

# Evaluation of Adherence to Highly Active Antiretroviral Therapy in Adults in Jamaica

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## ABSTRACT

**Background and Purpose:** Highly active antiretroviral therapy (HAART) has improved morbidity and mortality and quality of life, revitalized communities and transformed the perception of HIV/AIDS from being a “death sentence” to a chronic illness. Strict and sustained adherence to medication is essential long-term viral suppression. In April 2005, an Adherence Support Programme was introduced to Jamaica’s HIV Programme, whereby Persons Living with HIV/AIDS (PLWHA) who had achieved high levels of adherence were trained to provide support to other PLWHA in order to increase their adherence to HAART regimens.

**Methods:** A cross-sectional survey of 116 individuals with advanced HIV and on HAART was performed in June and July 2006.

**Results:** Many participants were unemployed, poor persons with limited education. Based on self-report of seven-day adherence, 54.8% of persons were 95–100% adherent, 37.5% were 80–94% adherent and 7.7% were < 80% adherent. Having interacted with an adherence counsellor was not associated with adherence levels. Factors associated with nonadherence were: being away from home (38%), sleeping through dose-time (37%), forgetfulness (37%) and running out of pills (31%). Having no food (26.9%), not wanting to be seen taking medication (20%) and intolerable side effects (18.8%) were also reasons given. Only 44% of persons used aids to remind them of dose times.

**Conclusion:** Adherence in this study group is low and may have worsened since 2005. More emphasis must be placed on preparing adults to start HAART. The use of pillboxes and other reminders such as alarm clocks and cell phones must be reinforced.

# Evaluación de la Adhesión a la Terapia Antiretroviral Altamente Activa en Adultos en Jamaica

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## RESUMEN

**Antecedentes y Propósito:** La terapia antiretroviral altamente activa (TARAA) ha producido un marcado mejoramiento en relación con la morbilidad y la mortalidad así como la calidad de la vida. Asimismo, ha revitalizado las comunidades y transformado la percepción del VIH/SIDA, de una “sentencia de muerte” a una enfermedad crónica. La adhesión estricta y sostenida a la medicación es esencial para una supresión viral a largo plazo. En abril de 2005, se introdujo un Programa de Apoyo a la Adhesión como parte del Programa de VIH de Jamaica, mediante el cual personas que viven con VIH/SIDA (PVCVS) y que han alcanzado altos niveles de adhesión, fueron entrenadas con el fin de ayudar a otras PVCVS a aumentar su adhesión a los regímenes de TARAA.

**Métodos:** En junio y julio de 2006 se llevó a cabo un estudio transversal de 116 individuos con VIH avanzado y bajo TARAA.

**Resultados:** Muchos participantes eran personas desempleadas y pobres, con un nivel de educación limitado. Según un auto-reporte de adhesión por 7 días, 54.8% de las personas mostraron una

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adhesión de 95–100%, 37.5% presentaban una adhesión de 80–94% y 7.7% tenían una adhesión de < 80%. El haber interactuado con un consejero de adhesión no guardaba relación con los niveles de adhesión. Los factores asociados con la adhesión fueron el estar fuera de casa (38%), pasar durmiendo la hora de la dosis (37%), olvido (37%), y el quedarse sin tabletas (31%). No tener alimentos (26.9%), no querer ser visto tomando medicamentos (20%) y efectos colaterales intolerables (18.8%) fueron también razones dadas. Sólo el 44% de las personas usaban ayudas para recordarles las horas de las dosis.

**Conclusión:** La adhesión en este grupo de estudio es baja y puede haber empeorado desde el 2005. Hay que hacer más énfasis en preparar a los adultos para que comiencen con TARA. El uso de cajas de tabletas y otros medios recordatorios tales como despertadores y celulares tiene que ser reforzado.

## BACKGROUND

Jamaica is the third largest Caribbean Island and had an estimated population of 2.6 million in 2006. It is estimated that 1.5% of the adult population is infected with the human immunodeficiency virus (HIV), with no significant change over the last decade. The epidemic is concentrated in vulnerable groups such as sex workers (9% prevalence) and men who have sex with men (20 to 30% prevalence) (1). Since the first case of HIV infection was reported in 1982, a cumulative total of 11 004 cases of the acquired immunodeficiency syndrome (AIDS) have been reported in Jamaica with > 600 AIDS deaths occurring each year. The majority (65%) of reported AIDS cases in Jamaica is in the 20 to 44-year old age group and the AIDS case rates among men exceed that among women (2).

Jamaica has developed treatment Guidelines for the use of HAART (Table 1). This was implemented at 18 treatment

Table 1: National antiretroviral treatment guidelines for adults

First line regime <sup>1</sup>		Second line regime <sup>2</sup>	
Column A NRTI	Column B NNRTI	Column C NRTI	Column D Protease inhibitors
Zidovudine + Lamivudine	Nevirapine	Emtricitabine + Tenofovir	Lopinavir + Ritonavir
Emtricitabine + Lamivudine + Stavudine	Efavirenz Lamivudine	Zidovudine + Ritonavir	Indinavir +Tenofovir

1 First line regimen is a combination of drugs from column A and B

2 Second line regimen is a combination of drugs from column C and D

sites islandwide. All drug regimens are in keeping with major international standards. Since public access to HAART began in September 2004, over 3000 persons with advanced HIV have been placed on HAART resulting in a 36% decrease in mortality between 2005 and 2006 [305 AIDS deaths from January–June 2005 compared to 196 AIDS deaths from January–June 2006] (2).

## Adherence to HAART

The goal of HAART is to achieve sustained suppression of viral load, maintenance and restoration of immunologic

function and an overall improvement in the patient's quality of life (1, 2). Since the advent of HAART, overall morbidity and mortality in persons infected with HIV has markedly decreased (1–4). Clinical experience has shown that strict and sustained adherence to prescribed medications is essential to long-term viral suppression (1). Intermittent exposure of the virus to antiretroviral agents results in the development of viral resistance and an increase in viral replication with a higher risk of death (1, 2). Therefore, once treatment is started, high levels of adherence, in excess of 95% (1), are required to ensure efficacy and prevent the emergence of resistance.

However, high levels of adherence are difficult to achieve and many studies report an average of 70% of the required doses being taken as prescribed (13).

A number of factors have been shown to predict patients' adherence to HAART. However, patient readiness and the availability of family support positively influence adherence. Negative perceptions such as fear of side effects and concerns about the strict adherence rules have been related to poor adherence (14). Demographic characteristics such as ethnic group and age are usually non-predictive of medication compliance.

Several methods exist by which adherence may be measured. These include patient self-report, pill counts, prescription refill monitoring, use of electronic devices, therapeutic drug monitoring and viral load/CD4 count (15–17). No one method is perfect. Self-report through doctor's office visits, questionnaires, structured interviews or diaries provide a simple and practical way of determining the self-perceived level of adherence (16). Due to the subjective nature of this method results have been inconsistent (18, 19) and tend to give higher values than other methods but may still be the best available tool (20).

This study sought to evaluate the Adherence Programme in Jamaica and assess the current rates of adherence. The objectives of the evaluation were:

- C To describe the demographic characteristics of adults taking HAART in Jamaica
- C To measure current patient-reported adherence and compare with rates measured in 2005
- C To determine the relationship between adherence levels and interaction with adherence counsellors

- \* To identify the current factors associated with non-adherence
- \* To determine the factors and mechanisms utilized by persons taking HAART to improve adherence levels
- \* To compare adherence levels and factors associated with non-adherence in rural and urban sites and
- \* To make recommendations with regards to strategies that may improve the delivery of the adherence programme in Jamaica.

## SUBJECTS AND METHODS

A cross-sectional survey was conducted among patients attending five government-designated Adult Treatment Sites: CHARES, the Comprehensive Health Centre and the Kingston Public Hospital in urban Kingston and the rural St Ann's Bay and Mandeville Health centres.

### Data Collection

After approval by the Ministry of Health, Jamaica, a structured questionnaire was administered to participants. The questionnaire consisted of standardized questions and was previously used in the same setting in 2005. It was pretested among PLWHA and necessary adjustments made. Questionnaires were administered by trained interviewers in face-to-face interviews. Their practice was observed prior to and intermittently during the process.

### Site Selection

The five treatment sites were conveniently selected to ensure that sufficient numbers of patients would be available to be interviewed in the limited time frame. A sample size of 126 participants was chosen based on the patient attendance rates of the previous year. The numbers were proportioned among the treatment sites accordingly; 116 persons participated (92% response rate).

### Participants

At each of the five sites, on any given day, patients over the age of 15 years who were registered to attend the clinic were approached and invited to participate. No data were collected from persons who refused (8% refusal rate). Data were collected in June–July, 2006.

### Inclusion Criteria

All participants were HIV-infected adults and adolescents 16 years or older who had been diagnosed with advanced disease ( $CD4^+$  T-cells  $< 350/\mu\text{L}$ ) previously and started on HAART. Participation was voluntary and all patients who agreed to take part in the study were requested to sign a consent form indicating that they were giving informed consent. All patient information was kept confidential. Refusal to participate did not affect provision of service at the treatment site nor were any incentives offered for participation.

### Adherence Definition

Adherence was measured using patient recall information about the number of doses missed in the previous 24 hours and over the previous seven days. For the 24-hour report, persons who did not miss any doses were defined as having good adherence while those missing one or more were reported as having poor adherence.

Based on the Jamaica's HAART regimens, all patients on first-line regimens would be taking medications twice daily; therefore, analyses were based on 14 doses per week for all patients as follows:

- No missed doses: 95–100% adherent
- 1–2 missed doses: 80–94% adherent
- 3 or more missed doses:  $< 80\%$  adherent.

### Statistical Methods

Data were coded and entered into an Epi-Info database and then analyzed using SPSS 10<sup>®</sup> software (Chicago, Illinois, USA). The Pearson Chi-squared ( $X^2$ ) test was used to assess statistical significance. No multivariable model was constructed.

## RESULTS

### Sociodemographics

The sample consisted of 116 patients (92% of those approached) with an average of 23 per site, range 11–34. Thirty-nine per cent of the sample attended clinic in rural districts and 61% attended clinic in Kingston. The participants ranged in age from 19 to 62 years, with a median age of 36 years (Table 2).

Table 2: Sociodemographic data for participants

Age n = 116		Marital status n = 116		Educational level n = 116	
Age Group/ years	Frequency	Relationship	Frequency	Level attained	Frequency
15–24	13%	Single	39%	Primary	25%
25–34	33%	Casual	35%	Secondary	61%
>35	53%	Common law/ married	25%	Tertiary	1.9%

Fifty-two per cent of the sample was unemployed, with significantly higher rates in men than women, 64% *versus* 38% respectively ( $p = 0.006$ ). Unemployment rates were also the same for men in rural or urban clinics. Those persons who were employed engaged in a wide variety of non-technical jobs such as hairdressing, telemarketing and catering.

### Adherence

Of the 93 patients who could recall if they missed a dose in the last 24 hours, 59% reported not missing any doses with 20% each reporting one missed dose or having missed all doses. One hundred and four persons recalled the number of doses taken over the last seven days, 54.8% reported not missing a dose, 37.5% missed one or two doses and 7.7% reported missing three or more doses. There were no significant differences based on gender and educational levels.

### Risk Factors for Non-adherence

Using the 24-hour recall measure, there were no significant differences in adherence levels when compared by gender, educational status or location of clinic. For the seven-day recall, there were also no differences based on gender or education.

Urban dwellers were more likely to take all their medications in the previous seven days than rural dwellers (62.0% to 44.2%,  $p = 0.03$ ). However, 53.5% of those in the rural areas missed only 1–2 doses (80–94% adherent) with only 2.3% being < 80% adherent. Of those in the urban areas 26.2% missed 1–2 (80–94% adherent) doses and 11.5% were < 80% adherent (Fig. 1).

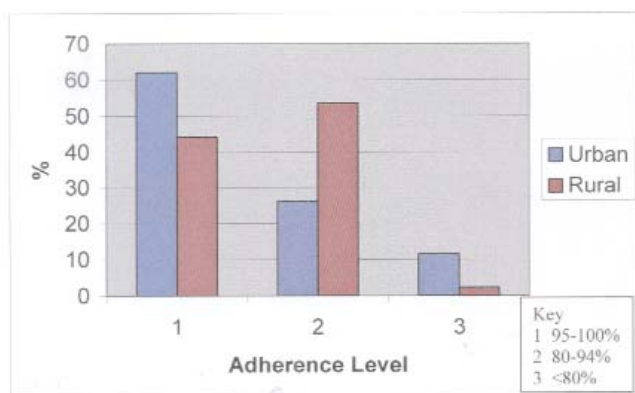


Figure: Comparative adherence by rural vs urban clinic attendees.

### Adherence and Interaction with a Counsellor

Eighty-seven per cent of patients reported having some interaction with an adherence counsellor. However, despite the high rate of interaction, there was no difference in adherence levels between those who interacted with a counsellor and those who did not (58% *versus* 57.5% for adherence levels of 95–100%). Additionally, only 20% of

those individuals who interacted with an adherence counsellor reported receiving support in adherence.

### Self-reported Reasons for Non-adherence

The major factors influencing adherence were being away from home, falling asleep, forgetfulness and running out of pills (Table 3). The majority of participants (56%) did not

Table 3: Reasons associated with missing ARVs

Reason	Number reporting	Percentage
<b>n = 116</b>		
Away from home	44	38
Fell asleep or slept through dose time	43	37
Simply forgot	43	37
Ran out of pills	36	31
Have no food to take with medication	31	27
Did not want others to notice	23	20
Intolerable side effects	22	19
Felt sick	13	11
Felt good	10	9
Felt depressed/overwhelmed	9	8

use specific aids to remind them of dose times. When mnemonic devices were used, they included assistance from the adherence counsellors, pillboxes and family members (Table 4).

Table 4: Methods utilized to support adherence

Methods utilized	Number reporting	Percentage
<b>n = 116</b>		
Self motivation	65	56
Adherence counsellors	23	20
Pill boxes	19	16
Family member or close friend	15	13
Other clinic staff	12	10
Reminders (eg beepers, phones)	9	8

### DISCUSSION

The reported adherence levels both by 24-hour recall and seven-day recall were low, 59% and 55% respectively. The average age of participants was similar to that of the reported AIDS cases in Jamaica with the highest prevalence being in the 24–35-year age group (2). The respondents were generally of a low educational level, not in a stable relationship and unemployed. The unemployment rate in the group was particularly high and not reflective of the general population rate of 9% (21).

Levels of self-reported adherence were even lower than those reported in the previous year, 68% and 60% (22). Nevertheless, the fraction of 37.5% of the population that was between 80–94% adherent would still see significant short-term benefits from the medications though they are at risk for developing antiretroviral drug resistance. The 7.7% who reported adherence levels of < 80% were at risk of developing drug resistance within a very short time frame (23). By geographic site, persons attending clinics in the urban area were more likely to be 95–100% adherent compared to



persons in rural clinics, 62% and 44% respectively. This may be attributed to higher levels of resources being available in the urban clinics. Persons in the rural areas were more likely to be 80–94% adherent with very few persons adhering below an 80% level.

Although most patients reported some interaction with the adherence counsellors, it is of concern that no significant difference was demonstrated in their adherence levels when compared to persons who had no interaction. The fact that only 20% of the sample reported that adherence counsellors provided support in adherence has significant implications for the cost effectiveness of the Adherence Programme warranting a review of the role and function of the counsellors. The methodology utilized by adherence counsellors will also need to be reviewed.

A high percentage of persons slept through their dose times or simply forgot to take their medications. Adherence counsellors, pillboxes and close family and friends all help to promote higher levels of adherence; however the majority of persons were in fact using no specific mechanism to remind them of dose times. A culture of using reminders such as beepers, alarm clocks and cellular phone reminders could enhance adherence levels.

The perception of stigma and discrimination also lead to individuals not wanting others to see them take ARVs. However, the recommendation of the Ministry of Health, Jamaica, for HAART has the vast majority of patients on a twice-daily regimen that facilitates taking the medication in the morning and twelve hours later at night outside of routine activities. Persons therefore need not take medication at work or in public if concerned about stigma and discrimination, a point that needs emphasis in the clinical setting.

This study has limitations. The reliance on self-report may be considered a maximum estimate of adherence; true adherence may be worse. We did not perform multivariable analyses to assess what predictors of non-adherence were most important and independent of other relationships. A comparison of reported adherence levels with viral loads, CD4<sup>+</sup> T-cell counts and clinical progression would be beneficial in providing a more comprehensive view of adherence to HAART.

In summary, the Jamaican Ministry of Health Adherence Programme needs revision. The use of pillboxes and other reminders must be reinforced to ensure wider use among the population. More emphasis must be placed on preparing individuals to start HAART.

## REFERENCES

1. Figueroa JP, Ward E, Walters C, Ashley DE, Wilks RJ. High risk health behaviours among adult Jamaicans. *West Indian Med J* 2005; **54**: 70–6.
2. National HIV/STI Programme, Ministry of Health, Kingston, Jamaica. Available at: [www.jamaica-nap.org](http://www.jamaica-nap.org).
3. Scientific Committee on AIDS. Recommended principles of antiretroviral therapy in HIV disease. Jan 2005. Available at <http://www.aids.gov.hk>
4. Sterne JA, Hernan MA, Ledergerber B, Tilling K, Weber R, Sendi P et al. Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study. *Lancet* 2005; **366**: 378–84.
5. Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *N Engl J Med* 1998; **338**: 853–60.
6. Dybul M, Fauci AS, Bartlett JG, Kaplan JE, Pau AK. Panel on Clinical Practices for Treatment of HIV. Guidelines for using antiretroviral agents among HIV-infected adults and adolescents. *Ann Intern Med* 2002; **137**: 381–433.
7. CASCADE collaboration. Determinants of survival following HIV-1 seroconversion after the introduction of HAART. *Lancet* 2003; **362**: 1267–74.
8. Mocroft A, Ledergerber B, Katlama C, Kirk O, Reiss P, D'Arminio MA et al. Decline in the AIDS and death rates in the EUROSIDA study: an observational study. *Lancet* 2003; **362**: 22–9.
9. Gulick RM. HIV treatment strategies: planning for the long term. *JAMA* 2004; **291**: 957–9.
10. Deeks SG. Treatment of antiretroviral-drug-resistant HIV-1 infection. *Lancet* 2003; **362**: 2002–1.
11. Vandamme AM, Sonnerborg A, Ait-Khaled M. Updated European recommendations for the clinical use of HIV drug resistance testing. *Antivir Ther* 2004; **9**: 829–48.
12. Wood E, Hogg RS, Yip B, Harrigan PR, O'Shaughnessy MV, Montaner JS. Effect of medication adherence on survival of HIV-infected adults who start highly active antiretroviral therapy when the CD4<sup>+</sup> cell count is 0.200 to 0.350 x 10<sup>9</sup> cells/L. *Ann Intern Med* 2003; **139**: 810–6.
13. Horne R, Cooper V, Gellaitry G, Leake H, Fisher M. Patients perception of highly active antiretroviral therapy in relation to treatment uptake and adherence. *JAIDS* 2007; **45**: 334–41.
14. Catt S, Stygall J, Catalan J. Acceptance of zidovudine (AZT) in early HIV disease: The role of health beliefs. *AIDS Care* 1995; **7**: 229–35.
15. Chesney M. Adherence to HAART regimens, *AIDS Patient Care STDS* 2003; **17**: 169–77.
16. Chesney MA, Ickovics JR, Chambers DB. Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. Patient Care Committee & Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG). *AIDS Care* 2000; **12**: 255–66.
17. Berg KM, Arnsten JH. Practical and conceptual challenges in measuring antiretroviral adherence. *J Acquir Immune Defic Syndr* 2006; **43 Suppl 1**: S79–87.
18. Nieuwkerk, PT, Oort FJ (abstract). Self-reported adherence to antiretroviral therapy for HIV-1 infection and virological treatment response: a meta-analysis. *JAIDS* 2005; **38**: 445–8.
19. Arnsten JH, Demas PA, Farzadegan H, Grant RW, Gourevitch MN, Chang CJ et al. Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: comparison of self-report and electronic monitoring. *Clin Infect Dis* 2001; **33**: 1417–23.
20. Fairley CK, Permana A, Read TR. Long term utility of measuring adherence by self report compared to pharmacy record in a routine clinic setting. *HIV Med* 2005; **6**: 366–9.
21. Statistical Institute of Jamaica (STATIN). Employment and earnings and hours worked in large establishments 2002 – 2005, Published by STATIN; 2007.
22. Harvey K, Jackson S, Hirshorn L. Adherence to Highly Active Antiretroviral Therapy (HAART) in Jamaica (abstract). NIMH/IAPAC International Conference on HIV Treatment Adherence; 2006.
23. Bartlett J, Gallant J. Medical Management of HIV Infection 2005–2006 edition, John Hopkins Medicine Health Publishing Business Group; 2005.