Facilitating Long-Term ART Adherence to Achieve Persistence

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• Adherence, Virologic Outcomes and Drug Resistance
• Adherence vs. Persistence
• Structural, Demographics, Regimen-Specific Barriers for Sustained Adherence and Persistence
• Evidence-Based ART Adherence Interventions
• Conclusions
The Lifesaving Impact of Highly Active Antiretroviral Therapy (ART)
Adherence to NNRTI-Based ART Predicts Virologic Response in a Linear Dose-Response Fashion

Levels of Adherence to ART Required for Virologic Suppression Among Type of ARV Regimens

Adherence to Antiretroviral Therapy Reduces Hospitalization Costs

Adherence vs. Persistence

Adherence (Adherence)

HIV-1 RNA (HIV-1 RNA)

Regimen change

Development of resistance

Lower limit of detection

Bae JW et al. AIDS 2011, 25:279–290
Estimated Risk of Resistance by Level of Adherence and Drug Class

Global HIV Treatment Cascade, 2021

- **People living with HIV who know their status**: 89% [80-98%]
- **People living with HIV who are on treatment**: 82% [70-95%]
- **People living with HIV who are virally suppressed**: 70% [61-82%]
- 74% [66-84%] for men
- 65% [56-75%] for women

**Legend**:
- **WOMEN (AGED 15+ YEARS AND OLDER) LIVING WITH HIV**
- **MEN (AGED 15+ YEARS AND OLDER) LIVING WITH HIV**
HIV Cascade of Care: Missed Opportunities in the US

HIV-Infected: >25 Years of Age (n=896,800)

- Diagnosed: ~88%
- Linked To Care: ~73%
- Retained in Care: ~40%
- Viral Suppression: ~28%

HIV-Infected: 13-29 Years of Age (n=78,949)

- Diagnosed: 40%
- Linked To Care: 25%
- Retained in Care: 11%
- Viral Suppression: 6%

Rates of Viral Suppression in People Diagnosed with HIV Infection, United States

- U.S. National Average: 59.8%
- Ryan White HIV/AIDS Program: 88.1%

Source: HRSA,
Relative Risk of VL Suppression in Adolescents vs. Adults

Time to VL rebound, comparing 154 adolescents (11-19 yod) to 1380 young adults (20-29 yod) and to 6242 adults
ART Adherence During & After Pregnancy in LMICs (Pre-Option B+ Era): Systematic Review and Meta-Analysis of 51 Studies with 20,153 Women

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

ART adherence in pregnancy (defined as % reporting >80% adherence to ART) is below that recommended for adequate virologic suppression. Optimal adherence remains a challenge during pregnancy, especially during postpartum period.
Adherence to HIV antiretroviral therapy among pregnant and postpartum women during the Option B+ Era: 12-month cohort study in urban South Africa and rural Uganda.

Cascade of HIV care for Brazilian MSM in Rio de Janeiro, Brazil.

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0157309
Barriers for HIV Control in US vs. Africa

• In US, barriers at the societal, healthcare system, and individual levels, such as stigma, racism, fragmented care, housing and food insecurity, poverty, and mental health and substance use issues are ongoing challenges.

• Meanwhile, demographics (e.g., 90% of global pediatric HIV infection occurs in sub-Saharan Africa, but there is only 50% pediatric ART coverage), and economic (poverty), socio-cultural (stigma), and political (e.g., criminalization of sexual minorities) are key challenges in Africa.
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

NIH Office of AIDS Research (OAR)
U.S. Department of Health and Human Services

International Association of Physicians in AIDS Care
Among regimens of similar efficacy and tolerability, \textit{once-daily regimens} are recommended for \textit{treatment-naive} patients beginning ART (II B).

Switching \textit{treatment-experienced patients} receiving complex or poorly tolerated regimens to \textit{once-daily regimens} is recommended, given regimens with \textit{equivalent efficacy} (III B).

Among regimens of equal efficacy and safety, \textit{fixed-dose combinations} are recommended to decrease pill burden (III B).
Antiretroviral Therapy Adherence Rate, Virological Response, and Pill Burden

FDA Approves First Extended-Release, Injectable Drug Regimen for Adults Living with HIV

- Cabenuva (cabotegravir + rilpivirine) administered by injection once every 4 weeks
- 8-week dosing under review
Long Acting Injectable Nano-Suspensions

TMC278LA (Rilpivirine; PATH)

- NNRTI (Rilpivirine)
- Oral formulation in Complera™
- Long acting: up to 3 months?
- Multiple trials:
  - Dose ranging PK; PK/PD
  - Phase-2: HPTN 076

Cabotegravir (GSK ‘744; ViiV)

- Integrase inhibitor
- Similar to Dolutegravir
- Safe in humans with oral run-in
- Activity up to 3 months
- NHP model efficacy
- Phase 2: Éclair and HPTN 077
Opportunities and Challenges of LA-ART

- Less frequent dosing
- Avoidance of “Pill Fatigue”
- Protection of health privacy
- Avoidance of stigma
- Improve Adherence???

- Injection volume
- Need for oral lead in
- INSTI/NNRTI resistance if missed doses
- Cold chain storage (for RPV)
- Dosing for children and pregnant women
- Cost
Differentiated Service Delivery (DSD) Model for Stable HIV Patients

- ART Initiation and refills
- Clinical monitoring
- Adherence support
- Laboratory tests
- OI treatment
- Psychosocial support

- Monthly
- Bimonthly
- Every 3 months
- Every 6 months

Service intensity

Service frequency

People living with HIV

Service location

Health worker cadre

- Physician
- Clinical officer
- Nurse
- Pharmacist
- Community health worker
- Patient, peers and family
Supplement: Short Report | Open Access

Community-based differentiated service delivery models incorporating multi-month dispensing of antiretroviral treatment for newly stable people living with HIV receiving single annual clinical visits: a pooled analysis of two cluster-randomized trials in southern Africa

Geoffrey Fati, Nicoletta Ngorima-Mabhena, Appolinaire Tiam, Betty Bawuba Tukel, Tonderai Kasu, Trish Muzenda, Khotso Maile, Carl Lombard, Charles Chasela, Ashraf Grimwood

Outcomes of Three- Versus Six-Monthly Dispensing of Antiretroviral Treatment (ART) for Stable HIV Patients in Community ART Refill Groups: A Cluster-Randomized Trial in Zimbabwe

Geoffrey Fati, MBCChB, MPH,1,2 Nicoletta Ngorima-Mabhena, MBCChB, MSc,2 Lalwa Motshis, MBCChB, FCP,1 Trish Muzenda, MPH,1,4 Regina Choto, MBCChB, MPH,1 Tonderai Kasu, MBCChB, MSc,3 Taunayi A. Tafuma, MBCChB, MPH,3 Nyika Mahachi, MBCChB, MPH,4 Kudakwashe C. Tukudzwa, PhD,4 Tezio Apollo, MBCChB, MPH, MPA,4 Owen Mharugwi, MBCChB, MSc,4 Charles Chasela, PhD,5,6 Risa M. Hoffman, MD, MPH,4 and Ashraf Grimwood, MBCChB, MPH4

Twelve-Month Outcomes of Community-Based Differentiated Models of Multimonth Dispensing of ART Among Stable HIV-Infected Adults in Lesotho: A Cluster-Randomized Noninferiority Trial

Tiku, Betty B. MD, BS,a,b,c,d,e,f,g,h,i Tiku, Geoffrey MBCChB, MPH,a,b,c,d,e,f,g,h,i Tiku, Appolinaire MBCChB, DPH,a,b,c,d,e,f,g,h,i Ngorima-Mabhena, Nicoletta MBCChB, MSc,c,d,e,f,g,h,i Tiku, Vincent J. MBCChB, MPH,a,b,c,d,e,f,g,h,i Tshabalala, Sibusiso,a,b,c,d,e,f,g,h,i Daliy S. Sebelo, Veronica M. BSc,a,b,c,d,e,f,g,h,i Mabuza, Trish MPH,a,b,c,d,e,f,g,h,i Wolowara, Linus M. BSc,a,b,c,d,e,f,g,h,i Selibago, Lehlohang B,a,b,c,d,e,f,g,h,i Marphong, Tsepo-Noko BSc,a,b,c,d,e,f,g,h,i Maumela, Justin K. MSc,a,b,c,d,e,f,g,h,i Momoko, Ian MPH,a,b,c,d,e,f,g,h,i Dzupa, Francis MSc,a,b,c,d,e,f,g,h,i Mphahlele, Motlhatla MSc,a,b,c,d,e,f,g,h,i Kanyalwana, Nyikate MSc,a,b,c,d,e,f,g,h,i Kulu, Thabo MB BCH, MPH,a,b,c,d,e,f,g,h,i Nels, Thomas MD, MPH,a,b,c,d,e,f,g,h,i Saima, Ian MB BCH,a,b,c,d,e,f,g,h,i Chakala, Charles BSc,a,b,c,d,e,f,g,h,i DUSPM,a,b,c,d,e,f,g,h,i for ECHO Health

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Research Article | Open Access

Twenty-four-month outcomes from a cluster-randomized controlled trial of extending antiretroviral therapy refills in ART adherence clubs

Tal Cassidy, Anna Grimsrud, Claire Keene, Keltumsetse Lebelo, Helen Hayes, Catherine Orrell, Nompumelelo Zukuta, Tabitha Mutseyekwa, Jacqueline Vogel, Riddi Gertshenhaber, Lynne Wilkinson

First published: 19 December 2020 | https://doi.org/10.1002/jia2.25649 | Citations: 8

Clinical Trial Number: FACTR201810631281009.
Community-based DSD models incorporating multi-month dispensing of ART for newly stable people living with HIV receiving single annual clinical visits: a pooled analysis of two cluster-randomized trials in southern Africa

Impact of the COVID-19 lockdown on HIV care in 65 South African primary care clinics: an interrupted time series analysis

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The Lancet HIV
Volume 8 Issue 3 Pages e158-e165 (March 2021)
DOI: 10.1016/S2352-3018(20)30359-3

Findings
Between Jan 1, 2018, and July 31, 2020, we recorded 1 315 439 HIV tests. Between Jan 1, 2018, and June 15, 2020, we recorded 71 142 ART initiations and 2 319 992 ART collection visits. We recorded a median of 41 926 HIV tests per month before lockdown (January, 2018, to March, 2020; IQR 37 838–51 069) and a median of 38 911 HIV tests per month after lockdown (April, 2020, to July, 2020; IQR 32 699–42 756). In the Poisson regression model, taking into account long-term trends, lockdown was associated with an estimated 47–6% decrease in HIV testing in April, 2020 (incidence rate ratio [IRR] 0·524, 95% CI 0·446–0·615). ART initiations decreased from a median of 571 per week before lockdown (IQR 498–678), to 375 per week after lockdown (331–399), with an estimated 46–2% decrease in the Poisson regression model in the first week of lockdown (March, 30, 2020, to April 5, 2020; IRR 0·538, 0·459–0·630). There was no marked change in the number of ART collection visits (median 18 519 visits per week before lockdown [IQR 17 074–19 922] vs 17 863 visits per week after lockdown [17 509–18 995]; estimated effect in the first week of lockdown IRR 0·932, 95% CI 0·794–1·093). As restrictions eased, HIV testing and ART initiations gradually improved towards pre-lockdown levels (slope change 1·183/month, 95% CI 1·113–1·256 for HIV testing; 1·156/month, 1·085–1·230 for ART initiations).

Interpretation
ART provision was generally maintained during the 2020 COVID-19 lockdown, but HIV testing and ART initiations were heavily impacted. Strategies to increase testing and treatment initiation should be implemented.
# Adherence/Retention in Care Interventions in Pregnant and Post-Partum Women Living with HIV

<table>
<thead>
<tr>
<th>Author/Study Name</th>
<th>Intervention(s)</th>
<th>Design, N &amp; Setting(s)</th>
<th>SMS Frequency</th>
<th>Primary Outcome(s)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kassaye et al&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Weekly one-way SMS</td>
<td>Cluster RCT, N = 550; Kenya</td>
<td>SMS 3-6 per week</td>
<td>ART Adherence, EID</td>
<td>Negative Study</td>
</tr>
<tr>
<td>WeiTel Retain van der Kop et al&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Weekly 2-way SMS</td>
<td>RCT, N = 700; Kenya</td>
<td>Weekly</td>
<td>Retention during the first year of HIV care</td>
<td>Negative Study</td>
</tr>
<tr>
<td>Mobile WAChX Kinuthia et al. &lt;sup&gt;3&lt;/sup&gt;</td>
<td>3 Arms RCT: 2-way vs. 1-way SMS vs. Control</td>
<td>RCT, N = 825; Kenya</td>
<td>Weekly</td>
<td>VL non-suppression, LFU, adherence, infant HIV-free survival</td>
<td>Negative Study</td>
</tr>
<tr>
<td>PRIME Mwapasa et al&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Reminder SMS if missed visit clinic vs. Integrated HIV care vs. SOC</td>
<td>Cluster RCT, N = 1350; Malawi</td>
<td>If missed clinic visit</td>
<td>12-month post-partum retention in care</td>
<td>Negative Study</td>
</tr>
<tr>
<td>MOTIVATE Odeny et al. &lt;sup&gt;5&lt;/sup&gt;</td>
<td>2-way Weekly SMS Peer-Support (Community Mentor Mothers or cMMs)</td>
<td>factorial, Cluster RCT, N = 1,331; Kisumu &amp; Homa Bay, Kenya</td>
<td>Weekly</td>
<td>retention in care and ART adherence at 12 months postpartum.</td>
<td>Negative Study</td>
</tr>
<tr>
<td>Odeny et al&lt;sup&gt;6&lt;/sup&gt;</td>
<td>2-way SMS</td>
<td>pragmatic, cluster, stepped-wedge RCT, N = 2515; Kenya</td>
<td>Weekly</td>
<td>EID and Retention in Care</td>
<td>Negative Study</td>
</tr>
</tbody>
</table>


Intervention: adolescent-based case management; peer-peer support and behavioral interventions to identify and address age-specific barriers to adherence; add-on such as free Wi-Fi and games to improve adherence to clinic and appointments; capacity building HCW and caregiver.
Optimizing ART and Viral Suppression Nigerian Adolescents
Reaching Impact, Saturation, and Epidemic Control (RISE)
Emerenini F et al. International Pediatric HIV Workshop Abs 32/IAS Virtual Abs OAD0505 July 2021

→Adolescent-specific programming and capacity; involvement of adolescents in their care resulting in improvement in commitment to self-care; and caregiver involvement in health care improved health outcomes among AYP.
Conclusions

- Although there has been progress toward achieving the third “90,” many challenges remain, particularly for vulnerable and key populations.

- Even as successes and challenges toward “90-90-90 by 2020” are outlined, new fast-track “95-95-95 by 2030” targets have been established due to concerns that the original targets may not achieve epidemic control.

- Regardless of a specific target, efforts to further research and scale up evidence-based strategies that are generalizable, cost-effective, community-based/led, and acceptable to persons living with HIV must be intensified.
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THANK YOU!!!

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