



MULTI-MONTH DISPENSING AND SCRIPTING FOR ADOLESCENTS AND YOUNG PEOPLE LIVING WITH HIV

LITERATURE REVIEW BRIEF

AUGUST 2020

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ACRONYMS

ART	Antiretroviral Therapy
ARV	Antiretroviral Drug
AYPLHIV	Adolescents and Young People Living with HIV
CATS	Community Adolescents Treatment Supporter
CAC	Community-based Adherence Club
CARG	Community ART Groups
CHW	Community Health Worker
DSD	Differentiated Service Delivery
FCD	Family Clinic Day
LTFU	Lost to follow-up
MMD/S	Multi-month Dispensing/Scripting
MMS	Multi-month Scripting
MMP	Multi-month Prescription
NGO	Non-governmental Organization
OHA	USAID Office of HIV/AIDS
OIs	Opportunistic Infections
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PYD	Positive Youth Development
SPEEDI	Standardized Pediatric Expedited Encounters for ART Drugs Initiative
SDGs	Sustainable Development Goals
SRH	Sexual and Reproductive Health
UNAIDS	Joint United Nations Programme on HIV/AIDS
USAID	United States Agency for International Development
VL	Viral Load
WHO	World Health Organization

INTRODUCTION

BACKGROUND

Nearly four million youth (10 to 24 years) are HIV positive, with an additional 200,000 infected annually.¹ HIV is one of the leading causes of death in adolescents (10-19 years) in Africa and the second leading cause globally, and adolescents are the only group in which HIV-related mortality has not decreased.² Adolescents and young people living with HIV (AYPLHIV) are at risk for poor outcomes even after initiation of antiretroviral therapy (ART), as they have significantly lower virologic suppression than older adults and higher rates of loss to follow-up (LTFU).³

Because of these issues, there has been increasing attention on AYPLHIV, and HIV programs have focused on provision of adolescent-friendly health services and use of disaggregated data to allow closer monitoring of programmatic outcomes for youth. Part of these efforts have aligned with the larger shift towards differentiated service delivery (DSD), an approach that aims to tailor delivery of HIV services to individual patient needs while improving the efficiency and quality of healthcare service delivery.⁴ A key feature of DSD is less frequent facility visits for stable patients as a way to reduce patient burden and decongest busy facilities. (Although the criteria for stability vary among countries, stable patients are generally defined as those who are clinically well, adherent to ART, and virologically suppressed.) These models were initially focused on stable adult patients due to concerns about the need for multiple dosing changes in growing children and poor retention and adherence in adolescents. However, DSD is now recognized as a critical part of efforts to improve care for all PLHIV, including children (<10 years of age), adolescents (10-19 years), and young people (15-24 years).⁵ Although literature on DSD models in these age groups is scarce, the WHO has already recommended some tailored approaches for AYPLHIV which include:

- Three- to six-month ART refills
- Appointments scheduled outside of school days
- Extended adolescent-specific service hours at health facilities
- Youth-friendly services provided by staff
- Psychosocial support for adolescents and youth
- An annual mental health assessment and drug and alcohol screening
- An annual viral load assessment for clinically stable adolescents

¹ UNAIDS 2019: https://www.unaids.org/sites/default/files/media_asset/2019-global-AIDS-update_en.pdf

² Reif LK, McNairy ML, Lamb MR, Fayorsey R, Elul B. Youth-friendly services and differentiated models of care are needed to improve outcomes for young people living with HIV. *Current Opinion in HIV and AIDS*. 2018 May;13(3):249-256.

³ UNAIDS. Start Free Stay Free AIDS Free. 2019. https://www.unaids.org/en/resources/documents/2019/20190722_UNAIDS_SFSAF_2019

⁴ IAS. Differentiated care for HIV: A decision framework for antiretroviral therapy. 2016. http://www.differentiatedcare.org/Portals/0/adam/Content/yS6M-GKB5EWs_uTBHkICIQ/File/Decision%20Framework%20REPRINT%20web.pdf

⁵ WHO, IAS. Key considerations for differentiated antiretroviral therapy delivery for specific populations: children, adolescents, pregnant and breastfeeding women and key populations. 2017 <https://www.who.int/hiv/pub/arv/hiv-differentiated-care-models-key-populations/en/>

- Peer and caregiver support

Multi-month dispensing/scripting (MMD/S) is a type of DSD in which patients are provided drug refills at intervals greater than the typical one-month refills required in conventional models. Providing stable patients with enough medication for two, three, or six months decreases the patient burden for travel to facilities and helps reduce daily patient load, allowing healthcare providers to focus their efforts on patients requiring more intensive clinical care. Acceptability among adult PLHIV for longer dispensing intervals is high; a study in Malawi found a high satisfaction with MMD/S in clients and providers, with half of clients preferring longer refill intervals of six or 12 months.⁶ Ethiopia has also had success with roll-out of six-month refills for stable adult patients, enrolling more than 100,000 eligible patients into the model between July 2017 and February 2018. However, 20% of eligible patients in Ethiopia have declined to participate, citing concerns over inadvertent disclosure with large quantities of medication at home and potential issues with safety and storage of medication for prolonged periods at home.⁷ MMD/S can be a stand-alone intervention for individual patients (with pickups at facilities or in the community) or can be a component of other DSD models such as community ART refill groups (CARGs) or adherence clubs. Most studies in the literature incorporate MMD/S within a broader intervention, making it difficult to ascertain its specific impact. However, several studies that incorporated MMD/S in adults have shown decreased facility waiting time and costs⁸, improved retention in care, and maintenance of high rates of viral suppression.^{9,10,11,12} Data on virologic suppression among patients on six-month refills are scarce.

As a result of this evidence, PEPFAR and the WHO have advocated for three- and six-month drug refills for stable patients, including adolescents and youth.^{13,14} In December 2019, the WHO released updated guidelines on adolescent-friendly services in which it re-emphasized the importance of MMD/S in

⁶ Hubbard J, Phiri K, Moucheraud C, et al. A Qualitative Assessment of Provider and Client Experiences With 3- and 6-Month Dispensing Intervals of Antiretroviral Therapy in Malawi. *Global Health: Science and Practice*. Published online February 3, 2020.

⁷ Six-month multi-month scripting: The Ethiopia experience. ICAP CQUIN Learning Network Webinar. 17 April 2019. https://cquin.icap.columbia.edu/wp-content/uploads/2019/04/CQUIN-webinar_Ethiopia-MMS_FINAL-1.pdf Accessed 9 July 2020.

⁸ Prust ML, Banda CK, Nyirenda R, et al. Multi-month prescriptions, fast-track refills, and community ART groups: results from a process evaluation in Malawi on using differentiated models of care to achieve national HIV treatment goals. *J Int AIDS Soc*. 2017;20(Suppl 4):21650.

⁹ Mody A, Roy M, Sikombe K, et al. Improved Retention With 6-Month Clinic Return Intervals for Stable Human Immunodeficiency Virus-Infected Patients in Zambia. *Clin Infect Dis*. 2018;66(2):237-243.

¹⁰ Mutasa-Apollo T, Ford N, Wiens M, et al. Effect of frequency of clinic visits and medication pick-up on antiretroviral treatment outcomes: a systematic literature review and meta-analysis. *J Int AIDS Soc*. 2017;20(Suppl 4).

¹¹ Lebelo K, Cassidy T, Grimsrud A, et al. Twelve-month retention and viral load outcomes from a noninferiority cluster randomized trial extending adherence club ART refill dispensing intervals to 6-monthly. Poster presented at: 10th IAS Conference on HIV Science; 21-24 July, 2019; Mexico City, Mexico.

¹² Fatti G, Ngorima-Mabhena N, Mothibi E, et al. 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. *J Acquir Immune Defic Syndr*. Published online March 23, 2020.

¹³ World Health Organization, 2016. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - Second edition. <https://www.who.int/hiv/pub/arv/arv-2016/en/>

¹⁴ PEPFAR 2019 Country Operational Plan Guidance for all PEPFAR Countries. <https://www.state.gov/wp-content/uploads/2019/08/PEPFAR-Fiscal-Year-2019-Country-Operational-Plan-Guidance.pdf>

adolescents.¹⁵ The document includes a review of five DSD models aimed at adolescents, and only three included MMD/S as a component of the packages.

It is widely acknowledged that further study is needed on adolescent and youth interventions, as the literature for DSD (and specifically, MMD/S) in these populations is limited. Because youth are still developing—that is, experiencing physical, developmental, and emotional changes and growth—what works for adult HIV care does not necessarily work for youth. As such, youth require specialized, non-judgmental, rights-based, and client-centered approaches to adherence support.¹⁶ Without tailored, effective interventions to improve adherence to ART, infections in youth will dramatically increase, threatening global progress in controlling the epidemic.¹⁷

PURPOSE OF THIS DOCUMENT

As programs work to develop and scale-up MMD/S among AYPLHIV, it is critical to use previous findings to inform development and roll-out of interventions. DSD is relatively new for adolescents and youth, and its use depends on the availability of services, national policies, and the knowledge and attitudes of healthcare providers. This brief summarizes the current literature on MMD/S for HIV-infected adolescents and young people and provides a summary review of policies related to MMD/S in 53 countries. Common terms used in the HIV treatment and care literature and in this brief can be found in Annex A.

LITERATURE REVIEW

METHODS

A review of the available literature published between 2017-2020 was conducted using Pubmed and Cochrane using key search terms (HIV, multi-month dispensing, multi-month scripting, adolescent, youth, differentiated service delivery).¹⁸ Reference lists of identified publications were used to identify additional resources. Websites from the International AIDS Society conference between 2017-2020 were also reviewed for additional unpublished studies. All types of literature that described MMD/S in AYPLHIV were included (e.g., program reports, webinar presentations, qualitative findings, etc.). Studies with predominantly older adults were included if age-disaggregated results on AYPLHIV were provided. If multiple publications were identified for the same model, the most relevant and rigorous study was summarized.

¹⁵ World Health Organization, 2019. Adolescent-friendly health services for adolescents living with HIV: From theory to practice. <https://www.who.int/publications/i/item/adolescent-friendly-health-services-for-adolescents-living-with-hiv> Accessed July 7, 2020.

¹⁶ Bekker L-G, Alleyne G, Baral S, et al. Advancing global health and strengthening the HIV response in the era of the Sustainable Development Goals: the International AIDS Society—Lancet Commission. *Lancet*. 2018;392(10144):312-358. doi:10.1016/S0140-6736(18)31070-5

¹⁷ Wong VJ, Murray KR, Phelps BR, Vermund SH, McCarragher DR. Adolescents, young people, and the 90–90–90 goals: a call to improve HIV testing and linkage to treatment. *AIDS*. 2017;31(Suppl 3):S191-S194.

¹⁸ Please note studies may have used data collected earlier than the 2017-2020 publish date.

STUDIES ON MMD/S IN AYPLHIV

Although there is an increasing amount of literature related to DSD and youth-friendly services, the literature on MMD/S in these populations is limited. Table I shows a summary of the nine MMD/S-specific papers or presentations identified in the review; all are from sub-Saharan Africa, and only three explicitly addressed MMD/S in adolescents and youth. Of those three, only one (a qualitative report of focus group discussions) discussed MMD/S of three to six month supplies; of the other two, one used two-month ART refills and the other did not explicitly delineate the MMD/S intervals for the included patients. In the two quantitative studies focused on MMD/S in youth, MMD/S was found to be feasible and was associated with maintenance of virologic suppression and retention in care. Although both articles noted potential supply chain challenges, MMD/S was provided as one component of much more complex interventions and/or was assessed retrospectively or at a limited number of sites. Only one report provided information on perspectives and/or acceptability of MMD/S among AYPLHIV.

Table 1. Select literature on MMD/S in Adolescents and Young People Living with HIV				
Country Participant Age Study Timeframe	Study design	Brief Model Description	Outcomes	Key author conclusions
Botswana, Lesotho, Swaziland, Malawi, Uganda, Tanzania 0-19 years¹⁹ <i>Timeframe: 2003-2015</i>	Retrospective review of medical records of 14,392 patients receiving multi-month prescription (MMP)	MMP of ART to children at Centers of Excellence Refill intervals varied between countries and were not specified	Outcomes at 5 years on MMP: <ul style="list-style-type: none"> • Mortality 2%; LTFU 2.6% • 93.1% with normal CD4 levels (CD4 >350 for patients >5 years; CD4%>25 for patients <5 years) • 76.1% good adherence (pharmacy pill count 95%-105%) • 82.3% VL <400 copies/mL Patients 15-19 years or <1 year at transition to MMP were at higher risk of LTFU and mortality compared with other age groups. 10-19-years had worse viral suppression (75%) than kids <10 years (88%) but MMP not associated with lower adherence in that age group.	Transition to MMP was feasible and had favorable HIV-related outcomes. Older adolescents had higher risk of mortality and LTFU even with MMP.
South Africa 16-24; 25+ years²⁰ <i>Timeframe: Joined AC: 2011-2014; data from 2014-2015</i>	Retrospective observational cohort study of random representative sample of patients enrolled in adherence club (AC) model in Cape Town	AC met five times/year in facility or community for symptom screen, discussion, and 2-month ART supply. A "buddy" could collect medication at alternate club meetings.	Outcomes: LTFU and viral rebound of patients in ACs; no comparison group. <ul style="list-style-type: none"> • Of 3,210 patients, only 119 (3.7%) aged 16-24 years. • Of AC members, those aged 16-24 years had higher LTFU (adjusted hazard ratio (aHR) 2.41) than club members 35-44 years old (absolute numbers not provided). • No significant differences in VL rebound were found between 16-24-year-old AC members and older patients, but small sample size limits analysis. Specific VL suppression rates by age group were not provided. 	Even with AC support, youth 16-24 years classified as stable have higher risk of LTFU than older adults; transitioning through difficult phases make them vulnerable to dis-engagement in care.
South Africa 16+ years²¹ <i>Timeframe: 2012-2013</i>	Retrospective analysis (using clinical databases) of patients initiating	Community-based adherence clubs (CAC) that met every two months for group counseling, symptom screening, and ART distribution (i.e., 2-month ART	Outcomes: LTFU and viral load rebound in CAC patients and those in standard CHC care	CACs were not associated with improved retention in 16-24-year olds, unlike in adults.

¹⁹ Kim MH, Waness RS, Caviness AC, et al. Multimonth Prescription of Antiretroviral Therapy Among Children and Adolescents: Experiences From the Baylor International Pediatric AIDS Initiative in 6 African Countries. *J Acquir Immune Defic Syndr.* 2018;78 Suppl 2:S71-S80.

²⁰ Tsondai PR, Wilkinson LS, Grimsrud A, Mdlalo PT, Ullauri A, Boule A. High rates of retention and viral suppression in the scale-up of antiretroviral therapy adherence clubs in Cape Town, South Africa. *J Int AIDS Soc.* 2017;20(Suppl 4):21649. doi:10.7448/IAS.20.5.21649

²¹ Grimsrud A, Lesosky M, Kalombo C, Bekker L-G, Myer L. Implementation and Operational Research: Community-Based Adherence Clubs for the Management of Stable Antiretroviral Therapy Patients in Cape Town, South Africa: A Cohort Study. *J Acquir Immune Defic Syndr.* 2016;71(1):e16-23.

	ART prior to end of 2012 at one community health center (CHC).	supply); 2,113 CAC patients included	<ul style="list-style-type: none"> LTFU not significantly different between 16-24-year-old CAC members and 16-24-year-olds in the CHC model. Higher LTFU for CAC patients 16-24 years (9.1%) compared with adults >25 years in CAC (5.9%). Only 3% of CAC members had viral rebound; CAC members 16-24 years were more than twice as likely to experience viral rebound than those >25 years in CACs (adjusted hazard ratio 2.17). No comparison with CHC. 	Youth in CAC models have higher rates of viral load rebound and LTFU than older patients in CACs.
Zimbabwe 13-19 years ²² <i>Timeframe:</i> 2015-2017	Cluster-randomized controlled trial; 16 rural primary care facilities randomized to Zvandiri model or standard of care (SOC).	Zvandiri: Community adolescent treatment supporters provided adherence and counseling support at facility and in community and tailored to patient needs; 3 month ART refills; monthly support groups; caregiver support	<p>Combined outcome: Death or viral load >1000 copies/ml at 96 weeks; 496 adolescents enrolled</p> <ul style="list-style-type: none"> Zvandiri 22% vs. control 36% (p=0.03) No difference in secondary outcomes (discontinuation of ART >3 months; <80% visit attendance; disclosure; SSQ-14 score; PHQ-9 score) Note: Control group seen every 3 months in clinic and unclear if received MMD/S 	"Qualitative data suggested that the multiple intervention components acted synergistically to improve the relational context in which adolescents with HIV live..."
Tanzania 1-26 years ²³ Mean age: 11.8 years <i>Timeframe:</i> 2013-2015	Retrospective review of 1164 patients on Standardized Pediatric Expedited Encounters for ART Drugs Initiative (SPEEDI) model in one site	Clinic visits and ART refills every 2 months, alternating between SPEEDI visit (collect ART without clinician visit) and regular visit (with clinician evaluation).	<p>51% of clinic patients enrolled in SPEEDI.</p> <p>Outcomes:</p> <ul style="list-style-type: none"> LTFU 0.6%, mortality 1.1%; Both indicators on a downward trend since SPEEDI After SPEEDI, overall satisfaction with clinical services remained high at 90.5%, wait times were reduced (wait >1 hour from 63.1% to 55%), and reporting wait was long or too long fell from 35.8% to 21%. No viral load data available. 	Expediting clinic visits is safe and feasible. Noted that dosing changes usually required only 5 times between ages 3 months and 8 years, so interval could be safely extended to three months.
Uganda and Kenya 2-14 years ²⁴ Median age: 8 years <i>Timeframe:</i> 2013-2015	Prospective cohort of 83 children who initiated ART with CD4>500 and received streamlined care model	A patient-centered care system, with nurse-driven visits focused on symptom-based ART toxicity screening, on-site nurse referral of complex cases to a physician, streamlined visit schedule with the provision of three months' ART refills, appointment reminders and patient tracking.	<p>Outcomes at 48-weeks:</p> <ul style="list-style-type: none"> 89 percent retention in care 92 percent of those tested had viral suppression (<500 copies/ml) 	Streamlined nurse-driven care systems can deliver safe and effective ART care to children in rural communities.
Malawi	Retrospective case-control	Adolescent-centered differentiated care model (teen	Primary outcome: Non-retention in care (attrition).	Older adolescents have higher risk of

²² Mavhu W, Willis N, Mufuka J, et al. Effect of a differentiated service delivery model on virological failure in adolescents with HIV in Zimbabwe (Zvandiri): a cluster-randomised controlled trial. *Lancet Glob Health*. 2020;8(2):e264-e275. doi:[10.1016/S2214-109X\(19\)30526-1](https://doi.org/10.1016/S2214-109X(19)30526-1)

²³ Bacha JM, Aririguzo LC, Mng'ong'o V, et al. The Standardized Pediatric Expedited Encounters for ART Drugs Initiative (SPEEDI): description and evaluation of an innovative pediatric, adolescent, and young adult antiretroviral service delivery model in Tanzania. *BMC Infect Dis*. 2018;18(1):448. doi:10.1186/s12879-018-3331-2

²⁴ Mwangwa, F., et al. "48-week outcomes of African children starting ART at CD4>500 with streamlined care." Poster presented at the Conference on Retroviruses and Opportunistic Infections (CROI), Boston, Massachusetts, USA, 2016. <https://www.croiconference.org/sessions/48-week-outcomesafrican-children-starting-art-cd4500-streamlined-care>.

10-19 years ²⁵ <i>Timeframe: 2010-2015</i>	study of 617 adolescents. Cases=ALHIV not retained in care; Controls=ALHIV retained in care	club) with dedicated weekend clinic time, sexual and reproductive health education, disclosure and ART adherence support, 3 month ART refills, individualized peer counseling and support, peer interaction.	<ul style="list-style-type: none"> Exposure to teen club package associated with 3.7 times lower odds of attrition compared to those not exposed to teen club. Regardless of teen club exposure, attrition was two times higher among those 15-19 years than those 10-14 years. 	attrition even with teen club, highlighting need for age-group specific programs and transitioning protocols.
Kenya Operation Triple Zero (OTZ) ²⁶ 10-24 years old <i>Started in 2016 (one facility) and at 400 facilities as of March 2018</i>	Program review using routine program data 2017-2018	All AYPLHIV receiving treatment can join OTZ clubs and commit to achieve the three zeros (zero missed appointments, zero missed medications, and zero viral load). Clubs involve monthly meetings, text messages, and other modalities to provide support and training and empower AYPLHIV to take charge of their health. Stable OTZ members receive 3-month ART refills. OTZ also has caregiver and healthcare worker modules.	Preliminary data from six implementing partners: <ul style="list-style-type: none"> Of 2,742 AYPLHIV, viral suppression increased from 71% (range 67% - 82%) to 82% (range 71% -96%) after 6 months of enrolment into OTZ. In data from Western Kenya: <ul style="list-style-type: none"> Self-reported adherence across programs increased from 88% in October 2017 to 96% in February 2018. 	Successful program that has been scaled up widely in Kenya and now being considered for adoption in other countries.
Kenya, Malawi, South Africa, Tanzania, Zimbabwe ²⁷ 10-26 years <i>2016-2017</i>	32 focus group discussions (FGD) with 393 'young people from diverse groups'	Per FGD, youth want: <ul style="list-style-type: none"> Fewer clinical visits and youth friendly clinics with shorter queues Alignment of ART refills with school terms; extended hours for pickup Quick, short, friendly 2 month ART refill visits <ul style="list-style-type: none"> Concern that 3-6 months in between refills may present a LTFU challenge in that adolescents who interrupt treatment or silent transfer will only be picked up after 3-6 months Integration of psychosocial support with clinical consultation and ART refill dates with virtual support groups in between visits 	Differentiated care approach should be used to support all AYPHIV, including those on ART <6 months and those not virally suppressed.	

²⁵ MacKenzie, R.K., et al. 2017. "Greater retention in care among adolescents on antiretroviral treatment accessing 'Teen Club' an adolescent-centered differentiated care model compared with standard of care: a nested case-control study at a tertiary referral hospital in Malawi," *Journal of the International AIDS Society*, no. 3: e25028.

²⁶ Operation Triple Zero: Empowering Adolescents and Young People Living with HIV to Take Control of Their Health in Kenya. PEPFAR Solutions Platform, Nov 2018. <https://www.pepfarsolutions.org/solutions/2018/10/30/operation-triple-zero-empowering-adolescents-and-young-people-living-with-hiv-to-take-control-of-their-own-health> (Accessed July 1, 2020).

²⁷ Ndlovu, Prosper. "Differentiated Service Delivery: Youth Perspectives," Presentation at the 9th IAS Conference on HIV Science, Paris, France, July 23-26, 2017. <https://slideplayer.com/slide/12771426/>

NATIONAL MMD/S POLICIES FOR AYPLHIV

A review of national policies related to MMD/S was conducted; full details and references can be found in Appendix B. Overall, most national policies permit this modality of treatment for patients who are defined as stable according to national criteria. Of the 30 countries that account for 89% of new HIV infections, 26 allow ART dispensing every three to six months. When including sub-Saharan African countries not accounted for in the above 30 countries, 87% of 53 countries permit MMD/S ranging from two to six months of ART. Four countries require monthly pickup (Benin, Equatorial Guinea, Gabon, and Pakistan). Most policies do not specify the age at which patients may receive MMD/S of ART. Exceptions include Ghana, where children may begin using MMD/S at age five years, and South Africa and Zimbabwe, where children 10 years and older may do so. Policies in Eswatini, Malawi, and Uganda include ART MMD/S for children, but do not declare a minimum age for qualification. Of note, policy is only one part of an enabling environment to promote MMD/S; others include ART availability, supply chain optimization, staff knowledge, and community awareness and acceptance.

KEY CONSIDERATIONS FOR SCALE-UP OF MMD/S IN AYPLHIV

1. **The data on ART MMD/S for AYPLHIV is scarce.** As demonstrated in this literature review, few studies have focused on MMD/S in youth, especially at intervals for ART refills >3 months. Although several AYPLHIV interventions have been evaluated and found to be effective, the models focus primarily on provision of psychosocial support, with MMD/S as a minor component. This makes it difficult to discern the impact of MMD/S in optimizing youth retention and viral suppression.
2. **Acceptability and preferences of AYPLHIV related to MMD/S are not well-defined and may not align with those of adults.** Although information is limited, the findings of the multi-country FGDs described above suggest that the longer intervals (e.g., six months) preferred by adults may be less appealing to AYPLHIV. Close consultation with youth on preferences related to MMD/S intervals (e.g., two, three, or six months) and locations (e.g., facility vs. community-based) should be an integral part of MMD/S scale-up, including determining what differences may be present between AYPLHIV living in rural and urban environments.
3. **More data is needed on clinical and programmatic outcomes of AYPLHIV who receive MMD/S.** Although the existing data on retention in care is promising, there is a particular dearth of data on virologic outcomes in AYPLHIV who receive MMD/S, especially at longer intervals. The maintenance of virologic suppression seen in older adults may not occur in youth, so evaluations of virologic suppression with varying intervals of MMD/S would be useful for program design.
4. **Older adolescents (15-19 years) and young people (15-24 years) are a particularly vulnerable group for disengagement from care in DSD models.** This review showed that participation in teen clubs or community adherence clubs did not necessarily mitigate issues with attrition and virologic suppression, and even those defined as stable and referred to DSD models exhibited higher rates of attrition than other age groups. These findings suggest that more tailored services are needed for this population.

Recommendations for designing interventions to improve retention and adherence among AYPLHIV can be found in Appendix C.

CONCLUSIONS

DSD has already had a significant positive impact on HIV service delivery by decreasing the burden of care for both patients and providers while improving retention in care and maintaining high rates of virologic suppression. Most DSD models thus far have incorporated ART refill intervals of two to three months, although more countries are using six-month intervals as experience and comfort with DSD grows and reassuring data accumulates. However, more focused attention on the preferences of AYPLHIV regarding MMD/S and its impact on clinical and programmatic outcomes is needed.

Ending the HIV/AIDS epidemic supports the achievement of several of the Sustainable Development Goals (SDGs) by 2030, such as SDG 3: Ensure healthy lives and promote wellbeing for all at all ages. While evidence shows improvements in the overall wellbeing of youth, these improvements have not been felt by AYPLHIV. We live in a time when we can realistically end the HIV epidemic if almost all people living with HIV are treated, adhere to treatment, and are virally suppressed. Yet in this high-potential environment, studies of what works for youth adherence are few. We must pilot and test what may work for young people, then learn, redesign, and pilot again or scale-up. In this way, we can control HIV/AIDS, support healthy lives for young people living with HIV today, and end new infections. Doing so requires that we perceive and engage AYPLHIV as individuals, partners, and experts with a great deal to contribute in promoting their health, well-being, and development.

APPENDIX A. KEY TERMS RELATED TO HIV TREATMENT

95-95-95 Goals

The 95-95-95 goals of the Joint United Nations Programme on HIV/AIDS (UNAIDS) aim to help end AIDS by 2030. Those goals are that 95 percent of people living with HIV knowing their HIV status; 95 percent of people who know their status are on ART; and 95 percent of people on ART have achieved suppressed viral loads. Goals include reducing the annual number of new HIV infections among adults to 200,000 and achieving zero AIDS-related discrimination.

HIV Continuum of Care

The HIV care continuum includes HIV prevention, testing, linkage to care, ART initiation, ART delivery, and chronic care.

Antiretroviral Therapy (ART)

Antiretroviral therapy (ART) is the primary means of treatment recommended by the World Health Organization (WHO) for all people living with HIV/AIDS. (Note that the 2016 WHO *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach* marked a paradigm shift with its “treat-all” recommendation; previous guidelines recommended limitations on eligibility based on CD4 count.)

Adherence

Adherence is taking medication as prescribed. ART adherence is intended for individuals to reach viral suppression, reduced risk of drug resistance, improved overall health and quality of life, and decreased risk of HIV transmission. Adherence is also linked with reduced risk of morbidity and mortality.

Retention

Retention refers to staying on ART (ART retention) and/or staying in HIV-related care (retention in care).

Viral Suppression

When ART reduces a person's viral load (number of copies of HIV ribonucleic acid (RNA) per milliliter of blood) to an undetectable level.

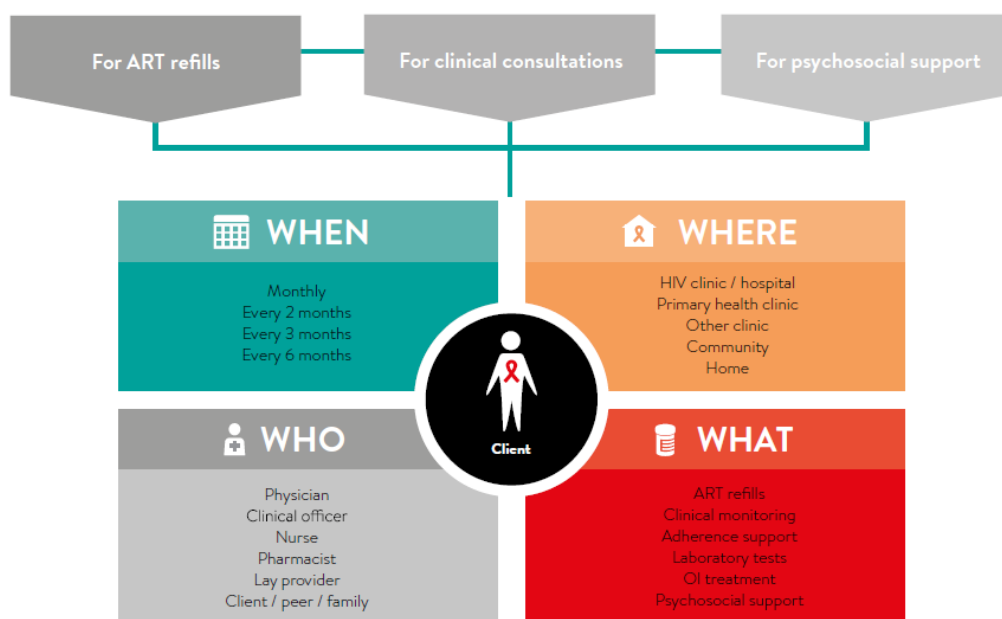
Differentiated Service Delivery (DSD)

Differentiated service delivery (DSD), also referred to as differentiated care, is a holistic, person-centered approach that applies across the HIV continuum of care. Differentiated service delivery (DSD) streamlines services as part of reaching the 95-95-95 goals to increase the number of people tested, treated, and virally suppressed by 2030. Differentiated ART delivery, on the other hand, refers to the part of the care continuum that includes treatment and viral suppression.

The WHO *Key Considerations for Differentiated Antiretroviral Therapy Delivery for Specific Populations: Children, Adolescents, Pregnant and Breastfeeding Women and Key Populations* is a guideline for ART for clinically stable people. Figure 1 illustrates the building blocks of differentiated ART delivery. Approaches using these building blocks are expected to overcome barriers to treatment and strengthen adherence

through a holistic model that includes medication, clinical attention, and psychosocial support. For adolescents and youth, clinics may offer Saturday adolescent days when youth-friendly trained staff focus on young people living with HIV.

Figure 1. Building Blocks for Differentiated ART Delivery²⁸



Multi-month Dispensing (MMD)

Multi-month dispensing (MMD) is one piece of differentiated ART delivery (see Figure 1 below). It allows health facilities and pharmacies to provide more than one month of ART medicine to a patient at once. The typical MMD range is two to six months.

Multi-month Scripting or Prescription (MMS/MMP)

Multi-month scripting or prescription (MMS/MMP) allows medical providers to prescribe more than one month of ART medicine to a patient at once.

Stable patient

In the context of differentiated service delivery, a stable patient is one who is clinically well, adherent to ART, and has a suppressed viral load. These patients require less intensive clinical services and thus are eligible for less frequent facility visits.

²⁸ IAS. Differentiated care for HIV: A decision framework for antiretroviral therapy. 2016. http://www.differentiatedcare.org/Portals/0/adam/Content/yS6M-GKB5EWs_uTBHkIClO/File/Decision%20Framework%20REPRINT%20web.pdf

Community ART Refill Groups (CARGs)

CARGs are an ART delivery model in which clinic patients voluntarily form groups and group members take turns traveling to the clinic to collect monthly ART refills for all group members.

Adherence clubs

Adherence clubs are groups of 20-30 patients that meet every 2-3 months for a counseling and medication pickup session in a clinic or community setting. The number of patients and intervals between meetings may vary depending on the country, setting (e.g., urban vs. rural), and/or population type (e.g., men, pregnant women, key population, etc.).

APPENDIX B. NATIONAL POLICIES RELATED TO MMD/S

* Indicates the policy did not explicitly reference the age at which MMD/S is permitted or if adolescents or youth can use MMD/S

Country	Policy Statements related to MMD/S	MMD/S permitted	MMD/S permitted for children	Reference
Angola	<p>"HIV /AIDS programs must ensure that ARV and related treatments are accessible to all people who need it, including pregnant women, children and key populations, in an environment free from discrimination."</p> <p>"It should be noted that access to ARVs is universal in the country and every effort must be made to withdraw medication free of charge and without constraints, including patients treated and medicated by the country's private network."</p> <p>- translations from Google Translate</p>	Yes	*	2015: REPÚBLICA DE ANGOLA MINISTÉRIO DA SAÚDE INSTITUTO NACIONAL DE LUTA CONTRA A SIDA. Normas de Tratamento Antiretroviral.
Bangladesh	<p>No specific mention of MMD/S, but two statements suggest MMD is available:</p> <p>1. First month: follow up visit every two weeks; Second month onward: follow up visit every month. Once stabilized and CD starts improving (after six months on ART) and the patient does not have any OI or adverse events, <i>the visit frequency can be once in two or three months depending on drug stocks, distance patient has to travel to reach CST Centre.</i></p> <p>2. After starting ART follow up visit ideally should be in two weeks and in one month after the start of ART. <i>After a month adherence measurement and counseling should be done every month or whenever the patient comes to collect ARV.</i></p>	Implied	*	2014: National AIDS /STD Program, Directorate General of Health Services, Ministry of Health and Family Welfare, Govt. of Bangladesh. National Guidelines for Antiretroviral Therapy. https://www.medbox.org/bd-guidelines-hiv-tb/national-guidelines-for-antiretroviral-therapy/preview
Benin	Monthly pickup	No	*	UNAIDS Laws and Policies Analytics
Botswana	<p>Two- to three-month ART will be permitted: central medical stores to inform health facilities when they can begin (securing supply chain needed).</p> <p>Teenagers cannot be denied treatment, though health providers must judge the person's maturity; parental accompaniment is advised. Pregnant adolescents do not need parental consent for HIV testing or treatment. Parental/ adult support recommended.</p>	Yes	*	2016: Handbook of the Botswana 2016 Integrated HIV Clinical Care Guidelines; Avalos, Ava. Nothing but the Best; Optimizing the ART Response in Botswana. AIDS 2016 Global HIV Clinical forum: integrase Inhibitors.

Brazil	ART pickup every three months for stable clients	Yes	*	2018: Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância, Prevenção e Controle das Infecções Sexualmente Transmissíveis, do HIV/Aids e das Hepatites Virais. Protocolo Clínico e Diretrizes Terapêuticas para Manejo da Infecção pelo HIV em Crianças e Adolescentes / Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Vigilância, Prevenção e Controle das Infecções Sexualmente Transmissíveis, do HIV/Aids e das Hepatites Virais. – Brasília : Ministério da Saúde; UNAIDS Laws and Policies Analytics;
Burkina Faso	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Burundi	ART pickup every six months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Cameroon	Underage adolescents must have parental consent to be tested. Refills are typically monthly, but the guidelines mention three-month follow-ups.	Yes	*	Ministry of Public Health. January 2015. National Guideline on the Prevention and Management of HIV in Cameroon.
Central African Republic	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Chad	Universal access to ART was officially declared in December 2006.	No policy	*	2013: Azétsop and Diop. Access to antiretroviral treatment, issues of well-being and public health governance in Chad: what justifies the limited success of the universal access policy? Philosophy, Ethics, and Humanities in Medicine.
China	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Comoros	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Cote d'Ivoire	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics

Democratic Republic of Congo	ART pickup every three to six months for stable clients	Yes	*	2018: République Démocratique du Congo, Ministère de la santé publique, Programme National de Lutte contre le VIH/Sida et les IST. Plan opérationnel d'offre des services différenciés en République Démocratique du Congo; République Démocratique du Congo Ministère de la santé publique, Secrétariat Général. 2018. Manuel d'Operationalisation des Modeles Differencies et du Guichet Unique VIH/TB> Programme de Lutte Contre le VIH et les IST (PNLS) et Programme de Lutte Contre La Tuberculose (PNLT).
Equatorial Guinea	Monthly pickup	No	*	UNAIDS Laws and Policies Analytics
Eswatini	Three-month ART through fast-track refills for stable patients. Only adolescents with an undetectable viral load are eligible for ART refills within a teen club. However, adolescents with a high viral load will be encouraged to participate in the group but will receive their ART refill through mainstream care with the engagement of the parent/guardian.	Yes	Yes	2016: Ministry of Health: Swaziland National AIDS Programme. Standard Operating Procedures for Implementing Community-centred Models of ART Service Delivery (CommART) in Swaziland.
Ethiopia	ART pickup every three months after six months on ART	Yes	*	2017: Ethiopia Federal Ministry of Health. National Guidelines for Comprehensive HIV Prevention, Care and Treatment.
Gabon	Monthly pickup	No	*	UNAIDS Laws and Policies Analytics
Ghana	Children >5 years of age, clinically stable and on adult doses, fully disclosed may have three-month ART refills through differentiated refill option. Recommends family approach for children through 10 years. Family group ART follow-up for mothers and children; facility-based adolescent group refill for adolescents who choose to receive their ART through a group approach.	Yes	Yes, at five years	2017: Ghana Health Services National AIDS/STI Control Programme (NACP).
Guinea	ART pickup every six months.	Yes	*	2019: Republique de Guinee, Ministere de la Sante. Guide de Mise en Place Rendez-vous à six mois : Un Modèle Différencié d'Accès au Traitement Antirétroviral :

				L'espace des visites pour les Personnes Vivant avec le VIH. PNLSH/ONUSIDA/MSF-B.
Guinea-Bissau	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Haiti	ART pickup every six months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
India	ART pickup every three months for stable clients:	Yes	*	2018: National AIDS Control Organization (NACO), Ministry of Health and Family Welfare Government of India. National Technical Guidelines on Anti-Retroviral Treatment.
Indonesia	Data unavailable		*	UNAIDS Laws and Policies Analytics
Iran	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Jamaica	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics; No reference found in CLINICAL MANAGEMENT OF HIV DISEASE Guidelines for Medical Practitioners
Kenya	ART pickup every three months for stable clients	Yes	*	2017: Ministry of Health, National AIDS and STI Control Program. Differentiated Care: Operational Guide. Nairobi, Kenya
Lesotho	ART refills lasting three to 6 months for stable patients	Yes	*	2016: Ministry of Health Government of Lesotho. National Guidelines on the Use of Antiretroviral Therapy for HIV Prevention and Treatment.
Liberia	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Malawi	Stable and adherent patients who have been on ART at least 6 months can be given up to 12-week (three-month) appointments Children (just like any other patients) who are adherent and stable on ART can be given three months of drug supply or more if necessary.	Yes	Yes	2016: Ministry of Health, Malawi. Malawi Guidelines for Clinical Management of HIV in Children and Adults.
Mali	ART pickup every six months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Mauritius	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics

Mozambique	ART every 3 months for stable clients	Yes	*	2018: Ministério da Saúde (MISAU), Direcção Nacional de Saúde Pública – Programa Nacional de Controlo das ITS/HIV e SIDA, Guião Orientador Sobre Modelos Diferenciados de Serviços em Moçambique
Namibia	ART pickup every three months for stable clients	Yes	*	2016: Republic of Namibia Ministry of Health and Social Services. National Guidelines for Antiretroviral Therapy.
Niger	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Nigeria	ART pickup every three months for stable clients	Yes	*	2016: Federal Ministry of Health, Abuja, Nigeria. National Guidelines for HIV Prevention, Treatment and Care for use in Nigeria.
Russian Federation	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Rwanda	ART pickup every three months for stable clients	Yes	*	2016: Republic of Rwanda Ministry of Health. National Guidelines for Prevention and Management of HIV and STIs.
Sao Tome and Principe	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Senegal	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Seychelles	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Sierra Leone	ART pickup every three to six months for stable clients	Yes	*	2018: National HIV/AIDS Control Programme, Ministry of Health and Sanitation. Guide of Differentiated care model in Sierra Leone: Who feels it knows it.
South Africa	ART pickup up to every six months for stable clients.	Yes	Yes, at 10 years	2017: Southern African HIV Clinicians Society. Guidelines for adherence to antiretroviral therapy in adolescents and young adults. Johannesburg, South Africa: Southern African HIV Clinicians Society.
South Sudan	ART pickup every three months for stable clients (adults and adolescents).	Yes	*	2017: Ministry of Health Republic of South Sudan. Consolidated Clinical Guidelines on Use of

				Antiretroviral Drugs for HIV Treatment and Prevention.
Togo	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Uganda	ART pickup every three months for stable adults and adolescents	Yes	Yes	2016: The Republic of Uganda Ministry of Health. Consolidated Guidelines for Prevention and Treatment of HIV in Uganda.
Ukraine	ART pickup every six months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
United Republic of Tanzania	ART pickup every 2 months after the first 6 months	Yes	*	2018: The United Republic of Tanzania Ministry of Health, Community Development, Gender, Elderly and Children. National Accelerated Plan on HIV Testing Services 2019 - 2020.
United States	Information about MMS/D not available		*	UNAIDS Laws and Policies Analytics; 2020: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. The National HIV/AIDS Strategy
Vietnam	ART pickup every three months for stable clients	Yes	*	UNAIDS Laws and Policies Analytics
Zambia	ART pickup every three months after 12 weeks on ART	Yes	*	2018: Republic of Zambia Ministry of Health. Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection.
Zimbabwe	Adolescents receive 3-month ART refills if disclosed to and on adult ART doses.	Yes	Yes, at 10 years	2017: Zimbabwe Ministry of Health and Child Care (MoHCC). Operational and Service Delivery Manual for the Prevention, Care and Treatment of HIV in Zimbabwe (OSDM). Zimbabwe MoHCC. Consolidated HIV and AIDS Job Aide.

APPENDIX C. RECOMMENDATIONS FOR DESIGN OF INTERVENTIONS FOR AYPLHIV

To improve AYPLHIV adherence, we recommend the following:

1. Make research, implementation, and testing part of a necessary learning cycle. To improve adherence among AYPLHIV, research what appears to be working, design interventions accordingly, test the intervention(s), learn, and redesign. Specifically, we propose to:
 - a. Include adolescents and youth in research to fill critical gaps in understanding how these groups perceive adherence, challenges with ART and having HIV, and how well they accept aspects of DSD.
 - b. Include key populations in research and implementation and use an intersectional lens that includes age, sex, adherence rate, and additional designations such as “pregnant,” “sex worker,” etc., as many adolescents and youth are also among key populations.
2. Give AYPLHIV a voice in designing, implementing, monitoring, and evaluating interventions to improve their adherence by applying a positive youth development (PYD) approach. Positive youth development is both a philosophy and an approach to youth development that “engages youth along with their families, communities, and governments so that youth are empowered to reach their full potential. PYD approaches build skills, assets, and competencies; foster healthy relationships; strengthen the environment; and transform systems.”²⁹ By seeing AYPLHIV as beneficiaries and participants in research and interventions to improve ART adherence, they will be empowered to be creative and co-design interventions for themselves and their peers. By engaging in monitoring and evaluation of interventions, they will help healthcare providers understand adherence challenges and change interventions to make them more effective, thereby improving ART adherence. The PYD framework describes four domains through which the vision of healthy, productive, and engaged youth can be achieved. Table 2 describes the domains and opportunities within each domain to support AYPLHIV.

Table 2. PYD Domains and Opportunities to Support AYPLHIV

Four Domains	Opportunities to support AYPLHIV
Assets: Youth have the necessary resources, skills, and competencies to achieve desired outcomes.	AYPLHIV know and understand: <ul style="list-style-type: none"> • Their HIV status • The need for a lifelong commitment to medicine • The value of ART and adherence • Who to talk with about HIV-related issues • How to get support with various challenges • How to ask questions

²⁹ <https://www.youthpower.org/positive-youth-development>.

	<ul style="list-style-type: none"> • How to develop healthy relationships
<p>Agency: Youth perceive and can employ their assets and aspirations to influence their own decisions about their lives and set their own goals, as well as act on those decisions to achieve desired outcomes.</p>	<p>AYPLHIV have:</p> <ul style="list-style-type: none"> • A positive self-identity • Self-efficacy vis-à-vis their health and commitment to self-care • Positive beliefs about the future supporting self-care in the present • Perseverance about adherence and health-related needs
<p>Contribution: Youth are engaged as a source of change for their own positive development and for their communities.</p>	<p>AYPLHIV can participate in:</p> <ul style="list-style-type: none"> • HIV-related research • HIV-related intervention design • Intervention monitoring and evaluation
<p>Enabling Environment: Youth are surrounded by an environment that develops and supports their assets, agency, and access to services and opportunities, and strengthens their ability to avoid risks and stay safe, secure, and protected, and live without fear of stigma or discrimination.</p>	<p>AYPLHIV are supported by:</p> <ul style="list-style-type: none"> • Family • Peers • Community • Clinic staff, healthcare workers, etc. • Youth-friendly services that are based on what AYPLHIV want and need, not just what providers and caregivers think they need • Public policy

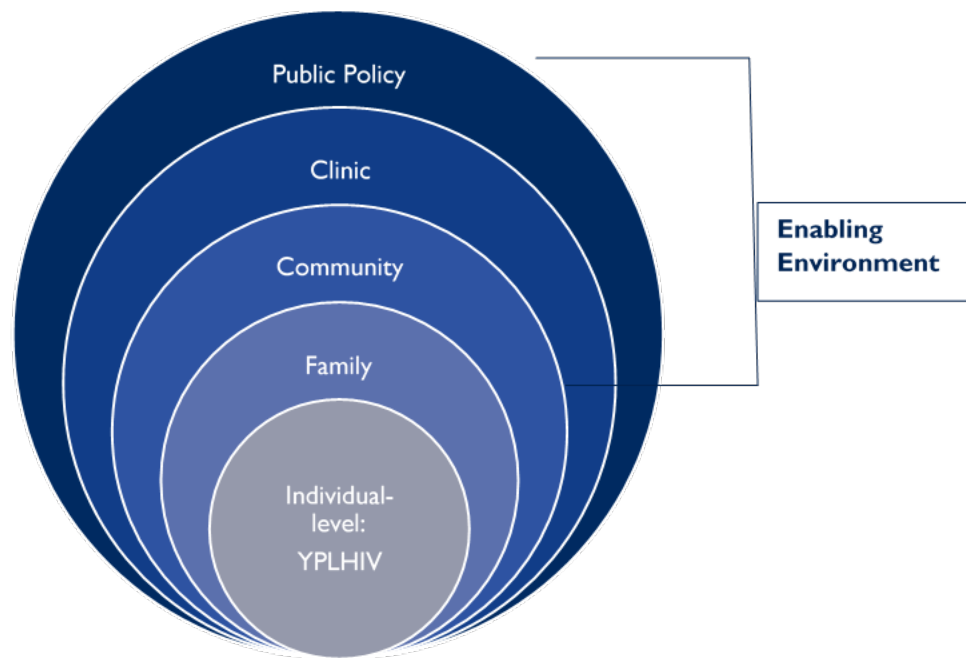


Figure 2. Social-ecological Model of AYPLHIV Adherence

In Figure 2, we envision the full range of factors that contribute to adherence using a social-ecological model, including the (A?)AYPLHIV themselves, their families, the clinics where they receive care, the communities in which they live and where they engage with peers, and the role of public policy. Each of the circles presents an opportunity for promoting youth health and wellbeing, as well as addressing stigma and discrimination, as described below.

Individual-level: The young person is either highly adherent to medication or not. S/he likely has one or more challenges to being adherent such as fear of inadvertent disclosure among peers or difficulty with medication side effects. Beyond the individual level, a positive enabling environment can support the growth of young people, including their self-efficacy in taking medicine. AYPLHIV need the social support of family, peers, community members, and clinic staff, as described below.

Family: Supportive family examples include the family supporting the individual to adhere to his/her medication and eat nutritious food and drink safe water and providing the financial resources for treatment and safe travel to and from the clinic. In unsupportive families, exposure to violence in the household, for example, undermines a young person's adherence.

Community: AYPLHIV may be afraid of discrimination and damaging relationships with peers and others. They may have a “buddy” (self-selected treatment supporter) who accompanies them to appointments or to pick up medication when they cannot.

Clinic: The clinic should be a safe space as relationships between the young person and clinic staff are special to AYPLHIV. Young people living with HIV protect those relationships by restricting what they say about taking medication, thereby avoiding judgment, anger, or disappointment. Expectations about

the clinic as a safe space include an adequate supply of medication so that AYPLHIV can get what they need; adolescent-only hours outside of school hours so they can interact with peers and avoid calling attention to themselves by regularly missing school; and friendly, trained staff who take the time to listen to AYPLHIV and refrain from expressing judgment about HIV or ART adherence. While ART adherence is critical to their health and wellbeing, the medicalization of ART adherence—making HIV care about taking medicine only—damages adherence when AYPLHIV feel they cannot talk about challenges managing their HIV status, storing and taking medicine, and doubts, questions, and concerns about their future. The focus needs to be on the young person’s wellbeing, which requires a more holistic approach to care.

Public policy: The AYPLHIV enabling environment includes public policy. Policies may support adolescent- and youth-friendly integrated services, such as family planning and sexual and reproductive health education to support the broad range of AYPLHIV needs. Policies to support the implementation of DSD with integrated services for adolescents and youth may be adequately resourced and implemented at one end of the spectrum or, at the other end, exist only on paper, with little support. Training may be necessary to help clinic staff see AYPLHIV holistically and support their empowerment and self-efficacy.

Each level and context must be understood and addressed to support ART adherence among young people.

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