



UPDATES IN HIV:
ADHERENCE
MARCH 2012,
ISSUE 3

UPDATES IN HIV: IMPROVING ADHERENCE TO ANTI-RETROVIRALS

Many people with HIV in Botswana are living longer, healthier lives because they are taking antiretrovirals (ARVs).

However, to be effective, ARVs need to be taken regularly, to ensure that the level of drugs in the patient's body are sufficient to achieve virologic suppression and to maximize the availability of future therapeutic options.

Unfortunately, maintaining this level of adherence is challenging for many persons living with HIV.^{1,2}

This edition of Tlaleletso offers an overview of the factors that influence adherence and highlights some of the strategies that can be used by doctors and nurses to help patients optimize their adherence to therapy.

WHY IS ADHERENCE IMPORTANT?

When ARVs are not taken all of the time, drug levels in the blood become sub-therapeutic and the HIV virus can multiply.

With increasing viral load in the presence of ARVs more mutations will occur that cause resistance to the ARVs.

Once resistance develops the ARVs are no longer effective and viral replication increases, CD4 count drops and clinical illness develops.

The short life cycle of HIV (1-2 days) means that whenever there is any non-adherence, viral load increases very quickly – within 3-7 days, sometimes even faster.

For this reason, if a person takes their ARVs less than **95%** of the time, the risk of resistance to the drugs increases significantly.

ASSESSING ADHERENCE

It is important that nurses, doctors and pharmacists assess adherence at every visit. Standard assessment in Botswana should include:

Direct questioning: Often patients don't tell their doctors if they are non-adherent. However patient self-reports of sub-optimal or poor adherence are very likely to be true and should be taken seriously.

Pill counts: At each visit the nurse or pharmacist should perform a pill count, to assess how many pills the patient has left since their last clinic visit. Pill counts can be a helpful marker of adherence although they are not a perfect indicator of adherence either.

Viral Load: An essential part of the adherence assessment is viral load measurement. An elevated viral load is a very sensitive marker of poor adherence. Anybody who has an elevated viral load warrants intensive adherence support and frequent viral load and CD4 monitoring.

WAYS TO IMPROVE ADHERENCE

- Adherence support is always important especially in the first two years on a new regimen.
- Adherence should be addressed at **every** visit to the IDCC
- Knowledge is a necessary component of adherence, but transfer of information *alone* is not sufficient to promote sustained adherence behavior. People need to understand why they need to take their pills.
- An open, collaborative, patient-provider partnership with shared decision-making maximizes



ADHERENCE IN BOTSWANA

Studies in Botswana have demonstrated that most patients are good at adhering to their ARVs >90% of the time.³

One study in Botswana found that even among patients with confirmed virologic failure, adherence was very good (average adherence 91%).⁴

In another Botswana-based study⁵ of 94 adults on ARV therapy responses showed that good adherence was associated with:

- Belief that the medications help
- Understanding the risks of not taking medications correctly
- Advice and support from doctors
- Family support
- Personal determination
- Improvement of symptoms on therapy

Finally, an extensive qualitative study of barriers to adherence in Botswana showed that transport costs and lost wages were important financial barriers to good adherence. The researchers recommended that providing transport and food support to patients who are too poor to pay, and that recurrent costs to users should be reduced by providing three-months, rather than the one-month supply of medication once optimal adherence levels have been achieved⁶.

RISK FACTORS FOR POOR ADHERENCE⁷

Characteristics of the individual associated with poorer adherence

1. Patient factors

- Lack of knowledge about HIV, the antiretroviral regimen, and the reason for adherence
- Literacy and language barriers
- Active substance abuse
- Mental illness, especially untreated depressive symptoms
- Treatment fatigue

2. Illness and treatment-related attributes

- Treatment-related comorbidities
- Regimen complexity
- Illness and/or treatment-related symptoms and comorbidities
- Multiple childcare responsibilities, travel commitments

3. Situational conditions

- Food insecurity, unstable housing, and/or poor transportation options related to cost, distance, and convenience
- Stigmatization and social isolation
- Demanding or erratic schedule, multiple childcare responsibilities, travel commitments
- Healthcare system related (e.g., limited access to HIV care and medications, poor clinic or poor patient-provider relationship).

4. Drugs

- Complicated dosing regimens and increased numbers of pills
- Bad side effects
- Cost (This is an issue for private sector patients and non-citizens without insurance)

Key Strategies To Improve Adherence

There has been a lot of research to evaluate interventions to improve adherence.^{8,9} Strategies that have been studied include:

- Patient education strategies¹⁵
- Addressing other medical and psychiatric problems¹⁰
- Cue-based reminders and monetary rewards¹²
- Social support/buddy systems
- SMS reminders¹³

The impact of any of these interventions on its own is generally modest.¹⁴ However, it has been shown that even small improvements in adherence enhance virologic outcomes and are cost-effective.

No single type of adherence intervention is clearly implied for clinic use by findings to date. However, an approach including a combination of strategies is likely to be effective. Adherence strategies also need to be individualized.

Practical adherence suggestions that can be used with all patients include:

1. Take pills with you to work and if you haven't disclosed your status at work/school take the pills in the bathroom
2. Set your cellphone to remind you or ask your adherence partner to text you
3. Take your pills at night if you are nauseated

4. Limit your alcohol intake

For each individual patient, regardless of which of these strategies is adopted, it is vital to assess the barriers and challenges to adherence as well as ensuring that they have the skills and knowledge necessary to do so.

All adherence strategies must be:

- **Ongoing** – every visit
- **Repetitive** – with consistent information
- **Revised** – to meet the changing needs of each patient
- **Multidisciplinary** – involving the patient, doctors, nurses, pharmacists, counselors, treatment partners, social workers, etc.

BOTSWANA GUIDELINES: MANAGING SUB-OPTIMAL ADHERENCE^A

- Suspect poor adherence in all patients with elevated viral load
- Initial strategies should include maintaining all patients with poor adherence on their current regimen, while the non-adherence is being addressed.
- Provide intensive adherence counseling to identify the adherence issues
- Continue patients on current regimen and repeat follow up priority viral load 4-6 weeks after intensive counseling adherence is completed or other medical issues are resolved.
- If repeat VL < 400 copies/mL, then repeat VL again at 3 months and then every return to 6 month viral load monitoring for adults, and every 3 month viral load monitoring for pediatric and adolescent patients.
- If repeat VL > 400 copies/ml and all correctable causes have been acted upon, assume that resistance has developed and change the regimen accordingly.

ASSESSMENT FOR VIROLOGIC FAILURE/ INTENSIVE ADHERENCE INTERVENTION

The Failure Management Team/Clinic should follow a protocol for prompt follow-up of treatment failure including the following:

- Assess patient motivation and understanding of the importance of adherence
- Involvement of adherence partner and/or care-giver(s) in clinical decisions
- Review of any side effects which might interfere with adherence
- Assess the complexity and inconvenience of the regimen
- Screen for depression or other mental illness and substance or alcohol abuse
- Determine if there are problems with stigma or disclosure, which might adversely impact adherence
- Assess for presence of any illness which might adversely affect adherence
- Review of potential drug-drug interactions
- Determine if there are any medical conditions interfering with oral intake or ARV absorption
- Diagnose any inter-current infections which might elevate viral loads

SUMMARY

- Potent antiretroviral drug regimens have significantly improved the life expectancy of persons living with HIV. However, to be maximally effective lifelong adherence is necessary.
- Unfortunately, even missing doses 10% of the time can have a significant impact leading to virologic failure and even development of drug resistance HIV.
- Suboptimal adherence is a pervasive problem and even the most reliable patients have a hard time taking their ARVs all of the time.
- The reasons why patients do not adhere to their antiretroviral regimen, even when it may prolong their lives, are not simple.
- Maximizing adherence and achieving the full potential of the antiretroviral therapies requires attention to many complex behavioral issues that compromise the success of HIV therapies.
- Adherence must be assessed at every visit and must involve a multidisciplinary team approach. Improving adherence requires a team effort from doctors, nurses, pharmacists and social workers – as well as the patient!

UPCOMING LECTURES

April	Guidelines Update: Diabetic Emergencies
May	Topics in HIV: Mental Health
June	Guidelines Update: Overdose
July	Topics in HIV: Tuberculosis Co-infection

BOTSWANA UPENN PARTNERSHIP

Got a clinical question about a complicated medical patient or a patient with HIV?

Mike Reid

267 724 78 777

OR

Miriam Haverkamp

267 76516520

WANT TO READ MORE? CHECK OUT THE REFERENCES BELOW:

1. Chesney MA, Ickovics J, Hecht FM, Sikipa G, Rabkin J. Adherence: a necessity for successful HIV combination therapy. *Aids* 1999;13 Suppl A:S271-8.
2. Lima VD, Harrigan R, Bangsberg DR, et al. The combined effect of modern highly active antiretroviral therapy regimens and adherence on mortality over time. *J Acquir Immune Defic Syndr* 2009;50:529-36.
3. Bussmann H, Wester CW, Ndwapi N, et al. Five-year outcomes of initial patients treated in Botswana's National Antiretroviral Treatment Program. *Aids* 2008;22:2303-11.
4. Bisson GP, Rowh A, Weinstein R, Gaothe T, Frank I, Gross R. Antiretroviral failure despite high levels of adherence: discordant adherence-response relationship in Botswana. *J Acquir Immune Defic Syndr* 2008;49:107-10.
5. Weiser S, Wolfe W, Bangsberg D, et al. Barriers to antiretroviral adherence for patients living with HIV infection and AIDS in Botswana. *J Acquir Immune Defic Syndr* 2003;34:281-8.
6. Hardon AP, Akurut D, Comoro C, et al. Hunger, waiting time and transport costs: time to confront challenges to ART adherence in Africa. *AIDS Care* 2007;19:658-65.
7. Reynolds NR, Testa MA, Marc LG, et al. Factors influencing medication adherence beliefs and self-efficacy in persons naive to antiretroviral therapy: a multicenter, cross-sectional study. *AIDS Behav* 2004;8:141-50.
8. Reinsner SL, Mimiaga MJ, Skeer M, Perkovich B, Johnson CV, Safren SA. A review of HIV antiretroviral adherence and intervention studies among HIV-infected youth. *Top HIV Med* 2009;17:14-25.
9. Simoni JM, Amico KR, Pearson CR, Malow R. Strategies for promoting adherence to antiretroviral therapy: a review of the literature. *Curr Infect Dis Rep* 2008;10:515-21.
10. Walkup J, Wei W, Sambamoorthi U, Crystal S. Antidepressant treatment and adherence to combination antiretroviral therapy among patients with AIDS and diagnosed depression. *Psychiatr Q*. 2008;79:43-53
11. Gaur AH, Belzer M, Britto P, et al. Directly observed therapy (DOT) for nonadherent HIV-infected youth: lessons learned, challenges ahead. *AIDS Res Hum Retroviruses* 2010;26:947-53.
12. Wise J, Operario D. Use of electronic reminder devices to improve adherence to antiretroviral therapy: a systematic review. *AIDS Patient Care STDS* 2008;22:495-504.
13. Lester RT, Ritvo P, Mills EJ, et al. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. *Lancet* 2010;376:1838-45.
14. Amico KR, Harman JJ, Johnson BT. Efficacy of antiretroviral therapy adherence interventions: a research synthesis of trials, 1996 to 2004. *J Acquir Immune Defic Syndr* 2006;41:285-97.
15. Rueda S, Park-Wyllie LY, Bayoumi AM, et al. Patient support and education for promoting adherence to highly active antiretroviral therapy for HIV/AIDS. *Cochrane Database Syst Rev* 2006;3:CD001442.