitoring in many key settings poses challenges

• Longer term outcomes (retention on ART, time to viral suppression, durable viral suppression) are not yet known.
  • Early data on retention are mixed (Rwanda, Haiti)
  • Outcomes may be worse for younger persons

• Treat All policies (backed up by implementation) are a key strategy for achieving UNAIDS 90-90-90 targets.

• Need identify implementation research priorities to inform and optimize the impact treat all implementation everywhere.
What’s in the pipeline?
What else is IeDEA is doing to advance priorities identified at the All-Africa meeting in Kigali, 2017?

Overview of Treat All Research Priorities from IeDEA Consensus Statement

Research priorities reflect consensus around:

- The importance of **generating critical metrics and estimates** to inform policies, planning, monitoring and evaluation of Treat All implementation.
- The need for focused **intervention effectiveness trials and economic evaluations** to improve rollout of Treat All.
- The importance of focusing on **key populations and groups who remain underserved** along each element of the HIV care cascade to better understand and meet their preferences through evidence-informed strategies and models of care.

- **IeDEA Site Assessment**
  - User fees for laboratory testing (A Kimmel)
  - Mental health services (Parcesepe)
  - Differentiated ART (Christ)
  - Substance use services (Lancaster)

- **CA IeDEA region**
  - Policy model in development (Kimmel)
  - Causal impact of treat all on long-term HIV care continuum outcomes (Zhang)

- **MR122**
  - Impact of ‘treat all’ on CD4 and VL monitoring

- **Sentinel Research Network**

- **MRXXX**
  - HIV-1 drug resistance to 1\textsuperscript{st}-3\textsuperscript{rd} line DTG-based regimens (Kouyos/Egger)

- **MR147**
  - Treat all ‘Dashboard’ for IeDEA SSA
IeDEA ‘Treat all’ SSA dashboard – Aims (1)

Overarching goal: develop and launch a user-friendly, interactive IeDEA Dashboard System to disseminate data and research focused on ‘Treat All’ in sub-Saharan Africa.

• Aim 1: We will develop and launch Version 1.0 of an interactive, web-based, visual ‘Treat All’ focused dashboard system to house aggregate site-level data on adolescents and adults from the patient-level databases in the African regions of IeDEA.
  • The dashboard will display trends in HIV care enrollment, ART initiation, ART regimens, and HIV care continua with ability to stratify by calendar time, country, age and sex.
  • The dashboard will also include ‘treat all’ focused modules with visualizations that draw on the IeDEA Site Assessment data (currently housed in REDCap) and the planned IeDEA Sentinel Research Network (SRN).
IeDEA ‘Treat all’ SSA dashboard – Aims (2)

• Aim 2: To serve as a clearing house for new published research that provides insights and direction to inform and assess the impact of ‘Treat All’ implementation in SSA.

  • Builds on momentum created by:
    • All-Africa IeDEA meeting in Kigali
    • Special issue of JVE focusing on ‘Treat all’ in SSA
    • Recent IeDEA Consensus Statement on Research priorities for ‘Treat All’ in SSA
    • Upcoming IeDEA All-Africa meeting in Jo’berg (October 2019)
IeDEA ‘Treat all’ SSA dashboard screen shots from test site

IeDEA Treat All Africa Dashboard

Since late 2015, the World Health Organization (WHO) has expanded their HIV treatment guidelines to recommend that all people living with HIV initiate antiretroviral treatment (ART), regardless of disease stage and CD4 cell count. The purpose of the Treat All Africa Dashboard is to disseminate data and research focused on Treat All at IeDEA clinics in sub-Saharan Africa.

4 Africa sub-regions  21 Countries  240 IeDEA clinics

1.4M people living with HIV ever enrolled
HIV Care Continuum among newly enrolled patients at IeDEA Clinics

- **1820** Patients newly enrolled in 2017
- **79%** Initiated ART within 12 mo. of enrollment
- **51%** Initiated ART within 30 days of enrollment
- **36%** Initiated ART within 14 days of enrollment
- **30%** Initiated ART within 7 days of enrollment
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Acknowledgements

• The IeDEA Consortium Regional PIs and teams

• IeDEA Treat All Dashboard team (Stephany Duda, Ben Katz, Ellen Brazier, Ashish Joshi)

• IeDEA Consensus Statement Working Group on ‘Treat all’ Research Priorities in sub-Saharan Africa
  • Diane Addison, Keri Althoff, Ellen Brazier, Barbara Castelnuovo, Craig Cohen, Morna Cornell, Mary-Ann Davies, Geraldina Dominguez, Stephany Duda, Aimee Freeman, Antoine Jaquet, Olivia Keiser, April Kimmel, Kathryn Lancaster, Valerie Leroy, Janne Markus, Rosemary McKaig, Pamela Murnane, Denis Nash (co-Chair), Dominque Nsonde, Amobi Onovo, Angela Parcesepe, Jean d’Amour Sinayoby, Annette Sohn, Per Von Groote, Rachel Vreeman, Gilles Wandeler, Radhika Wikramanayake, Carolyn Williams, Kara Wools-Kaloustian, Constantin Yiannoutsos, Marcel Yotebieng (co-Chair)

• Jacquelyne Alesi, Musah Lumumba, Lucy Wanjiku Njenga, S. Wakefield, Thomas LaSalvia and the End AIDS Coalition

• IeDEA Working Groups

• IeDEA All-Africa Meeting attendees, November 5-6, 2017, Kigali, Rwanda

• IeDEA consensus statement coordinating team: Ellen Brazier, Diane Addison, Radhika Wikramanayake, Marcel Yotebieng, Denis Nash

• **Funding**: National Institutes of Health Award Numbers R13AI134393, U01AI096299, U01AI069911, U01AI069924, U01AI069919, the US President’s Emergency Plan for AIDS Relief (PEPFAR), and travel support from the NIH Office of AIDS Research.