



90-90-90 Targets Workshop

July 21-22, 2018 • Amsterdam

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GLOBAL NETWORK OF
PEOPLE LIVING WITH HIV



HIV Care Engagement: Maximizing Individual and Population Health Outcomes

Jean B. Nachega, MD, PhD, MPH, DTM&H, FRCPE

Associate Professor of Epidemiology, Infectious Diseases & Microbiology
Graduate School of Public Health; University of Pittsburgh, PA, USA
JBN16@PITT.EDU

Adjunct Associate Professor of Epidemiology & International Health
Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
jnacheg1@jhu.edu

Professor of Medicine

Director, Center for Infectious Diseases

Stellenbosch University School of Medicine, Cape Town, South Africa
jnachega@sun.edu

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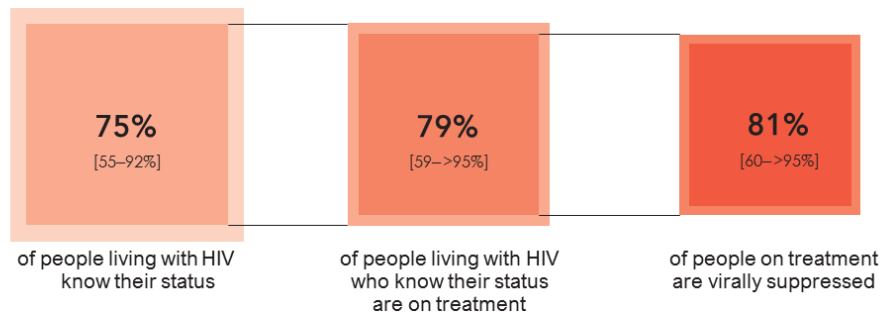


GLOBAL NETWORK OF
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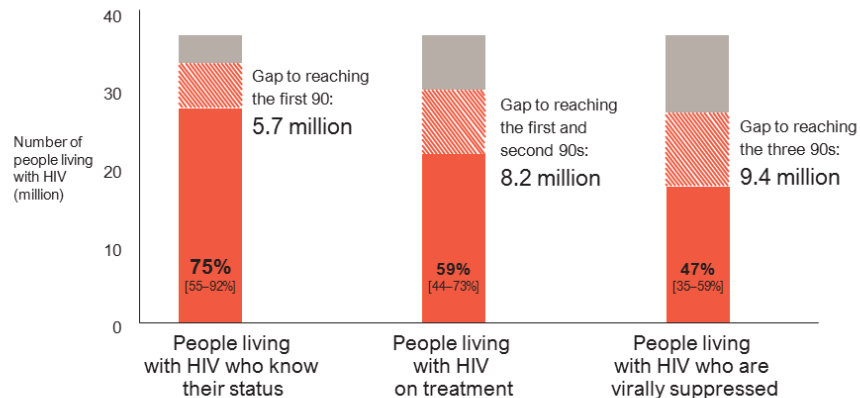


Remarkable progress on HIV testing and treatment

Progress towards 90–90–90, global, 2017



HIV testing and treatment cascade, global, 2017



Source: UNAIDS special analysis, 2018; see annex on methods for more details.

Implications of poor engagement

✓ Individual Level

- Delayed ART initiation & ART non-adherence
- Poor CD4 count & VL outcomes
- Emergence of HIV resistance
- Disease progression & death

✓ Population Level

- Role in transmission
 - Change in risk transmission behaviors
 - Impact of ART in reducing transmission

Keruly et al. *AJPH* 2002;92, Robbins et. al. *JAIDS* 2007;44, Park et al. *J Intern Med* 2007;261, Giordano et al. *Clin Infect Dis* 2007;44, Mugavero et al. *JAIDS* 2009;50, Marks et al. *AIDS* 2006;20, Metsch et al. *Clin Infect Dis* 2008;47, Cohen et al. *N Engl J Med* 2011;365

US Estimated Transmission, HIV Care Continuum

RIGHT PRACTICES



Widespread HIV testing and linkage to care enabling people living with HIV to access treatment early.



Full access to PrEP services for those whom it is appropriate and desired, with support for medication adherence for those using PrEP.



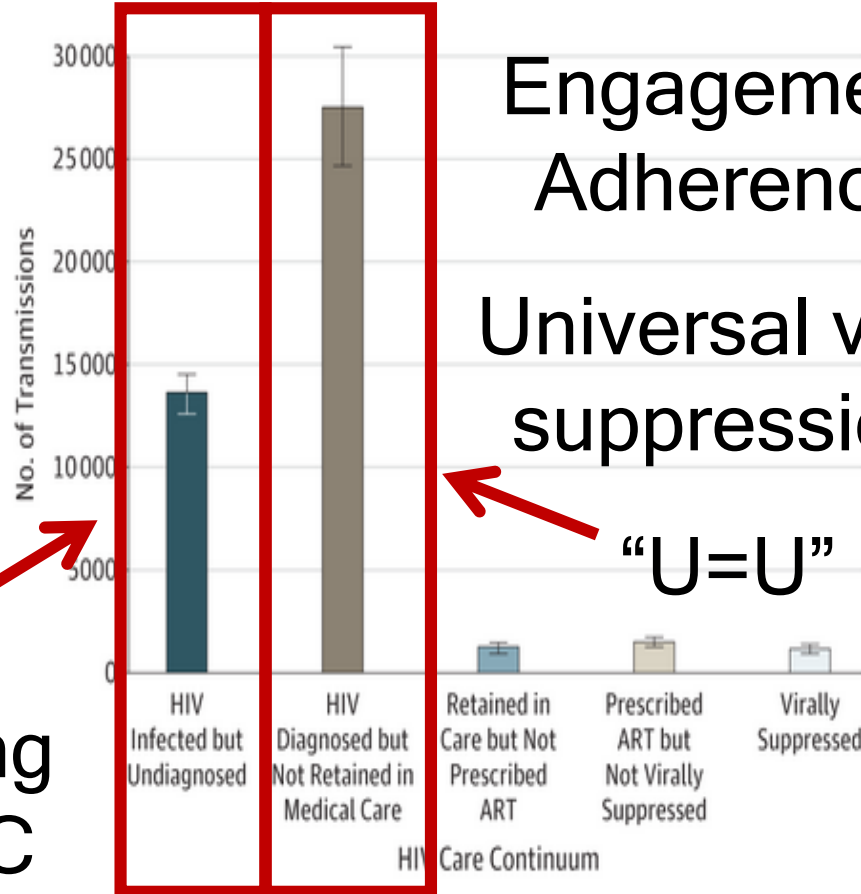
Broad support for people living with HIV to remain engaged in comprehensive care, including support for treatment adherence.



Universal viral suppression among people living with HIV.



Testing
& LTC



Engagement
Adherence



Universal viral
suppression

“U=U”



U=U: Undetectable=Untransmittable



HIV & AIDS – sharing knowledge, changing lives

“The scientific evidence is clear. Someone whose HIV is undetectable does not pose an infection risk to their sexual partners.”

For information on HIV you can rely on: www.aidsmap.com

#UequalsU

U=U Undetectable
Equals Untransmittable

New York State Becomes the First State in the U.S. to join U=U
September 28, 2017



Department
of Health



HEALTHY
CHICAGO

City of Chicago and Community Leaders Join U=U Campaign as Part of
New Effort to Reduce HIV Transmissions to Zero

CHICAGO DEPARTMENT OF PUBLIC HEALTH September 28, 2017

<https://www.preventionaccess.org/about>,

https://www.health.ny.gov/diseases/aids/ending_the_epidemic/,

https://www.cityofchicago.org/city/en/depts/cdph/provdrs/health_services/news/2017/september/city-of-chicago-and-community-leaders-join-u-u-campaign-as-part-.html

There has never been a more hopeful time in the history of AIDS.
Revolutionary advances in HIV prevention and treatment can now
bring the epidemics of HIV stigma and HIV to a halt.



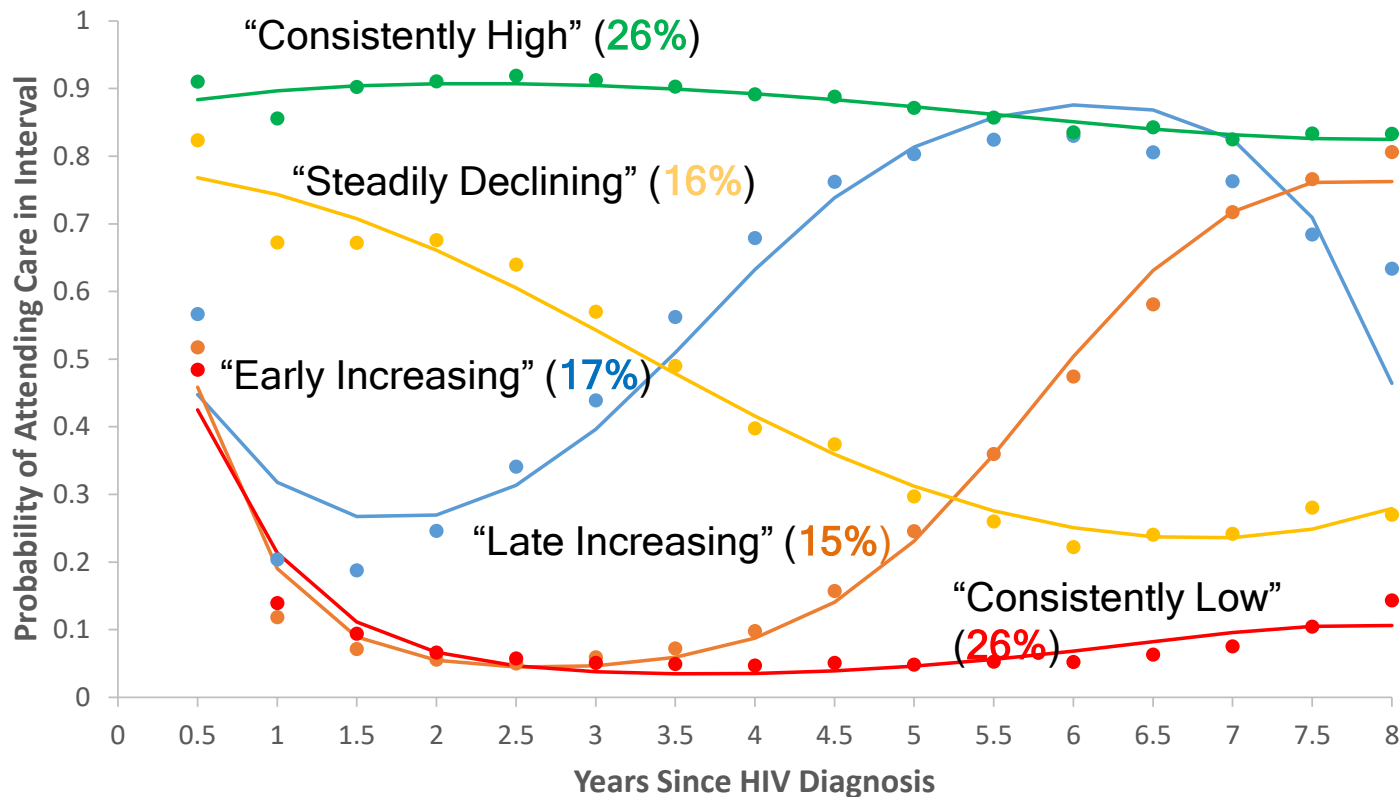
U=U

UNDETECTABLE
=
UNTRANSMITTABLE

A PERSON LIVING WITH HIV
WHO HAS AN UNDETECTABLE
VIRAL LOAD DOES NOT
TRANSMIT THE VIRUS TO THEIR
PARTNERS.

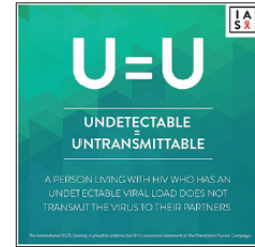
to endorse the U=U consensus statement of the Prevention Access Campaign.

Engagement in Care is Dynamic



Viral Suppression (VS): A Dynamic Biomarker

- 1-year clinic-based cohort study (n=10,942)
 - VS=83% based upon most recent VL
 - 66% with durable VS (all VL<200 c/mL)
 - 25% with ≥ 1 VS & 9% with NO measured VS
- 2-year surveillance-based study (n=425,624)
 - VS=83% based upon most recent VL
 - 62% with durable VS (all VL<200 c/mL)
 - Among 38% w/o durable VS, estimated time >200 c/mL=60% and >10,000 c/mL=30%



For more on U=U see <https://www.preventionaccess.org/undetectable>

For the letter from the CDC see https://docs.wixstatic.com/ugd/de0404_1f9f737da1674cdda5a42f7857cd4fa6.pdf

For the HPTN 052 trial interim analysis results see <http://www.nejm.org/doi/full/10.1056/NEJMoa1105243#t=article>

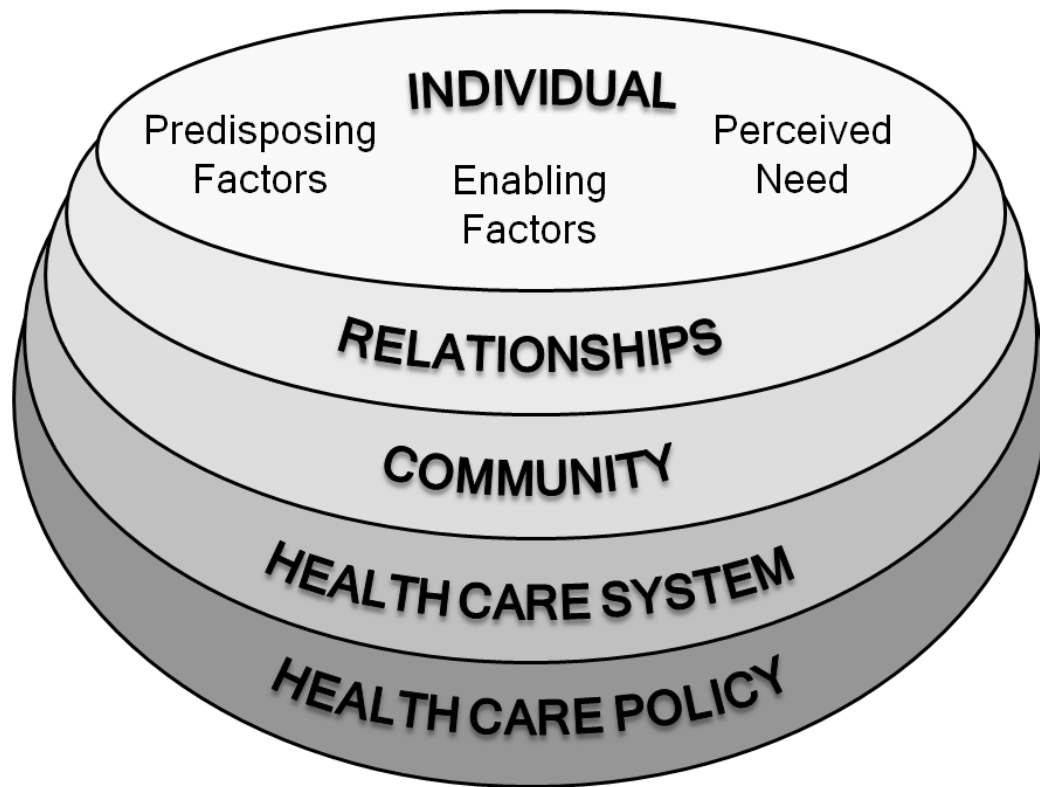
For the HPTN 052 trial final results see <http://www.nejm.org/doi/full/10.1056/NEJMoa1600693#t=article>

For the PARTNER study see <https://jamanetwork.com/journals/jama/fullarticle/2533066>

For the Opposites Attract study see <http://programme.ias2017.org/Abstract/Abstract/5469>

Marks et al. *JAIDS* 2016;73, Crepaz et al. *Clin Infect Dis* 2016;63, *Lancet* 2017;4

Factors associated w/ poor engagement



Factors associated w/ poor engagement

- ✓ Younger age
- ✓ Male sex in LMICs
- ✓ Racial / ethnic minority in US
- ✓ Psychosocial (Stigma, etc.)
- ✓ Pregnant and post-partum women
- ✓ Structural (Lack of health insurance, distance to clinic, unstable housing, food insecurity, etc.)
- ✓ Mental illness (depression, etc.)
- ✓ Substance abuse (alcohol, drugs, etc.)
- ✓ Unmet needs for supportive services

Keruly et al. *AJPH* 2002;92, Robbins et. al. *JAIDS* 2007;44, Giordano et al. *Clin Infect Dis* 2007;44, Mugavero et al. *JAIDS* 2009;50, Metsch et al. *Clin Infect Dis* 2008;47, Hall et al. *JAIDS* 2012;60, Hightow-Weidman et al. *AIDS Pt Care and STDs* 2011;S1:S31, Torian et al. *Arch Intern Med* 2008;168:1181

Retention in HIV care among adolescents

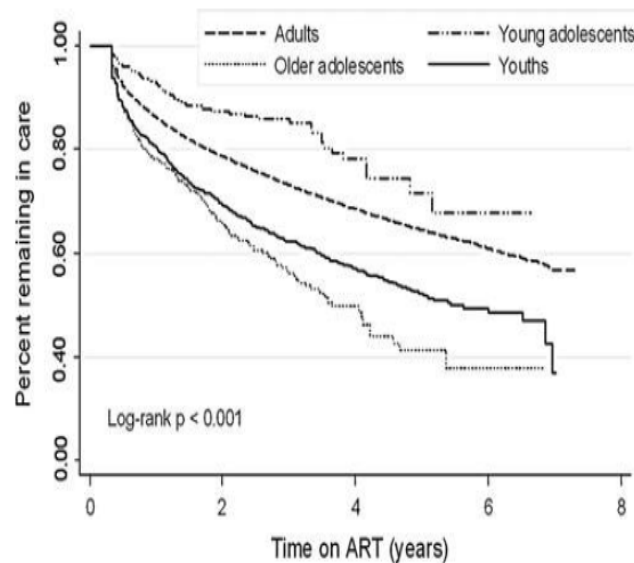
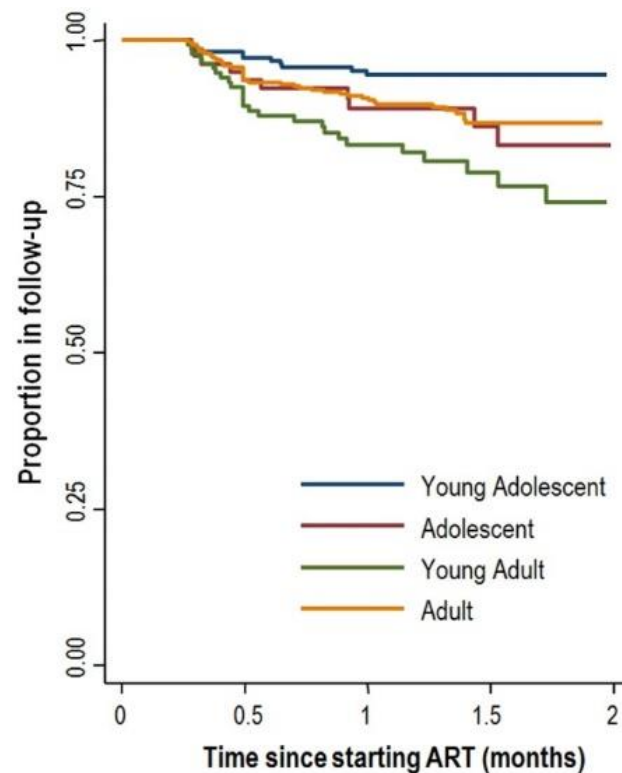


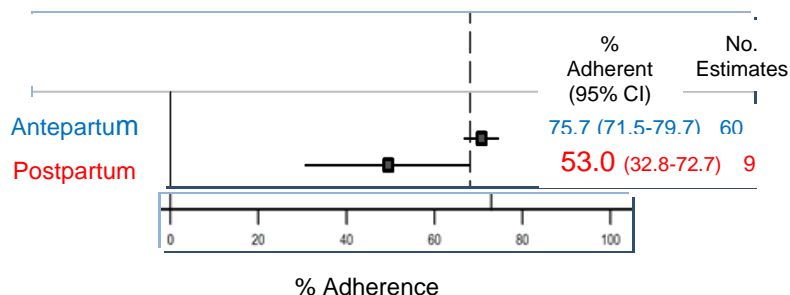
FIG. 1. Crude Kaplan-Meier survival curve showing percentage remaining in care any time after ART initiation, stratified by age category [young adolescents ($n=310$), older adolescents ($n=342$), young adults ($n=1,599$) and adults ($n=40,176$)]. The log-rank test for the percentage remaining in care was $p<0.001$.



Challenge: ART Adherence During Pregnancy and Postpartum

Nachega J et al. AIDS 2012;26:2039-52

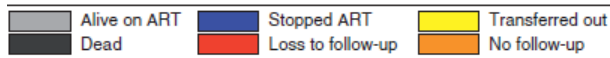
- Meta-analysis 51 studies in 20,153 pregnant women.
- Adequate adherence defined as >80% adherence to doses.
- Overall, only 73% reported >80% adherence.



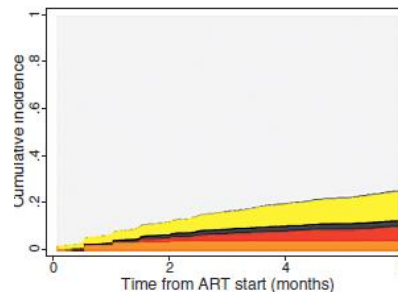
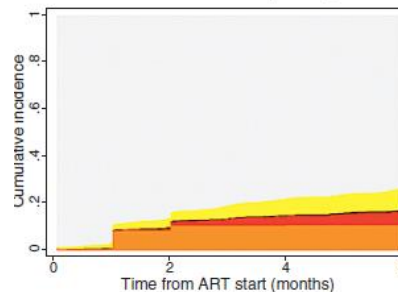
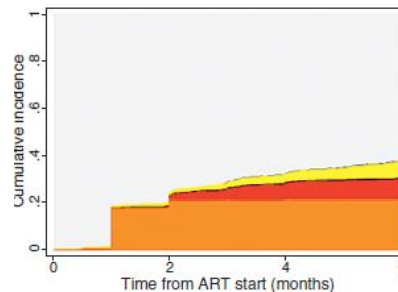
- Adherence was significantly worse in the postpartum period

Retention in Care Option B+ Malawi

Tenthani L et al. AIDS 2014;28:589-98



- Option B+ indication and ART start during pregnancy
 - No f/u or lost f/u, **29.4%**
- Option B+ indication and ART start after delivery while BF
 - No f/u or lost f/u, **16.1%**
- WHO stage 3/4 and/or CD4 <350
 - No f/u or lost f/u, **9.6%**



Retention of Pregnant/Breastfeeding Women on ART in Option B+ Era Still Not Optimal

Haas AD et al. Lancet HIV 2016;3:e175-182

- Data from Malawi ART program 2011-2013; 14,630 start ART for Option B+ and 14,515 start ART for own health.
- Option B+ women had higher risk of LTFU in 1st 2 years on ART compared to those starting ART for clinical reasons:
 - aOR 2.5 (2.1-2.9) ↑ risk LTFU starting ART during BF
 - aOR 4.7 (4.3-5.2) ↑ risk LTFU starting ART during pregnancy
- Overall, 69.7% in Option B+ retained at 3 years:
 - **1st year LTFU high, 21.6%**
 - 2nd year LTFU moderate, 5.7%
 - 3rd year LTFU low, 0.8%

Clinical Guidelines

Guidelines for Improving Entry Into and Retention in Care and Antiretroviral Adherence for Persons With HIV: Evidence-Based Recommendations From an International Association of Physicians in AIDS Care Panel

Melanie A. Thompson, MD; Michael J. Mugavero, MD, MHSc; K. Rivet Amico, PhD; Victoria A. Cargill, MD, MSCE; Larry W. Chang, MD, MPH; Robert Gross, MD, MSCE; Catherine Orrell, MBChB, MSc, MMed; Frederick L. Altice, MD; David R. Bangsberg, MD, MPH; John G. Bartlett, MD; Curt G. Beckwith, MD; Nadia Dowshen, MD; Christopher M. Gordon, PhD; Tim Horn, MS; Princy Kumar, MD; James D. Scott, PharmD, MEd; Michael J. Stirratt, PhD; Robert H. Remien, PhD; Jane M. Simoni, PhD; and Jean B. Nachega, MD, PhD, MPH



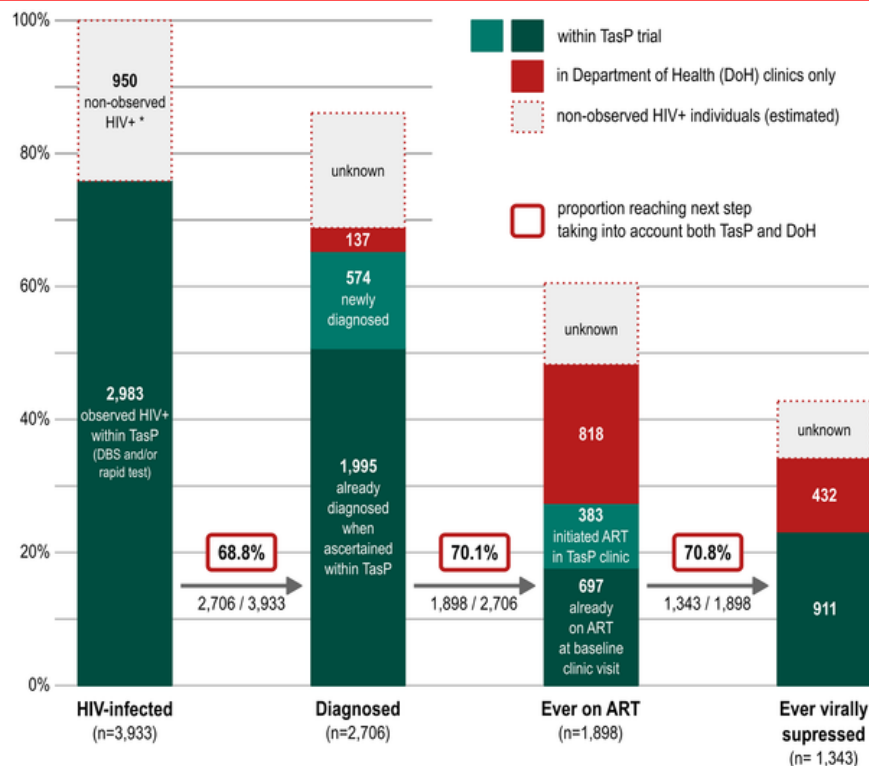
Entry Into & Retention In HIV Care

- Systematic **monitoring** of successful **entry** into HIV care (II A) and **retention** in HIV care (II A) is recommended for all individuals diagnosed with HIV.
- Brief, **strengths-based case management** for individuals with a new HIV diagnosis is recommended (II B).
- **Intensive outreach** for individuals not engaged in medical care within 6 months of a new HIV diagnosis may be considered (III C).
- Use of **peer or paraprofessional patient navigators** may be considered (III C).

Novel Evidence-Based Interventions to Address the Second & Third “90s” Targets Globally

- “Test and treat” reflecting the new cascade
 - Universal home-based HIV testing ^{ANRS TasP 12249}
 - Hybrid mobile HIV testing ^{SEARCH}
 - RAPID ART ^{Pilcher C.}
- Integration, Task shifting, and Decentralization
 - Cash transfer ^{Yotebieng M.}
 - Mothers2mothers mentor models ^{Sam-Agudu N., Phiri S.}
 - Differentiated service delivery models (DSD) ^{Grimsrud A.}
- Implementation challenges of mHealth to scale ^{Lester R.}

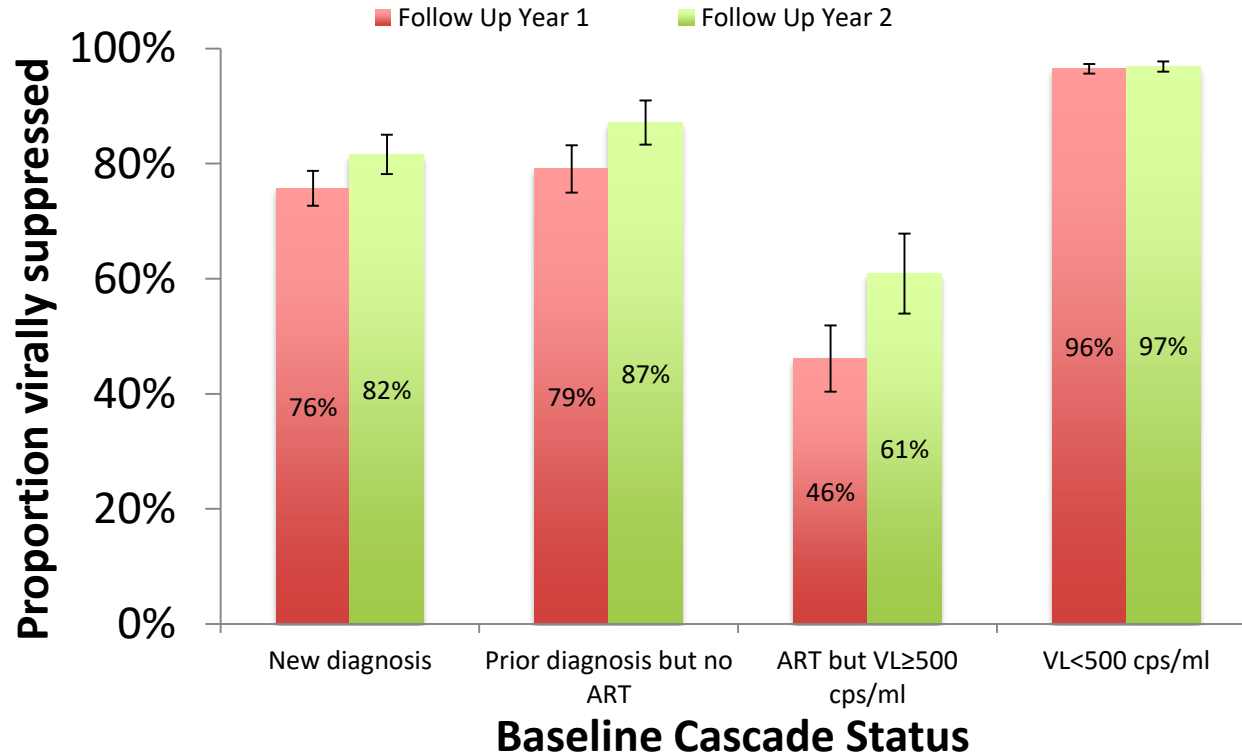
ANRS 12249: Estimated HIV care cascade among all HIV-infected individuals at the population level, KZN Province, South Africa



Iwuji CC, Orne-Gliemann J, Larmarange J, Okesola N, Tanser F, et al. (2016) PLOS Medicine 13(8): e1002107.

SEARCH Test & Treat Study in Kenya and Uganda: Viral Suppression Over Time Among Baseline HIV+

Petersen M et al. JAMA 2017



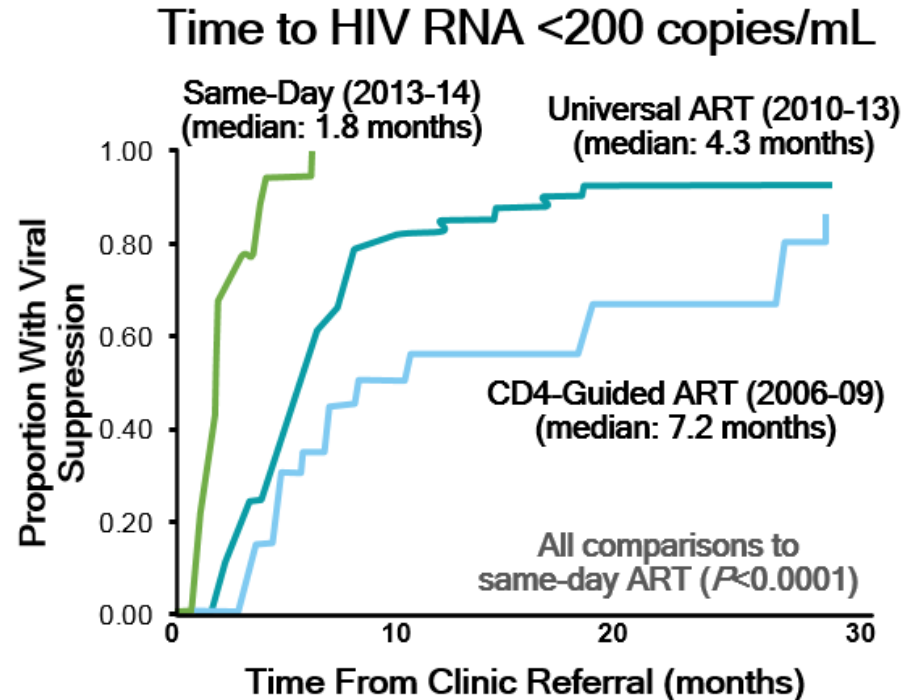
RATIONALE FOR RAPID ART

- LTFU is high during the period from HIV testing to ART initiation
- Multiple visits increase the risk of LTFU
- Contributes to late initiation of ART, higher mortality rates, and ongoing transmission

San Francisco RAPID: Same Day ART Initiation

Time from HIV Dx to:	RAPID (n=39)	SOC (n=47)
ART	1 (0-7)	22 (14-48)
Clinic referral	6 (2-11)	11 (3-4)
VL<200 c/mL	65 (52-119)	170 (79-363)

Prospective Cohort (consecutive pts with new HIV diagnosis, 2013-2014).¹
Same-day ART initiation cohort: pts with acute or recent infection (<6 months) or CD4 <200 cells/mm³.

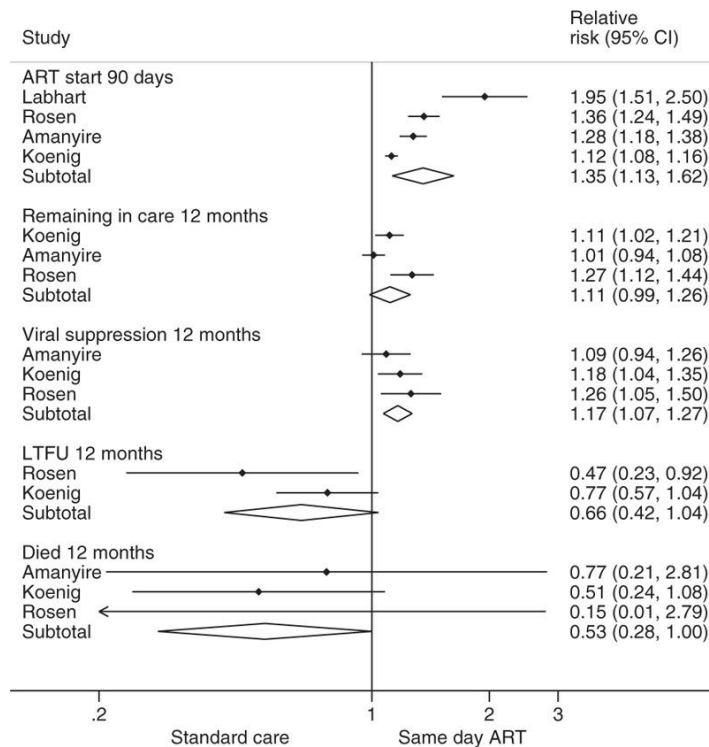


RAPID ART: Three Randomized Trials

- South Africa – RapIT (Rosen et al. *PLOS Med*, 2016)
- Uganda – START-ART (Amanyire et al, *Lancet HIV*, 2016)
- Haiti – (Koenig et al, *PLOS Med*, 2017)

Benefits and risks of rapid initiation of ART

Ford N et. Al. AIDS. 2018 Jan 2; 32(1): 17–23



Evidences for Rapid ART

- 3 RCTs
 - Increased likelihood of starting ART within 90 days (RR 1.3)
 - Increased 12-month retention (RR 1.12)
 - Increased viral suppression (RR 1.18)
 - Decreased 12-month mortality (RR 0.47)
- 11 Observational studies
 - Increased likelihood of starting ART within 90 days (RR 1.53)
 - Shorter time to Viral Suppression
 - Rapid ART did not increase retention (RR 0.97)

WHO Recommendations for Rapid ART Initiation

- “Rapid ART initiation should be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment.”
 - “Rapid” defined as within 7 days
- “ART initiation should be offered on the same day to people who are ready to start.”
- Goal: To improve linkage to care and reduce LTFU
- ART should be deferred if documentation of clinical symptoms suggesting TB or cryptococcal meningitis to avoid paradoxical worsening of the existing infection that can be life threatening (CNS-IRIS)

Guidelines for managing advanced HIV disease and rapid initiation of ART, July 2017. Geneva: WHO; 2017.



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GLOBAL PUBLIC HEALTH



EFFECTIVENESS OF CONDITIONAL CASH TRANSFERS TO INCREASE RETENTION IN CARE AND ADHERENCE TO PMTCT SERVICES: A RANDOMIZED CONTROLLED TRIAL, KINSHASA, DRC

M. Yotebieng, H. Thirumurthy, K.E. Moracco, B. Kawende, J.L.
Chalachala, L.K. Wenz, N.L.R. Ravelomanana, A. Edmonds,
D. Thompson, E. Okitolonda, F. Behets

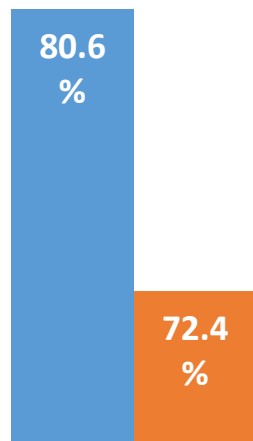


R01 HD075171

Yotebieng M. et al. Lancet HIV 2016

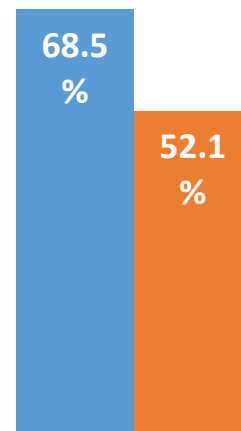
Cash Transfer & Retention and adherence to PMTCT Services at Six Weeks, Kinshasa, DR Congo

Retention in care



RR: 1.11 (95% CI 1.00-1.24)

Adherence



RR 1.26; (95% CI 1.08-1.48)

Mothers2mothers Mentors Models

Malawi, Option B+
21 sites, 1,269 women
SOC v Facility v Community PS
24 month retention: 66 v 80 v 83%

*Levison Chivaula, PhD, MA,||| Michael Eliya, MPH, Dip Nursing,¶¶ Frank Chimbwandira, MBBS, MPH,¶¶
Mina C. Hosseinipour, MD, MPH,†† and the PURE Malawi Consortium*

Nigeria, Option B
20 sites, 497 women
Unstructured v structured PS
6 month retention: 25 v 62%

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Zimbabwe, Option B+
30 sites, 350 women
SOC v Facility-based mother support
groups
12 month retention: Regular vs non-
regular attendance 3x higher

*Patt
Joanna
Abig
Geo*

*roups in
)
DS, MBChB,‡
gezi, PhD,¶
ocSc,‡
study group*

JAIDS 2017; 75 INSPIRE Supplement

Differentiated Service Delivery (DSD) Models for “Stable” Patients in LMICs

	Individual	Group
Facility-based	Fast track Appointment spacing	ART clubs Teen clubs Family pick up
Community-based	Outreach model PODI model*	Community ART Groups or Clubs (CAGs or CACs)

* PODI: Points de Distribution Communautaires

	Appointment spacing and fast-track drug refill	Adherence Clubs	Community ART Distribution Points (PODI)	Community ART Groups (CAGs)
Project	Chiradzulu, Malawi	Khayelitsha, South Africa	Kinshasa, DR Congo	Tete, Mozambique
Context	Rural	Urban	Urban	Rural
ART refill	3-monthly	2-monthly	3-monthly	Monthly
Mode	Individual	Group	Individual	Group
Where	Health facility	Health facility or community venues	Community distribution points	Patients' homes
Led by	Lay worker	Lay worker	Lay worker of network of PLHIV	Self-formed group of patients
Clinical consultation	6-monthly	Yearly	Yearly	6-monthly
Blood drawing	Yearly viral load	Yearly viral load	Yearly CD4	6-monthly CD4

Clubs as models of ART delivery & Adherence Support to Stable Patients, Khayelitsha, South Africa

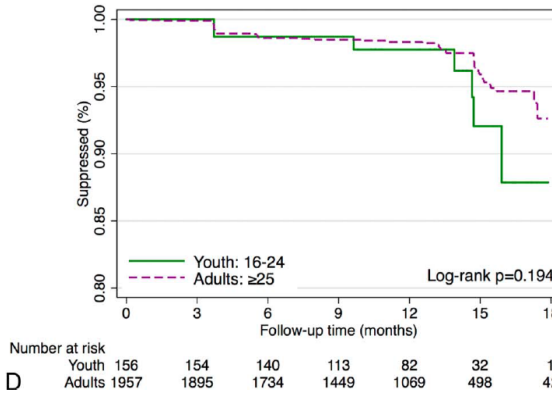
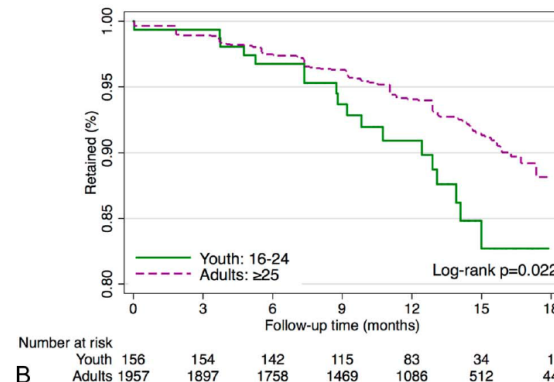
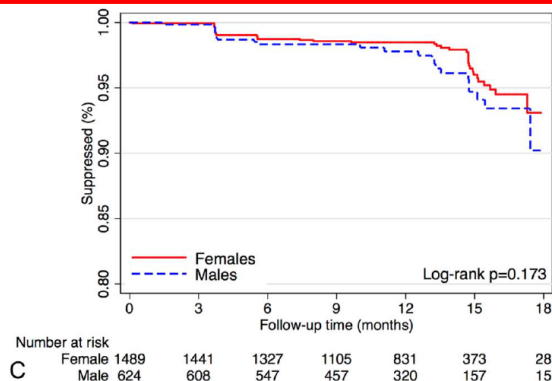
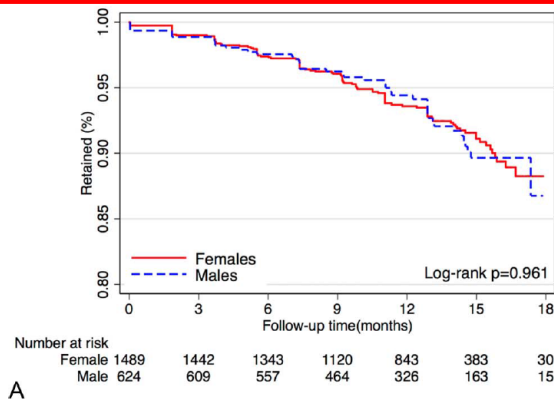


Slide courtesy of Dr. Gilles Van Cutsem, Médecins Sans Frontières, Cape Town, South Africa

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Community Adherence Clubs (CAC) in South Africa: Retention and Virologic Suppression



- CAC participation was associated with a 67% reduction in the risk of LTFU (aHR: 0.33, 95% CI: 0.27 to 0.40) compared with community health centre
- LTFU and viral rebound were twice as likely in youth compared with older patients, but no difference was observed by sex

Improving Engagement in HIV Care for HIV-Infected Adolescents

Malawi: MacKenzie et al JIAS 2017

Nested case-control study, 1 hospital
Adolescent 'Teen Club' model
Lower treatment dropout (OR .27)

South Africa: Zandoni et al PLOSOne 2017

Retrospective cohort, 1 hospital
Adolescent-friendly clinic
Higher viral suppression (OR 3.7)
Higher retention in care (OR 8.5)

South Africa: Fatti et al JIAS 2018

Retrospective cohort study, 47 clinics
Kheth'Impilo community based support by lay workers
Less mortality (AHR .52)
40% lower loss-to-follow-up (AHR .60)
Less viral failure (OR .24)

PMTCT *mHealth* Adherence & Retention Trials

	Message topics	Design, N & Setting (s)	Frequency	Outcomes	End
Kassaye ¹ cRCT	PMTCT services, reminders, adherence, motivation, MCH	Cluster RCT, Kenya	SMS 3-6 per week	No effect on maternal ARV uptake, EID	2016
WelTel ²	WelTel 'shida' with escalation call	RCT, 600; Kenya	weekly	Retention, adherence 24 m pp, CEA	2017
Mobile WACH ³	2-way or 1-way SMA vs. control	RCT, 825; Kenya	weekly	Retention, adherence, VL 24 m pp, CEA	2019
Mwapasa ⁴ PRIME	Reminder SMS if missed visit clinic vs. Integrated HIV care vs. SOC	Cluster RCT, 1230; Malawi	If missed clinic visit	Retention	2018
Nachega ⁵ SANTU	2-way Weekly SMS vs. male involvement vs. control	Factorial Design, 1200; South Africa, Nigeria, Tanzania, Uganda	weekly	MTCT Rates, Maternal VL, Adherence, Retention, CEA	2021

1. Kassaye AIDS Res&Treat 2016; 2. Awiti BMC Med Inf Dec Mak 2016; 3. Drake Clin Trials 2017; 4. Mwapasa JAIDS 2014; 5. Nachega et al., Protocol Under Submission)

Conclusions

- Engagement in HIV care is not a one-off event-require maintenance life-long and critical to individual and population health outcomes.
- Engagement is determined by multiple factors: individual, social and structural
- Need a menu of interventions tailored to context and resources
- Interventions need to combine a public health approach *AS WELL AS* being responsive to individual needs

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Slides

Lynne Mofenson
Michael Mugavero
Richard Lester
Nadia Sam-Agudu
Marcel Yotebieng



Thank You!

