



Facilitating Long-Term ART Adherence to Achieve Persistence

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Roadmap

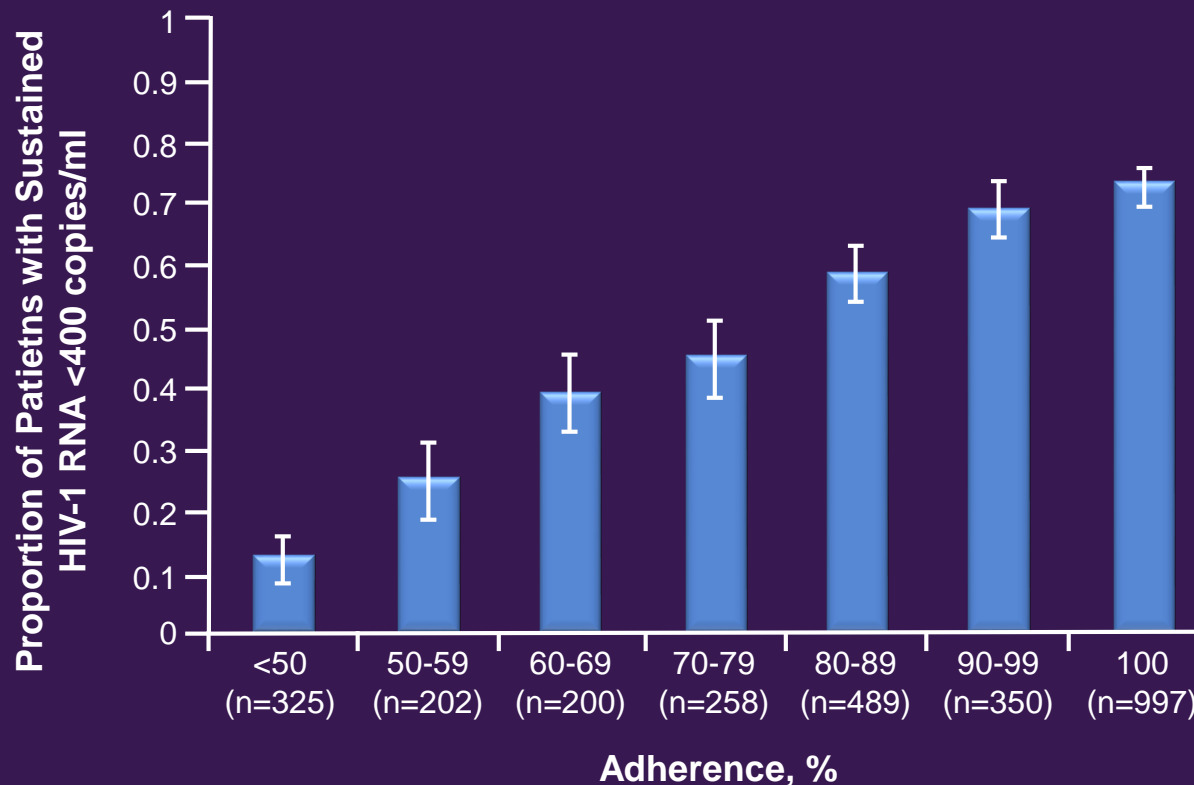
- Adherence, Virologic Outcomes and Drug Resistance
- Adherence vs. Persistence
- Structural, Demographics, Regimen-Specific Barriers for Sustained Adherence and Persistence
- Evidence-Based ART Adherence Interventions
- Conclusions

The Lifesaving Impact of Highly Active Antiretroviral Therapy (ART)



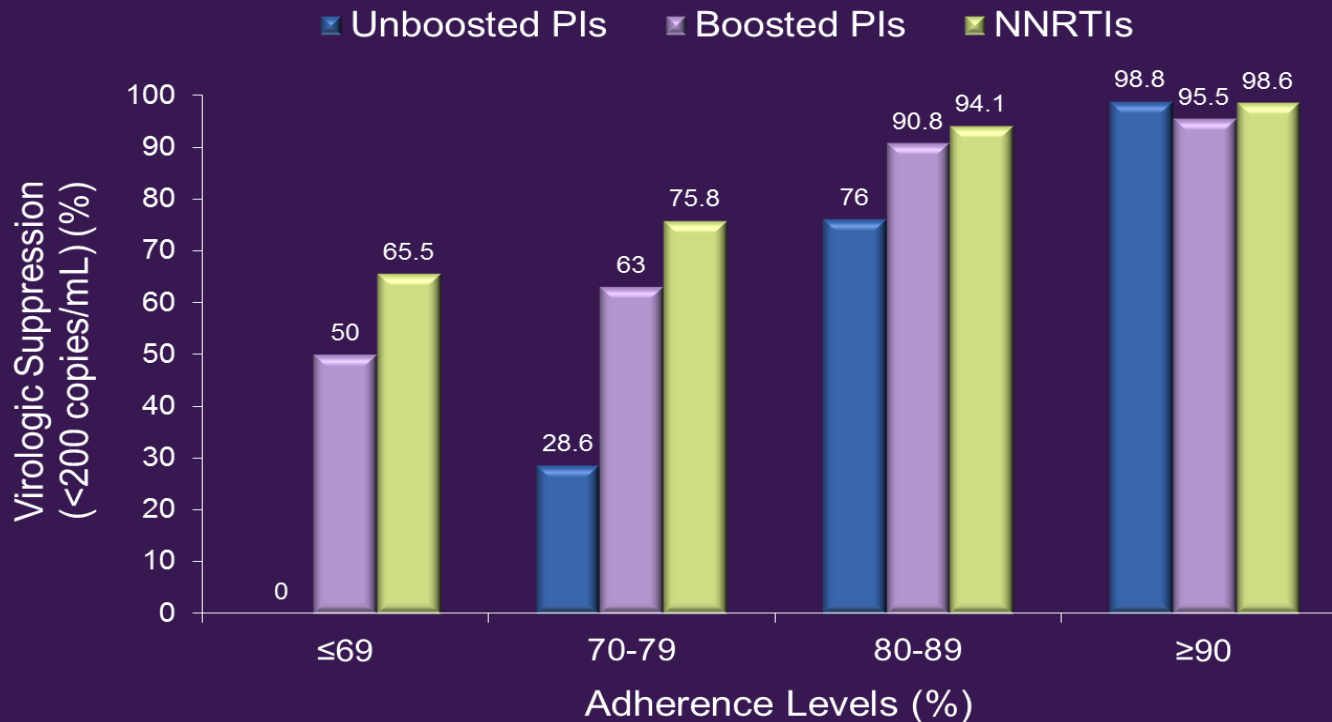


Adherence to NNRTI-Based ART Predicts Virologic Response in a Linear Dose-Response Fashion

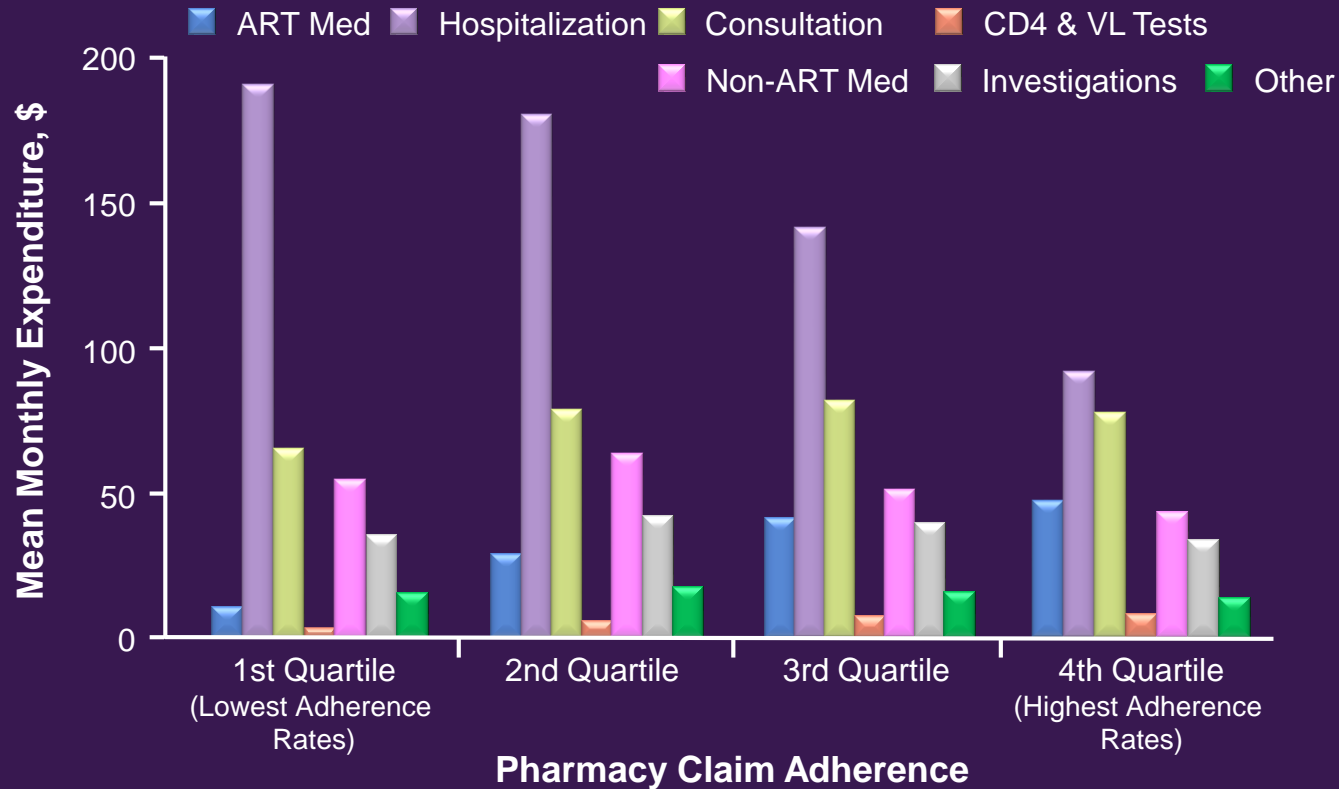




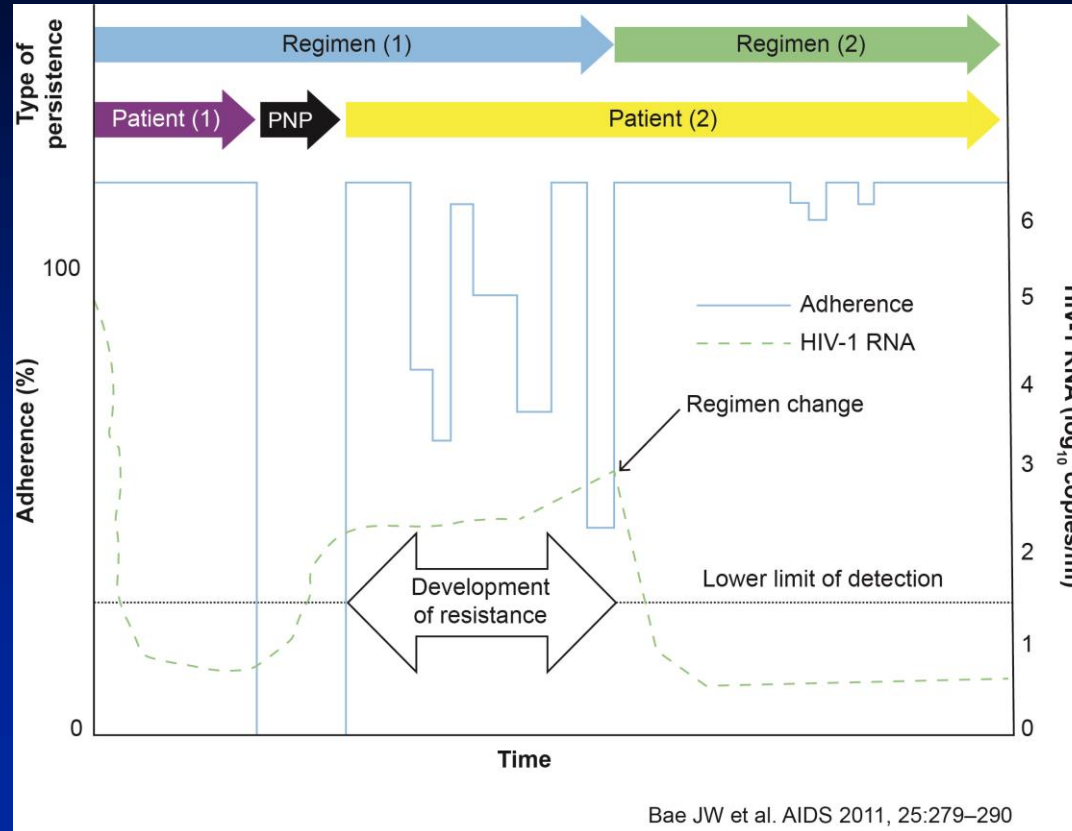
Levels of Adherence to ART Required for Virologic Suppression Among Type of ARV Regimens



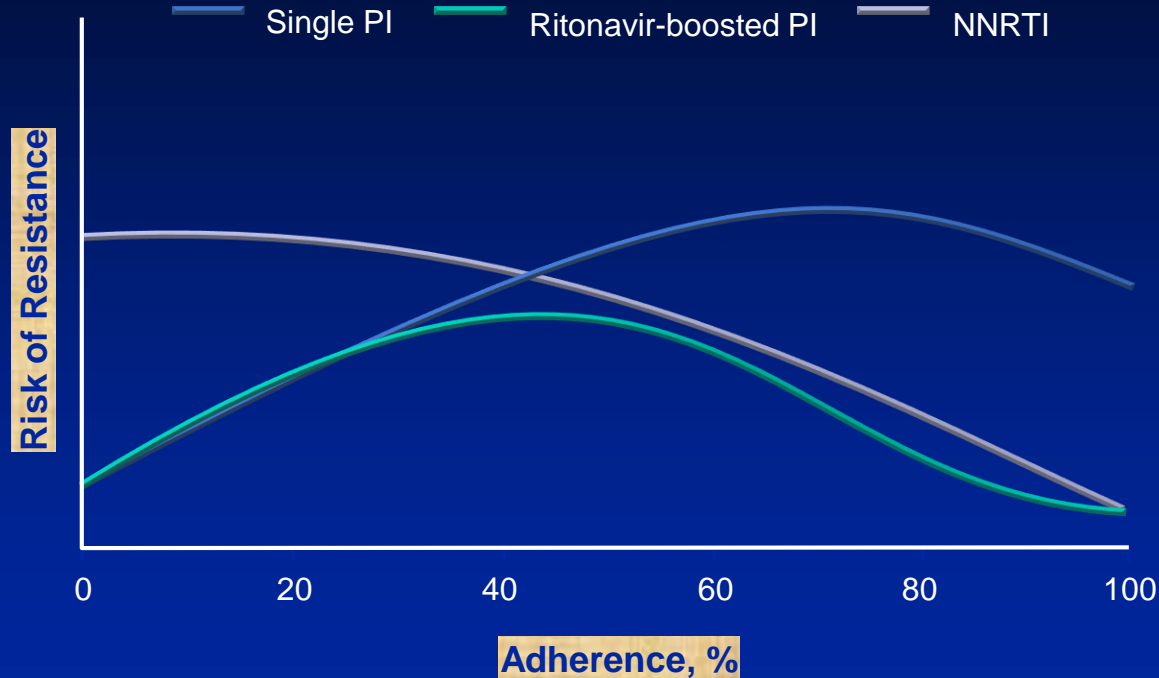
Adherence to Antiretroviral Therapy Reduces Hospitalization Costs



Adherence vs. Persistence

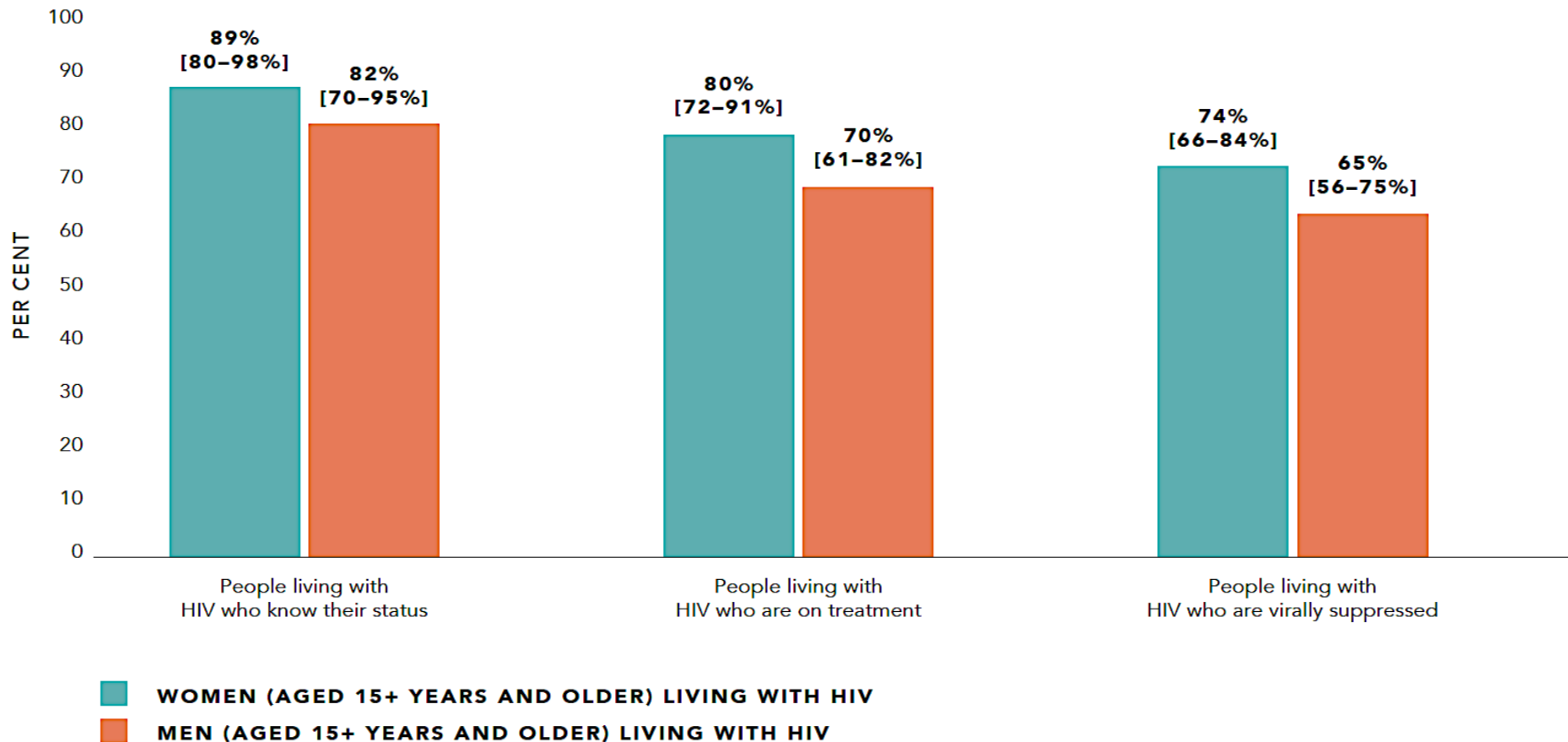


Estimated Risk of Resistance by Level of Adherence and Drug Class

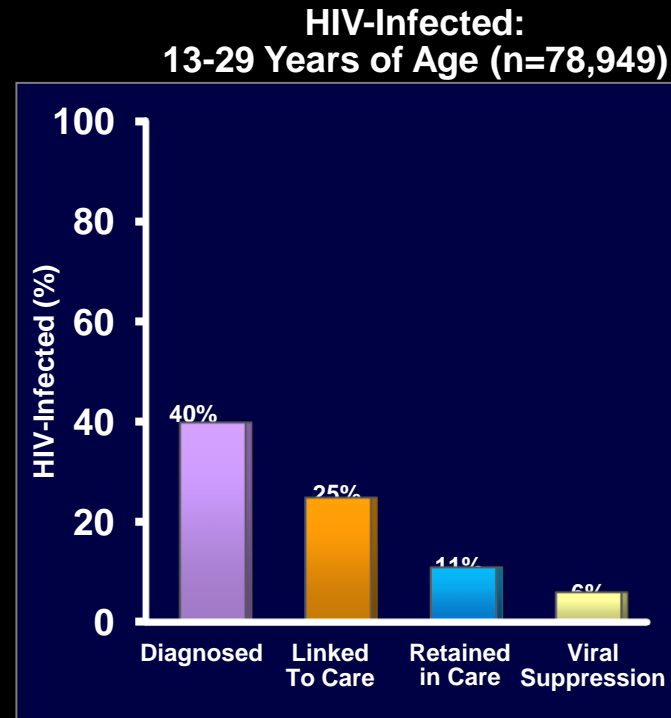
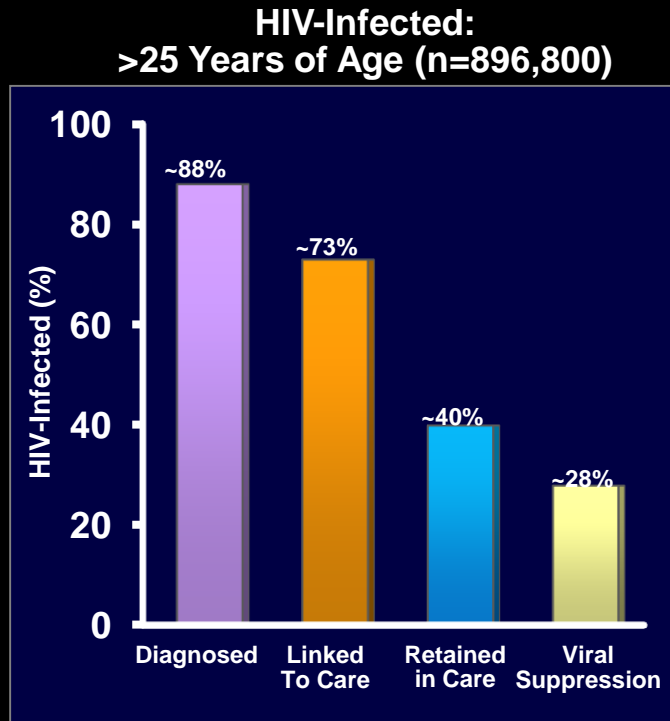


Bangsberg DR, Moss AR, Deeks SG. *J Antimicrob Chemother.* 2004;53:696-699.

Global HIV Treatment Cascade, 2021

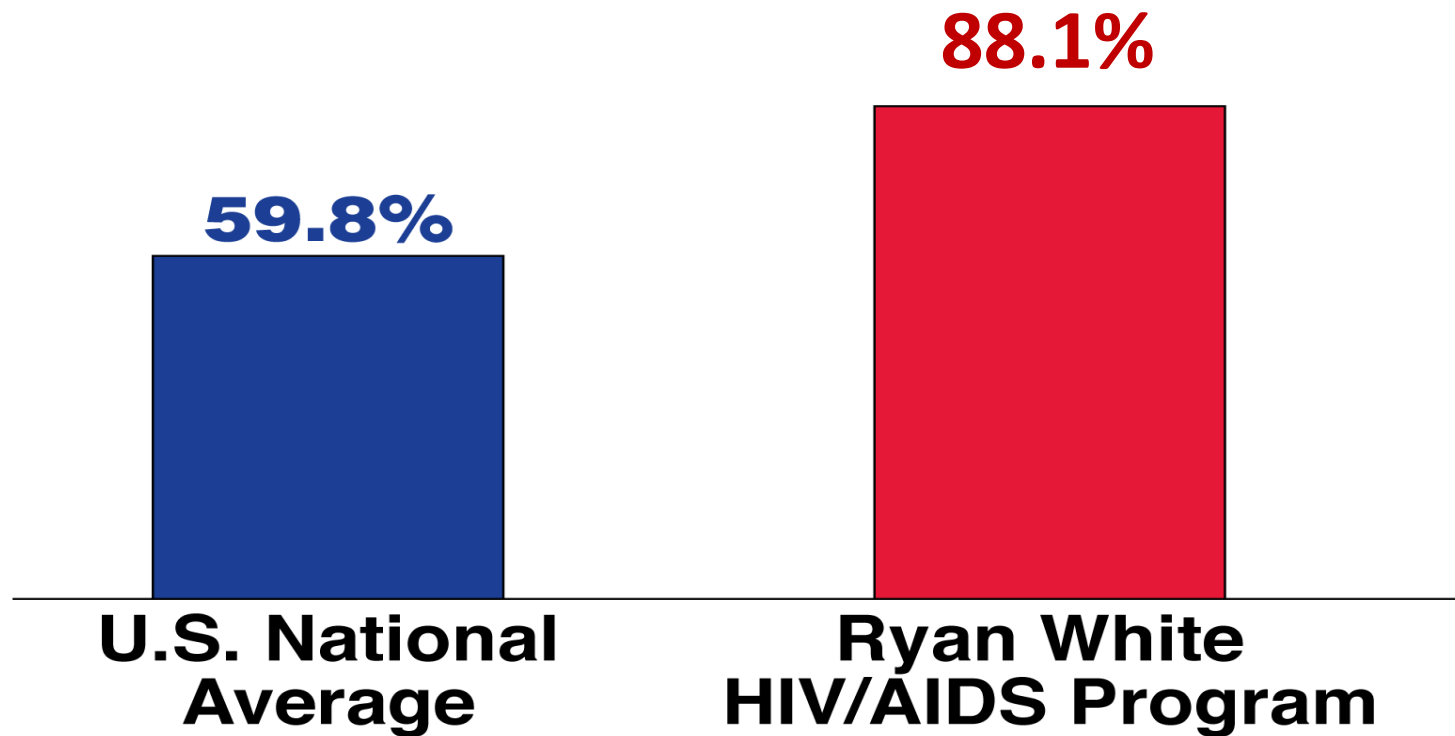


HIV Cascade of Care: Missed Opportunities in the US



Zanoni BC, et al. *AIDS Patient Care STDS*. 2014;28:128-135.
Hall HI, et al. *JAMA Intern Med*. 2013;173:1337-1344.

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



Source: HRSA,

Antiretroviral Therapy Adherence, Virologic and Immunologic Outcomes in Adolescents Compared With Adults in Southern Africa

Jean B. Nachega, MD, PhD,*† Michael Hislop, MSc,‡ Hoang Nguyen, MD, MPH,*
David W. Dowdy, MD, PhD,§ Richard E. Chaisson, MD,*§|| Leon Regensberg, MBChB, MRCP,‡
Mark Cotton, MBChB, PhD,¶ and Gary Maartens, MBChB, FCP†

JAIDS 2009;51:65–71)

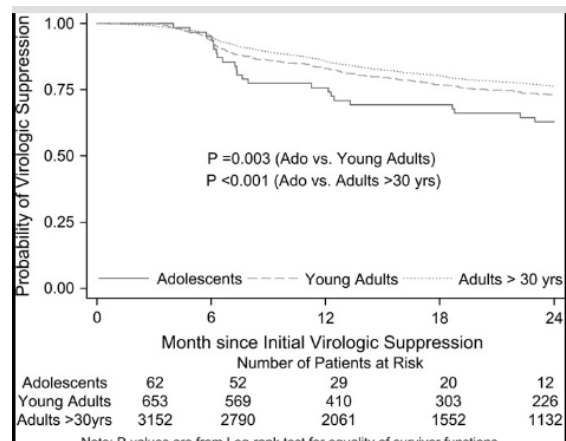
Time of follow-up	Unadjusted		Adjusted for All Variables Other Than Adherence*		Completely Adjusted†‡	
	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
At 6 months‡	0.91 (0.78 to 1.07)	0.24	0.88 (0.74 to 1.05)	0.16	0.96 (0.79 to 1.16)	0.65
At 12 months‡	0.74 (0.57 to 0.95)	0.02	0.65 (0.48 to 0.90)	0.01	0.74 (0.53 to 1.03)	0.08
At 18 months‡	0.75 (0.56 to 1.01)	0.06	0.84 (0.60 to 1.17)	0.31	—	—
At 24 months‡	0.70 (0.49 to 1)	0.05	0.72 (0.49 to 1.06)	0.10	0.78 (0.53 to 1.15)	0.22

CI, confidence interval; RR, relative risk.

*Includes gender, race, baseline CD4, baseline viral load, ART regimen (NNRTI based vs. PI based), ART initiation before 2003, and number of viral load measurement per patient-months.

†Adherence categorized in strata of ≤50%, 51%–67%, 67%–84%, 85%–99%, and 100% and baseline variables as described in (*). No adherence data at 18 months.

‡Time is measured in months after HAART initiation.

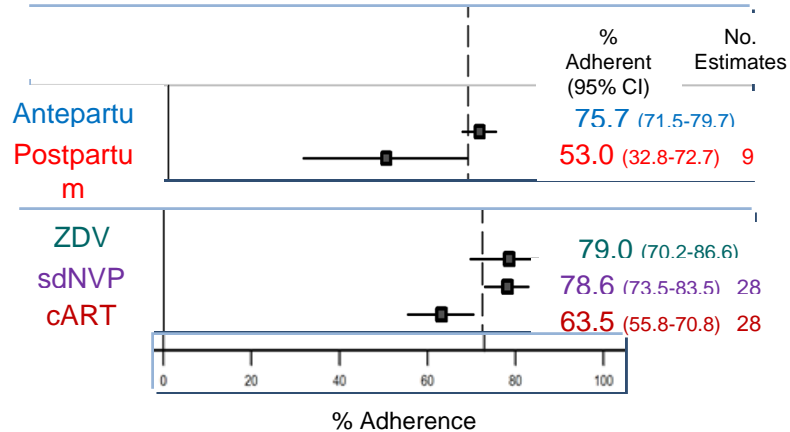
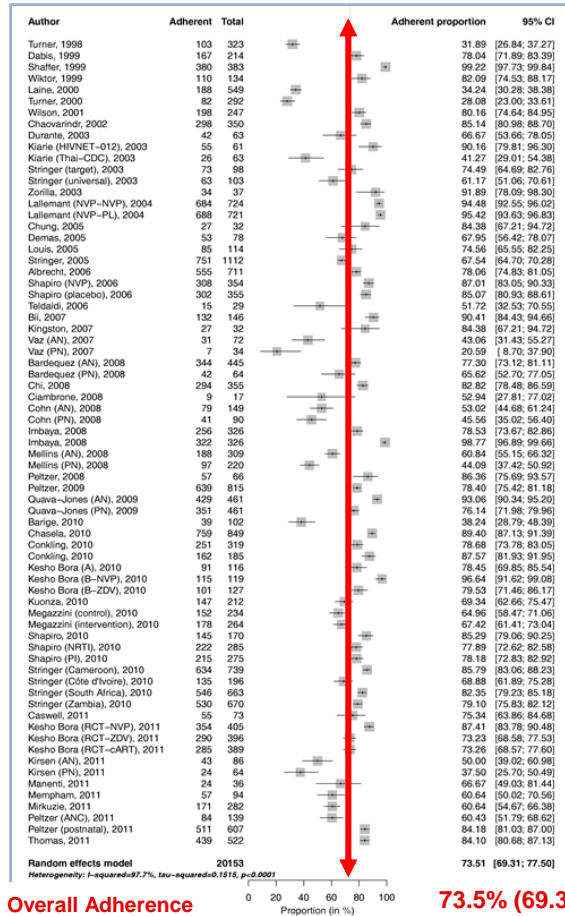


Relative Risk of **VL Suppression** in
Adolescents vs. Adults

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

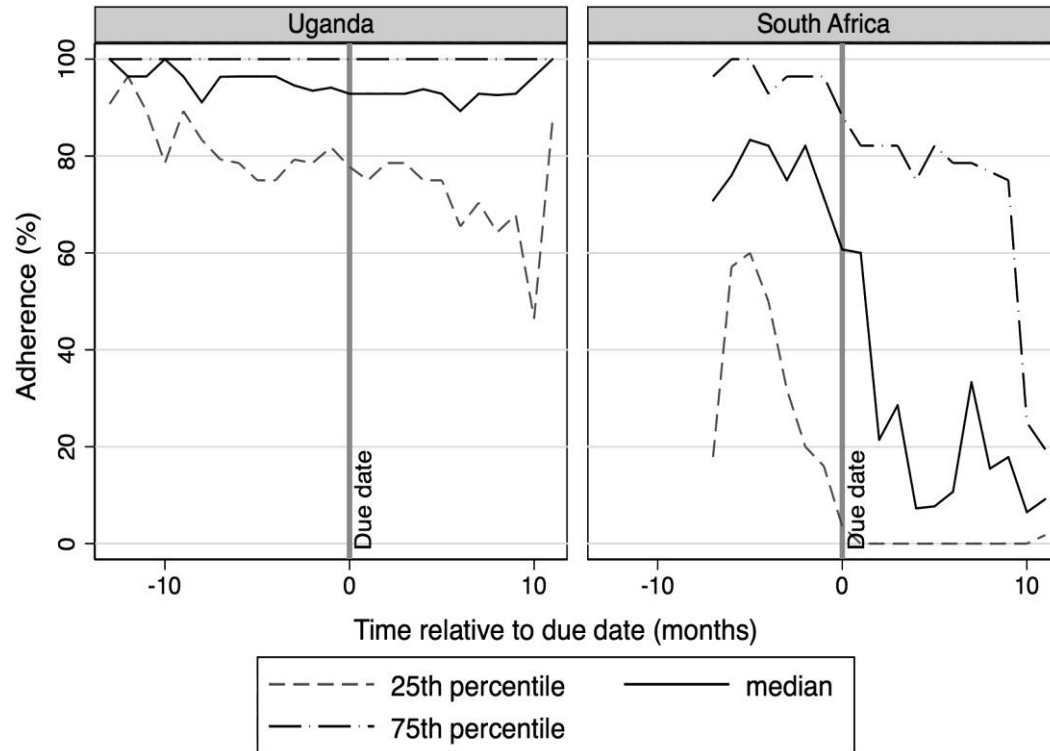
Nachega J et al. AIDS 2012;26:2039-52



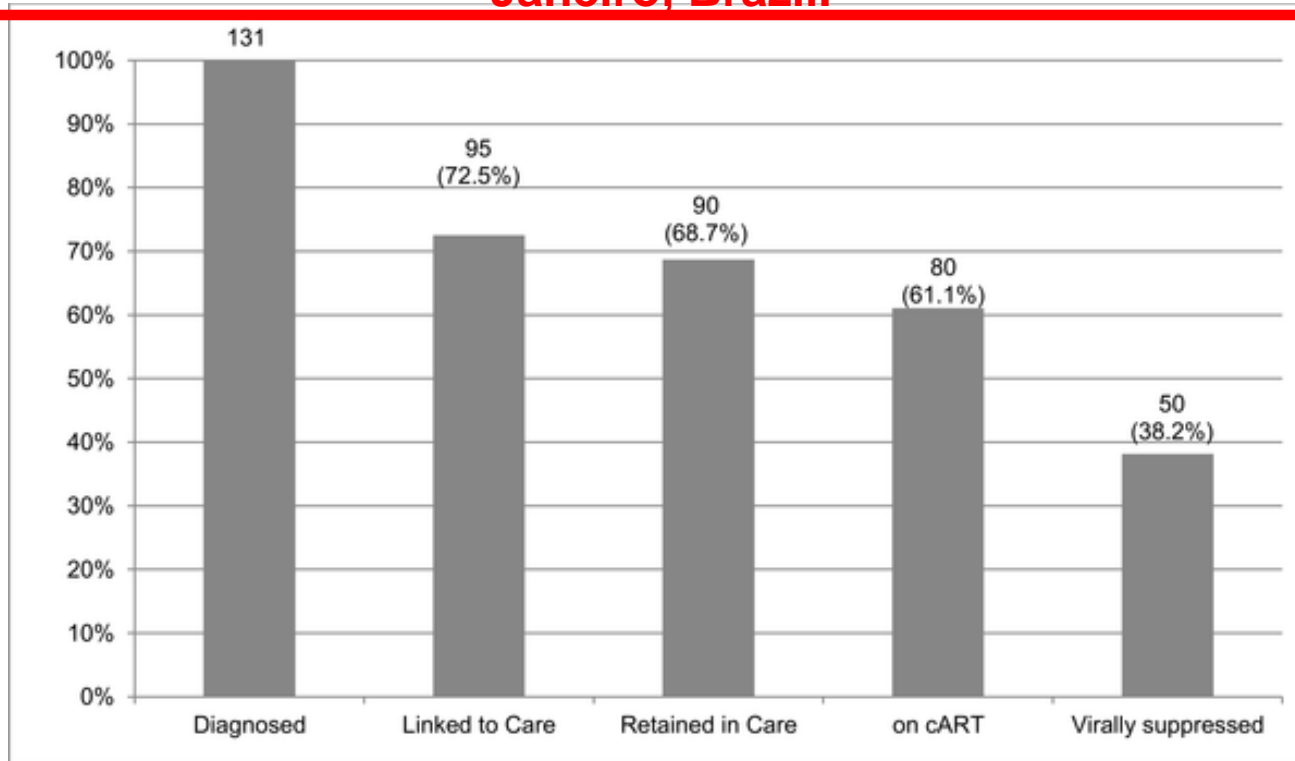
ART adherence in pregnancy (defined as % reporting >80% adherence to ART) is below that recommended for adequate virologic suppression. Optimal adherence remains a challenge during pregnancy, especially during postpartum period

73.5% (69.3, 77.5) had adherence of $\geq 80\%$ to ARV

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.



Castro R, Ribeiro-Alves M, Corrêa RG, Derrico M, Lemos K, et al. (2016) The Men Who Have Sex with Men HIV Care Cascade in Rio de Janeiro, Brazil. PLOS ONE 11(6): e0157309. <https://doi.org/10.1371/journal.pone.0157309>
<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

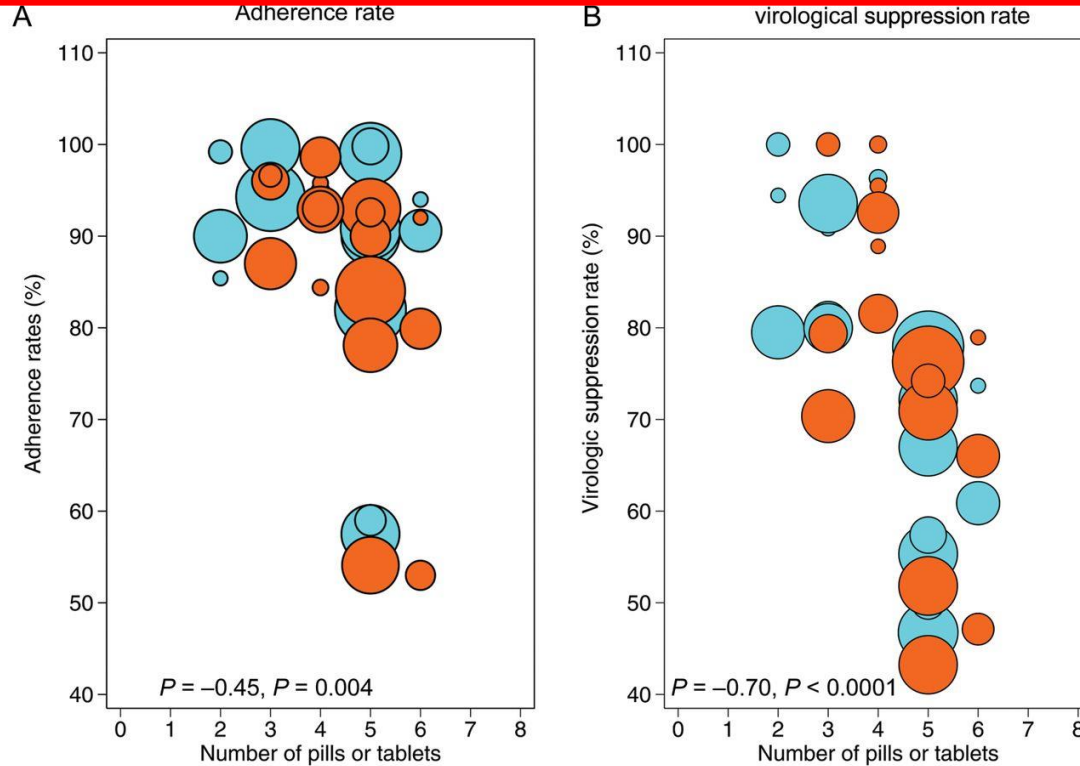


ART Regimen Simplification and ART Adherence

- Among regimens of similar efficacy and tolerability, **once-daily regimens** are recommended for **treatment-naïve** patients beginning ART (II B).
- Switching **treatment-experienced patients** receiving complex or poorly tolerated regimens to **once-daily regimens** is recommended, given regimens with **equivalent efficacy** (III B).
- Among regimens of equal efficacy and safety, **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**

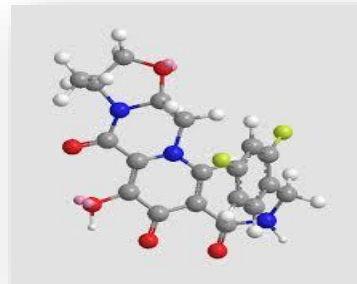
Long Acting Injectable Nano-Suspensions

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)

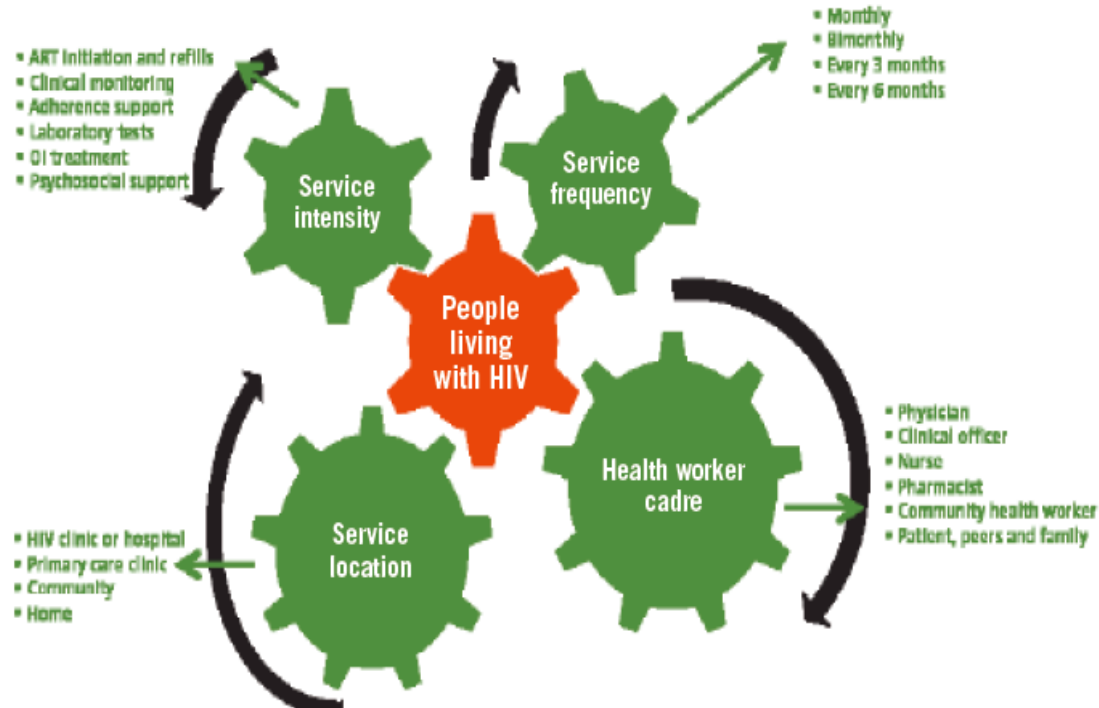


- Integrase inhibitor
- Similar to Dolutegravir
- Safe in humans with oral run-in
- Activity up to 3 months
- NHP model efficacy
- Phase 2: Éclair and HPTN 077

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





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

IMPLEMENTATION SCIENCE

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 Fatti, MBChB, MPH,^{1,2} Nicoletta Ngorima-Mabhena, MBChB, MSc,³
Eula Mothibi, MBChB, FCP,¹ Trish Muzenda, MPH,^{1,4} Regis Choto, MBChB, MPH,⁵
Tonderai Kasu, MBChB, MPSM,⁵ Taurayi A. Tafuma, MBChB, MPH,⁶ Nyika Mahachi, MBChB, MPH,⁶
Kudakwashe C. Takarinda, PhD,⁵ Tsitsi Apollo, MBChB, MPH, MBA,⁵ Owen Mugurungi, MBChB, MSc,⁵
Charles Chasela, PhD,^{7,8} Risa M. Hoffman, MD, MPH,⁹ and Ashraf Grimwood, MBChB, MPH¹

IMPLEMENTATION SCIENCE

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

Tukei, Betty B. MSc, BSc⁴; Fatti, Geoffrey MBChB, MPH^{1,2}; Tiam, Appolinaire MBChB, DipHIVMan, MMed^{1,6}; Ngorima-Mabhena, Nicoletta MBChB, MSc³; Tukei, Vincent J. MBChB, MMed, MPH²; Tshabalala, Itumeleng Dipl.¹; Sejana, Veronica M. BSc⁴; Muzenda, Trish MPH²; Mokoroane, Lincoln M. BSc⁴; Sehlabo, Lebelang BA⁴; Maotoe, Thapelo MBChB, MD⁵; Miremba, Justine K. MBChB³; Membe, Ian MPH³; Akpan, Francis MBChB, MPH⁵; Maile, Khotso MSc⁴; Faturiyeye, Iyiola MBChB, MPH³; Xulu, Thembi MB BCh, MPH⁵; Minor, Thomas MD, MPH¹; Sanne, Ian MB BCh⁵; Chasela, Charles BSc, MSc, DLSHTM, PhD⁸; for EQUIP Health

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JAIDS Journal of Acquired Immune Deficiency Syndromes: November 01, 2020 - Volume 85 - Issue 3 - p 280-



Research Article | [Open Access](#) |

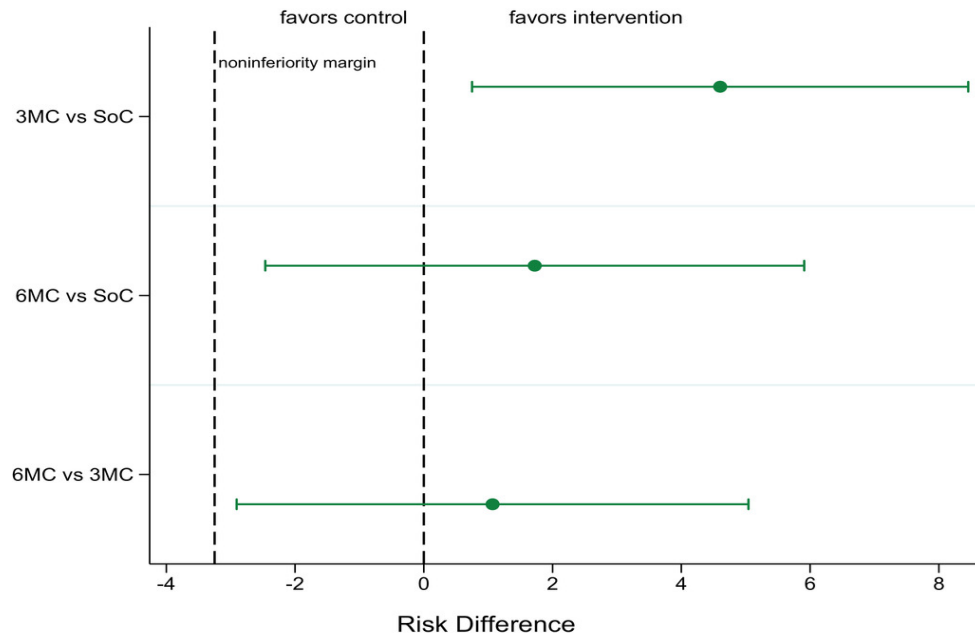
Twenty-four-month outcomes from a cluster-randomized controlled trial of extending antiretroviral therapy refills in ART adherence clubs

Tali Cassidy , Anna Grimsrud, Claire Keene, Keitumetse Lebelo, Helen Hayes, Catherine Orrell, Nompumelelo Zokufa, Tabitha Mutseyekwa, Jacqueline Voget, Rodd Gerstenhaber, Lynne Wilkinson

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

Clinical Trial Number: PACTR201810631281009.

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

Jienchi Dorward, MBChB, Thokozani Khubone, BTech, Kelly Gate, FCFP, Hope Ngobese, BCurr, Yukteshwar Sookrajh, MBChB, Siyabonga Mkhize, HSIDCCert, Aslam Jeewa, BEng, Christian Bottomley, PhD, Lara Lewis, MSc, Kathy Baisley, MSc, Prof Christopher C Butler, FMedSci, Nomakhosi Gxagxisa, MD, Nigel Garrett, PhD

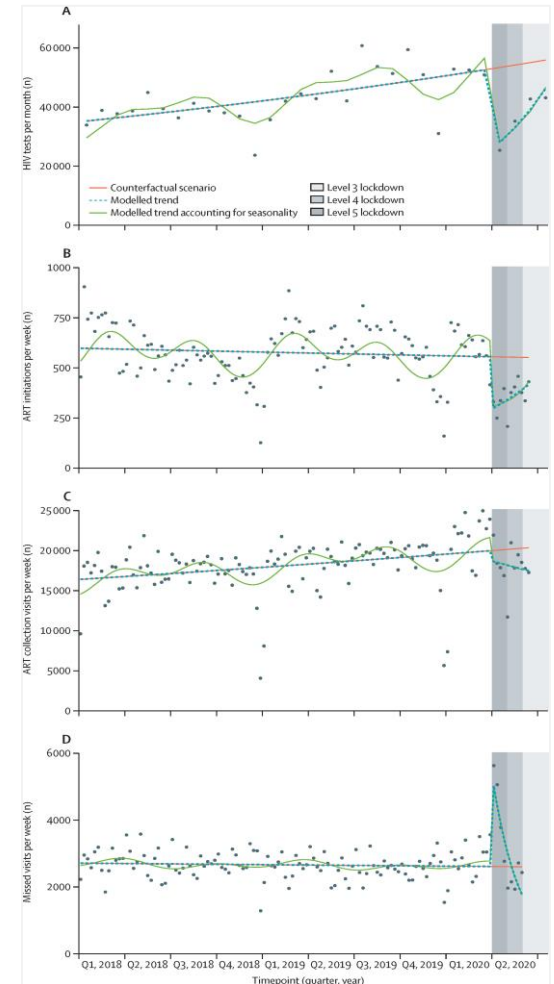
The Lancet HIV

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 71142 ART initiations and 2 319 992 ART collection visits. We recorded a median of 41926 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.



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

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Adherence/Retention in Care Interventions in Pregnant and Post-Partum Women Living with HIV

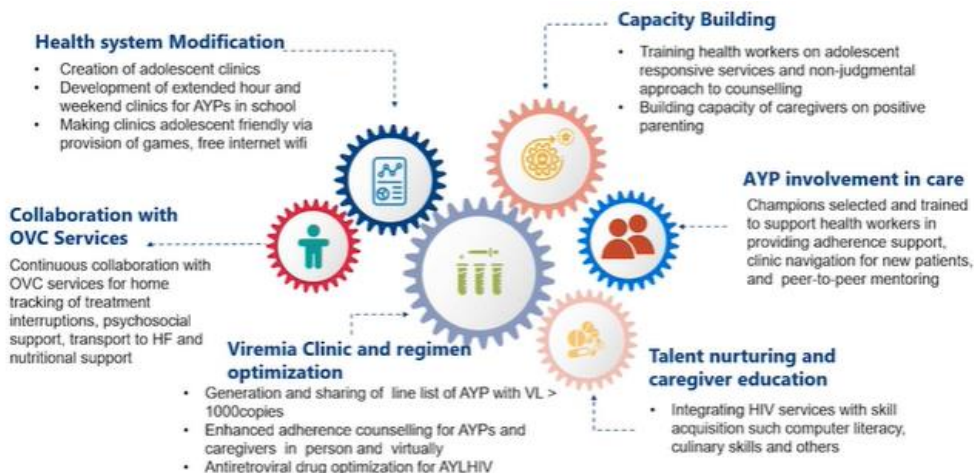
Author/Study Name	Intervention (s)	Design, N & Setting (s)	SMS Frequency	Primary Outcome (s)	Results
Kassaye et al ¹	Weekly one-way SMS	Cluster RCT, N =550; Kenya	SMS 3-6 per week	ART Adherence, EID	Negative Study
WelTel Retain van der Kop et al ²	Weekly 2-way SMS	RCT, N= 700; Kenya	Weekly	Retention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

1. Kassaye AIDS Res&Treat 2016; 2. van der Kop ML et al. Lancet Public Health 2018; 3. Kinuthia J, et al. PLoS Med 2021; 4. Mwapasa et al. JAIDS 2017; 5. Abuogi LL et al. JIAS 2022; 6. Odeny et al. PlosMed 2019

Optimizing ART and Viral Suppression Nigerian Adolescents Reaching Impact, Saturation, and Epidemic Control (RISE)

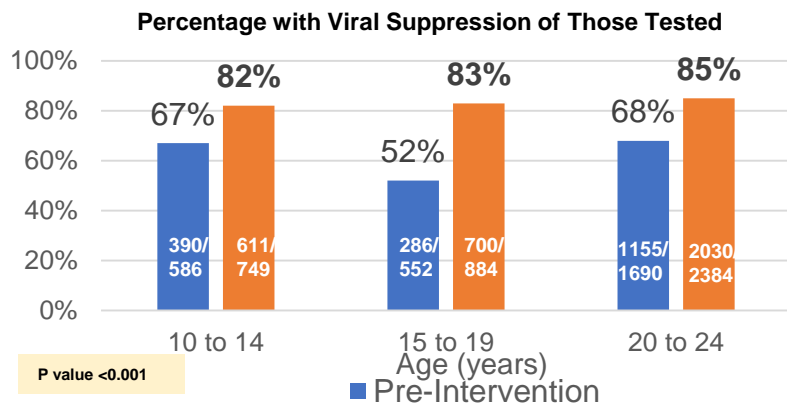
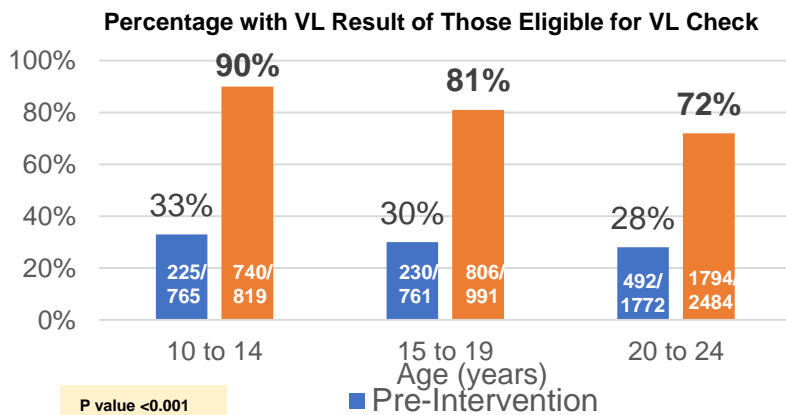
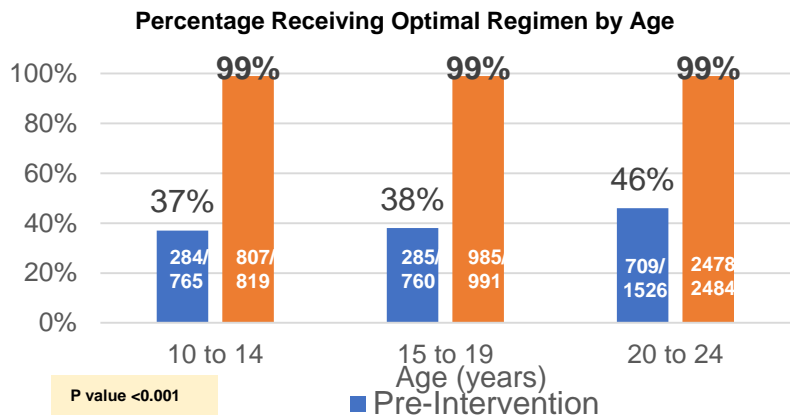
Emerenini F et al. International Pediatric HIV Workshop Abs 32/IAS Virtual Abs OAD0505 July 2021

- Implementation of integrated multi-disciplinary intervention for 4,617 adolescents/youth 10-24 years in 103 facilities in 4 states in Nigeria; compared regimen optimization, VL testing and suppression 6 mos **pre-intervention** (Oct 2019-Mar 2020) and 6 mos **post-intervention** (Ap-Sept 2020) chart review.
- 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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University of Pittsburgh



SA collaborators

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NIH/FIC D43TW010937-02
NIH/FIC D43TW011827-01A1



National Institute of Allergy and Infectious Diseases
National Institutes of Health

PITT collaborators

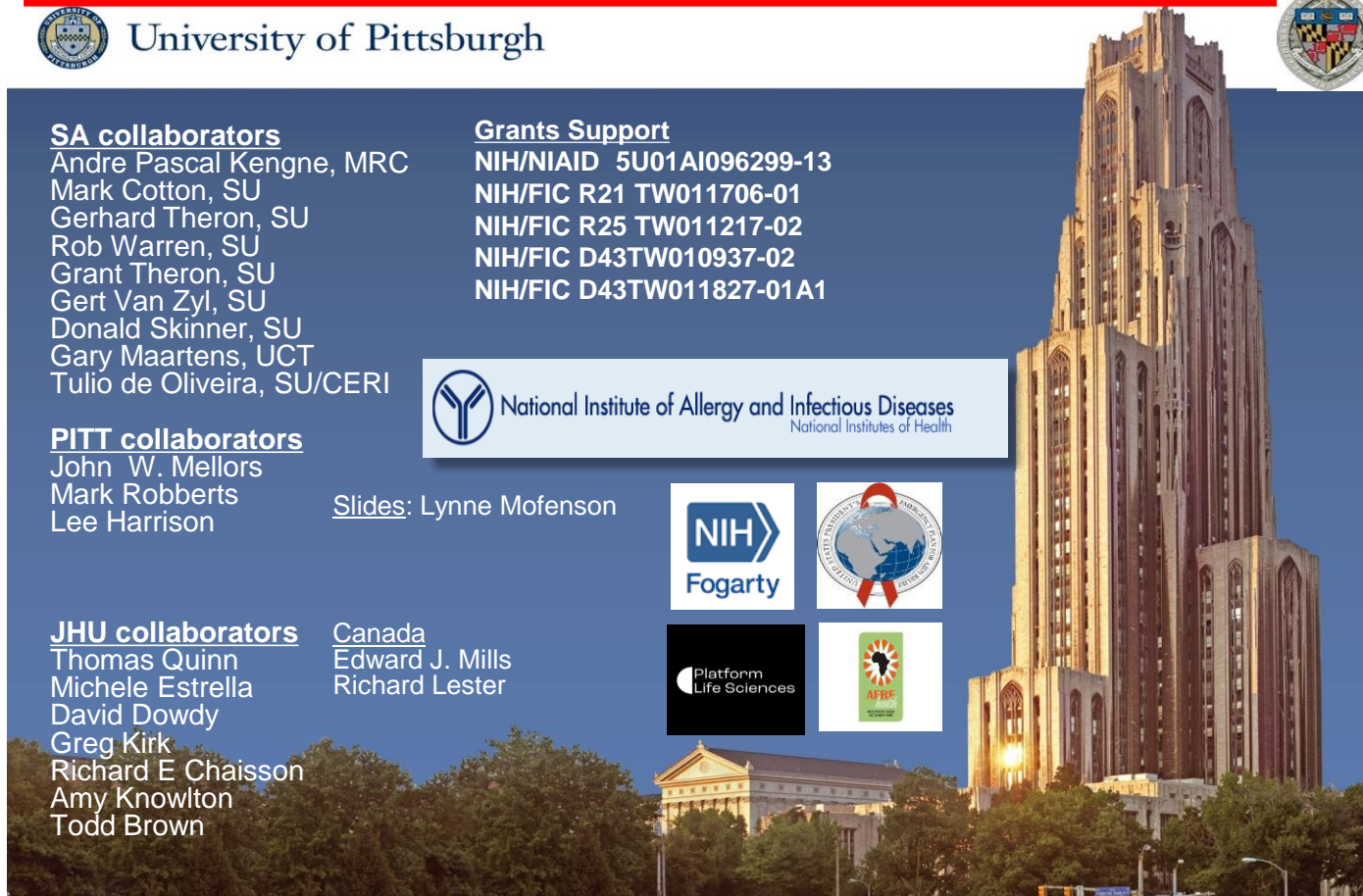
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THANK YOU!!!
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