90-90-90 Targets Workshop
July 21-22, 2018 • Amsterdam

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BRITISH COLUMBIA CENTRE FOR EXCELLENCE in HIV/AIDS
GLOBAL NETWORK OF PEOPLE LIVING WITH HIV

IAS
HIV Care Engagement: Maximizing Individual and Population Health Outcomes

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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

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.

Engagement Adherence

Universal viral suppression

"U=U"

Testing & LTC

Skarbinski et al. JAMA Intern Med 2015;175
U=U: Undetectable=Untransmittable

"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

New York State Becomes the First State in the U.S. to join U=U
September 20, 2017

Department of Health

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

https://www.preventionaccess.org/about,
https://www.health.ny.gov/diseases/aids/ending_the_epidemic/,
Engagement in Care is Dynamic

“Consistently High” (26%)

“Steadily Declining” (16%)

“Early Increasing” (17%)

“Late Increasing” (15%)

“Consistently Low” (26%)

Powers et al, JAIDS 2017; 74(S2), Slide courtesy of Julie Dombrowski
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%

Factors associated with poor engagement

Adapted from: Mugavero et al. Clin Infect Dis 2011;52(S2)
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

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

<table>
<thead>
<tr>
<th></th>
<th>% Adherent (95% CI)</th>
<th>No. Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antepartum</td>
<td>75.7 (71.5-79.7)</td>
<td>60</td>
</tr>
<tr>
<td>Postpartum</td>
<td>53.0 (32.8-72.7)</td>
<td>9</td>
</tr>
</tbody>
</table>

% Adherence
Retention in Care Option B+ Malawi


- 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


- 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
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 \(^{\text{ANRS TasP 12249}}\)
  - Hybrid mobile HIV testing \(^{\text{SEARCH}}\)
  - RAPID ART \(^{\text{Pilcher C.}}\)
- Integration, Task shifting, and Decentralization
  - Cash transfer \(^{\text{Yotebieng M.}}\)
  - Mothers2mothers mentor models \(^{\text{Sam-Agudu N., Phiri S.}}\)
  - Differentiated service delivery models (DSD) \(^{\text{Grimsrud A.}}\)
- Implementation challenges of mHealth to scale \(^{\text{Lester R.}}\)
ANRS 12249: Estimated HIV care cascade among all HIV-infected individuals at the population level, KZN Province, South Africa

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

Petersen M et al. JAMA 2017

Proportion virally suppressed

Baseline Cascade Status

0% 20% 40% 60% 80% 100%

New diagnosis 76% 79% 46% 96%
Prior diagnosis but no ART 82% 87% 61% 97%
ART but VL≥500 cps/ml
VL<500 cps/ml
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

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

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/mm\(^3\).
RAPID ART: Three Randomized Trials

- **South Africa** – RapIT (Rosen et al. *PLOS Med*, 2016)
Benefits and risks of rapid initiation of ART

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART start 90 days</td>
<td></td>
</tr>
<tr>
<td>Labhart</td>
<td>1.95 (1.51, 2.50)</td>
</tr>
<tr>
<td>Rosen</td>
<td>1.36 (1.24, 1.49)</td>
</tr>
<tr>
<td>Amanyire</td>
<td>1.28 (1.18, 1.38)</td>
</tr>
<tr>
<td>Koenig</td>
<td>1.12 (1.06, 1.16)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>1.35 (1.13, 1.62)</td>
</tr>
<tr>
<td>Remaining in care 12 months</td>
<td></td>
</tr>
<tr>
<td>Koenig</td>
<td>1.11 (1.02, 1.21)</td>
</tr>
<tr>
<td>Amanyire</td>
<td>1.01 (0.94, 1.08)</td>
</tr>
<tr>
<td>Rosen</td>
<td>1.27 (1.12, 1.44)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>1.11 (0.99, 1.26)</td>
</tr>
<tr>
<td>Viral suppression 12 months</td>
<td></td>
</tr>
<tr>
<td>Amanyire</td>
<td>1.09 (0.94, 1.26)</td>
</tr>
<tr>
<td>Koenig</td>
<td>1.18 (1.04, 1.35)</td>
</tr>
<tr>
<td>Rosen</td>
<td>1.26 (1.05, 1.50)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>1.17 (1.07, 1.27)</td>
</tr>
<tr>
<td>LTFU 12 months</td>
<td></td>
</tr>
<tr>
<td>Rosen</td>
<td>0.47 (0.23, 0.92)</td>
</tr>
<tr>
<td>Koenig</td>
<td>0.77 (0.57, 1.04)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>0.66 (0.42, 1.04)</td>
</tr>
<tr>
<td>Died 12 months</td>
<td></td>
</tr>
<tr>
<td>Amanyire</td>
<td>0.77 (0.21, 2.81)</td>
</tr>
<tr>
<td>Koenig</td>
<td>0.51 (0.24, 1.08)</td>
</tr>
<tr>
<td>Rosen</td>
<td>0.15 (0.01, 2.79)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>0.53 (0.28, 1.00)</td>
</tr>
</tbody>
</table>
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)

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

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

Retention in care

- Intervention: 80.6%
- Control: 72.4%
- RR: 1.11 (95% CI 1.00-1.24)

Adherence

- Intervention: 68.5%
- Control: 52.1%
- 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%

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

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

JAIDS 2017; 75 INSPIRE Supplement
Differentiated Service Delivery (DSD) Models for “Stable” Patients in LMICs

<table>
<thead>
<tr>
<th></th>
<th>Individual</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Facility-based</strong></td>
<td>Fast track Appointment spacing</td>
<td>ART clubs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Teen clubs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family pick up</td>
</tr>
<tr>
<td><strong>Community-based</strong></td>
<td>Outreach model PODI model*</td>
<td>Community ART Groups or Clubs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(CAGs or CACs)</td>
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</tbody>
</table>

* PODI: Points de Distribution Communautaires
<table>
<thead>
<tr>
<th>Project</th>
<th>Chiradzulu, Malawi</th>
<th>Khayelitsha, South Africa</th>
<th>Kinshasa, DR Congo</th>
<th>Tete, Mozambique</th>
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</thead>
<tbody>
<tr>
<td>Context</td>
<td>Rural</td>
<td>Urban</td>
<td>Urban</td>
<td>Rural</td>
</tr>
<tr>
<td>ART refill</td>
<td>3-monthly</td>
<td>2-monthly</td>
<td>3-monthly</td>
<td>Monthly</td>
</tr>
<tr>
<td>Mode</td>
<td>Individual</td>
<td>Group</td>
<td>Individual</td>
<td>Group</td>
</tr>
<tr>
<td>Where</td>
<td>Health facility</td>
<td>Health facility or community venues</td>
<td>Community distribution points</td>
<td>Patients’ homes</td>
</tr>
<tr>
<td>Led by</td>
<td>Lay worker</td>
<td>Lay worker</td>
<td>Lay worker of network of PLHIV</td>
<td>Self-formed group of patients</td>
</tr>
<tr>
<td>Clinical consultation</td>
<td>6-monthly</td>
<td>Yearly</td>
<td>Yearly</td>
<td>6-monthly</td>
</tr>
<tr>
<td>Blood drawing</td>
<td>Yearly viral load</td>
<td>Yearly viral load</td>
<td>Yearly CD4</td>
<td>6-monthly CD4</td>
</tr>
</tbody>
</table>
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
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: Zanoni et al PLOSOOne 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

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

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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