Adherence to Anti-Retroviral Treatment and Factors Associated with Optimal Adherence among Adolescent and Adult PLWHA Attending Comprehensive Care Centres in Selected Hospitals in Nairobi County

Mulia Wilfred Kisingu[1 & 2*]   Charles F L. Mbakaya[1]   Anselimo Makokha[2]   Gabriel G. Mbugua[3]
James Kariuki[1]   Erastus Muniu[1]

1 Centre for Public Health Research, Kenya Medical Research Institute, P.O Box 20752-0202, KNH, Nairobi-Kenya
2 Jomo Kenyatta University of Agriculture and Technology (JKUAT), P.O Box 62000 – 00200, Nairobi - Kenya
3 Meru University of Science and Technology (MUST), 972-60200, Meru, Kenya

Abstract
Background: Anti-retroviral therapy (ART) has saved many lives from imminent deaths among PLWHA. However, the success is pegged on optimal (>95%) adherence to the ART by the PLWHA. The main objective of this study was to determine the ART adherence level by the PLWHA and the factors associated with the adherence.**Methods:** This was a cross sectional descriptive study on 454 PLWHA, attending Comprehensive Care Centres (CCCs) in selected hospitals in Nairobi County. A structured questionnaire was used to collect data. The Data was analysed using SPSS version 17.0. **Results:** There were 180 (39.6%) males and 274 (60.4%) females in the study. Majority (53.3%) PLWHA were aged between 40 and 49 years. Only 265 (58.4%) had optimal adherence to ART and duration on the ART was found to be significantly associated with optimal adherence to ART drugs.**Conclusion:** Optimal adherence was far below the recommended (>95%) mark and duration on ART was found to be significantly associated with optimal adherence. That is, the shorter the time one had been on ART, the more the chances of being more adherent. Most PLWHA blamed forgetfulness as the main reason for their failure to take the ART drugs as required. Since Anti-Retroviral Treatment is a lifelong process, targeted counselling including reminders (ringing of a bell in the phone) and formation of groups for calling each other for remembrance would suffice.
Keywords: PLWHA; ART; optimal adherence; Forgetfulness.

Background

Antiretroviral therapy (ART) has been recommended as a standard form of treatment for use by People Living with HIV/AIDS (PLWHA). The recommendation on the use of antiretroviral therapy in resource-limited settings recognized the critical role of adherence in order to achieve clinical and programmatic success (WHO, 2006). The long lasting efficiency of ART starts with the initial decision to start ART. Good adherence to ART has been shown to achieve the best virological response, lower the risk of drug resistance, and reduce morbidity and mortality; (Harrigan; et al. 2005). Optimal adherence is the compliance to ART that achieves a sustained plasma drug concentration that will inhibit viral replication. Studies have indicated that at least 95% adherence to ART regimens is optimal (Arnsten; *et al*. 2000). According to Arnsten; *et al*.(2000), the 95% adherence makes viral suppression to below detectable levels occur in 80% of cases. A fall in adherence to 70% (25% less than optimal) drastically decreases viral suppression to 33% (less than 50% achieved with optimal adherence). However, adherence barriers are many and vary in different settings; (Turner; 2002). The benefits critically depend on patients achieving and maintaining high levels of medication adherence; (Gill, et al. 2005). Very high level of adherence of more than 95% is required for ART to be effective for long term and to prevent the emergence of resistant viral strains; (Paterson et al. 2000).

There has been a concern about the capability of patients in resource-limited settings to adhere to ART, especially in the African context; (Harries et al. 2001). Both clinical experience and emerging data suggest that many patients with chronic HIV disease do not fully adhere to their ART regimens; (Signh, et al. 1999). Incomplete adherence to antiretroviral agents can have serious consequences, including loss of plasma HIV suppression and in turn lead to disease progression, inability to suppress HIV even with very intensive regimens, and development of drug resistant HIV strains. This can lead to transmission of resistant HIV to others; (Havlix. et al. 1998). In Kenya, National AIDS Control Council (NACC, 2011) revealed that over 450, 000 PLWHA were on ART and 79, 294 of those were in Nairobi with 73,050 being adolescents and adults aged between 15 and 49 years. Kenya AIDS Indicator Survey (KAIS, 2012) confirmed that ART is widely available in Kenya and can be accessed at private and public facilities. The ART drugs appear in two lines: 1st line and 2nd line. The first line is the desired but for some reason, the PLWHA become resistant to them and are then switched to 2nd line. The 1st line drugs include: Zidovudine(AZT)+Lamivudine(3TC)+Nevirapine (NVP)or Evafirenz (EFV) or Tenofovir(TDF)+3TC+NVP/EFV and the 2nd line drugs include: Tenofovir (TDF)+3TC+Lopinavir

(LPV)/ritonavir or AZT+3TC+LPV/ritonavir.

The main objective of this study was to determine adherence levels and establish factors associated with optimal ART adherence among PLWHA attending comprehensive care centres in selected hospitals in Nairobi.

Materials and Methods

This was a cross-sectional study which elucidated factors that are associated with ART adherence levels of the PLWHA. The study was purposively undertaken at CCCs of Karen, St. Mary's, Mbagathi and Kenyatta National Hospitals in Nairobi county, among adult PLWHA, attending CCCs in the four hospitals. Fisher's formula of 1998 was used to calculate sample size which came to 385 PLWHA. Calculated sample size was increased by 20% to cater for possible failure of some PLWHA to come for interview due to stigma associated with HIV and AIDS giving a sample size of 460. However sample size of 454 PLWHA was realized. Proportional allocation was carried out to determine sample size required in each CCC of the four hospitals. Simple Random sampling was used to select the PLWHA in each of the four hospitals. Those selected were contacted to visit their respective CCCs on a set date to be informed about the study and their consent to participate. PLWHA aged between 15 and 49 years who had been on ART for more than one year were included in the study. The age inclusion criterion was guided by the fact that, 15 to 49 year olds is where majority PLWHA and indeed on ART where obtained. In case of those PLWHA below 18 years of age, a legal guardian was requested to sign the consent form for the PLWHA for Participation after the assenting. Given the level of stigma associated with HIV/AIDS in Kenya and indeed the whole world, confidentiality was paramount. Research assistants were recruited from the institutions where the study was being carried out and trained on the data collection procedure and tools (structured questionnaires). The main issues which were captured were socio-economic characteristics of the PLWHA, duration on ART, number of times ART drugs were missed and reasons for missing. Prior to the data collection, the questionnaire was pre-tested for its suitability for the study.

Data management and analysis

The lead author counter-checked the questionnaires to ensure that there were no mistakes or omissions. The questionnaires were stored in a confidential lockable cabinet after entry into a microcomputer using SPSS Software. The entered data was cleaned for errors and any inconsistent entries to ensure quality before analysis. Data analysis was done using SPSS version 17. Chi-square and where applicable, Fisher's exact probability were used as most of the data was categorical. All variables that had a p-value <0.25 were subjected to Binary Logistic regression analysis to identify those associated with optimal adherence.

RESULTS

Socio-demographic characteristics

A total of 454 PLWHA were recruited into the study and 180 (39.6%) were males while 274 (60.4%) were females giving a Male : Female ratio of 1 : 1.5. Majority 53.3% were aged 40 to 49 years and only 1.3% were below 20 years, Over a half (53.5%) were married, 21.6% were single and the rest were either separated (8.1%) divorced (7.5%) or widowed (9.3%). Over three quarters (77%) had attained secondary education and above with only 1.3% having no formal education. Christians were the majority (95.2%), Muslims 3.7%, Traditional 0.7% and others 0.4%. The main sources of income were employment (48.5%) and business (44.9%) with 5.3% relying on donations and 1.3% on other sources.

Anti-Retroviral Treatment Adherence

A total of 265 (58.4%) PLWHA had optimal (>95%) adherence to Anti-Retroviral treatment, while 189 (41.6%) had sub-optimal (<95%) adherence. The following were advanced as reasons for sub-optimal adherence.

Table 1: Reasons for sub-optimal adherence to Anti-Retroviral treatment (N = 189).

Reason for sub-optimal adherence	Frequency	Percent
Forgetfulness	135	71.4
When on Safari	48	25.4
Stigma	23	12.2
Luck of regular drug supply	6	3.2
No food in the stomach	7	3.7

Forgetfulness and being on safari were the two major reasons cited for sub-optimal adherence with stigma following in third position (table 1).

Challenges while on ART

Table 2: challenges while on ART (N = 454).

Challenges while on ART	Frequency	Percent
To remember to swallow the drugs	209	46.0
Search for food	31	6.8
Search of income	36	7.9
Recurrent illnesses	28	6.2
Fear of stigma	96	21.1
Fear of drug failure	24	5.3
Uncertain future	30	6.6

The most mentioned challenge while on ART by almost half of the study participants was remembering to swallow the drugs. Other challenges are indicated in table 2.

Challenges most difficult to tackle

Table 3: challenges most difficult to tackle (N = 454).

Challenges most difficult to tackle	Frequency	Percent
To remember to swallow the drugs	166	36.6
Search for food	46	10.1
Search of income	50	11.0
Recurrent illnesses	48	10.6
Fear of stigma	134	29.5
Fear of drug failure	52	11.5
Uncertain future	68	14.9

Remembering to swallow drugs and fear of stigma stood out as the main challenges most difficult to tackle (table 3).

Family support in relation to taking of ART drugs

Table 4: Family support in relation to taking of ART drugs (N = 454).

Family support in relation to taking of ART drugs	Frequency	Percent
No support given	174	38.3
Money for transport	54	11.9
Money for food	45	9.9
Accommodation	9	2.0
Moral support	238	52.4

A total of 38.3% of study participants did not receive any form of support from their family and for those who received support; it was mainly moral support (table 4).

Table 5: Support given by community organized groups (N = 181).

Support by community organized groups	Frequency	Percent
Financial support	8	4.4
Reduction of stigma	96	53.0
Encourage PLWHA to form self- help groups	91	50.3
Mobilize funds for expensive drugs	6	3.3
Vocational & occupational rehabilitation	6	3.3

For 181 (39.9%) study participants who had community organized groups to support them, only 4.4% received individual financial support. The other kinds of support were general (table 5).

Factors associated with optimal adherence

Table 6: Distribution of participant characteristics by adherence

Variable	Adherence		P-value
	Suboptimal (N=189) %	Optimal (N=265) %	
Sex Male	37.0	41.5	
Female	63.0	58.5	0.337
Age in years <30	16.4	11.3	
30-39	31.2	34.7	0.276
40-49	52.4	54.0	
Marital status Single	23.3	20.4	
Married	51.9	54.7	0.741
Div./Sep./widowed	24.9	24.9	
Education None/primary	22.2	23.4	
Secondary	43.4	41.9	0.938
College/University	34.4	34.7	
Source of income			
Employment	47.6	49.1	0.948
Business	45.5	44.5	
Donation/others	6.9	6.4	
Amount earned in Kshs.			
<3000	6.3	7.5	
3000 - 6000	11.6	12.5	
7000 - 9000	9.5	10.6	0.768
10000 - 12000	14.3	13.2	
13000 - 15000	16.9	12.1	
>15000	41.3	44.2	
Line of ART drugs			
1st	44.4	46.0	
2nd	43.4	45.3	0.478
Don't know	12.2	8.7	
Duration on ART (years)			
1-2	22.8	20.0	
3-4	14.3	30.9	<0.001
5-6	24.9	15.1	
>6	38.0	34.0	

On the factors associated with optimal adherence, only duration on ART was found to be significantly associated with optimal adherence to ART drugs (table 6).

Discussion:

Optimal ART adherence of more than 95% is necessary if we expect to: attain sustained HIV suppression; reduce risk of drug resistance; improve overall health and quality of life and survival (Chesney, 2006); and (Cohen, et al. 2011). However, from a patient perspective, failure to adhere is often a consequence of one or more behavioral, structural, and psychosocial barriers (e.g., depression, neurocognitive impairment, low health literacy, stressful life events, homelessness, poverty, stigma, and inconsistent access to medications); Carr, et al. (2004) and Halkitis, et al. (2005). In addition, failure to adopt practices that facilitate adherence, such as linking medication taking to daily activities or using a medication reminder system or a pill organizer, is also associated with treatment failure; (Fisher, et al. 2006). In our study findings, 265(58.9%) had attained optimal adherence of ≥ 95% to ART, while 189(41.6%) had suboptimal adherence within a one month (30 days) recall period. This finding was comparable to that of a study done in Nigeria where optimal adherence of 59.9% was realized in a self-reported 30 days recall period; Agu et al. (2011), but slightly higher than earlier reports by Iliyasu and colleagues in Kano (Northern Nigeria), Nwauche and colleagues (Southern Nigeria) and a study done in Kenya, who reported adherence levels of 54.5%. 49.2% and 43.2% respectively; Iliyasu et al. (2005). These findings compare fairly with studies conducted in developed countries which demonstrated that the rates of adherence by self-report (30 days recall) ranged from 40% to 70%; Chesney, et al. (2000).

In our study findings, duration on ART was the only factor that was found to be significantly associated with optimal adherence to ART (P =<0.001). That is, the shorter the time one had been on ART, the more the chances of being more adherent. For example, fewer (37.1%) PLWHA who had been on ART for 1-4 years had

suboptimal adherence, compared to more (62.9%) PLWHA who had suboptimal adherence after being on ART for ≥5 years. This compares with a study by Habtamu et al. (2013) which indicated that adherence rate was inversely proportional to the length of time on ART. That is, the longer the respondents were on ART, the lesser they adhered. Another study by Afiong et al. (2013) significantly showed that the PLWHA who had been on ART for ≥ 24 months had poorer adherence than those who had been on ART for ≤ 24 months. In our study, the reasons given for non-adherence to ART were: forgetfulness (71.4%); traveling (25.4%); stigma (12.2%); luck of drugs (3.2%); and fear to swallow drugs on an empty stomach (3.7%). Similar reasons were reported in other studies conducted in Yirgalem Hospital, Gondar, and Harari in Ethiopia and in South Africa and Guatemala, Endrias et al. (2008), Tessema et al. (2010), Habtamu et al. (2013), Magutu et al.(2010) and Campbell et al.(2010). Many other studies had forgetfulness as the main reason for poor adherence to ART, for example: in South West Ethiopia (Amberbir, 2008), found that the principal reasons reported for skipping doses were forgetfulness 38 (43.7%), falling sick or ill at that time 17 (19.5%), and running out of medication 11 (12.6%); in another study of 173 patients, by Haubrich et al. (1999), 102(59%) patients who reported as having missed ART doses did so for a variety of reasons, the most common being forgetfulness 42(41%). Other reasons included being away from home (9%), being busy with other activities (6%), and taste perversion (5%), or concern about toxicity (4%).

Study limitations.
Certain limitations of this study need to be recognized. The cross-sectional nature of the study did not give space for inferences to be drawn as to causal relationship among variables. Besides the use of self-report in 30 days recall period to assess ART adherence was a limitation because of the possibility that the PLWHA would either over-or underestimate their adherence level. Additionally, the study did not corroborate the self-report on adherence with other parameters such as viral load and CD4 counts.

Conclusion. HIV/AIDS is a lifelong disease and requires lifelong measures of health care. ART happens to be the most prominent type of health care required for PLWHA so far and requires lifelong utilization with optimal adherence. However, there are multidimensional obstacles that hinder optimal adherence with the most commonly mentioned being; forgetfulness, busy work schedules, travelling and stigma and hence the need for tailored interventions. For example, suggesting reminders like setting alarms on the mobile phones, incorporating ART drugs taking with meals, formation of group network which would involve calling each other on daily basis for remembrance and encouraging the PLWHA to make ART away of life.

Declaration: We (the authors) declare that there are no conflicts of interest regarding the publication of this article.

References
Agu KA, Okojie O, Oqua D, King RC, Omonaiye O, Onuoha C, et al.: Medication Adherence and Risk factors for Non-adherence among Patients taking Highly Active Antiretroviral Therapy. West Afr J Pharm 2011,22(1):19–26.

Al-Khindi, T., Zakzanis, K. K., & van Gorp, W. G. (2011). Does antiretroviral therapy improve HIV-associated cognitive impairment? A quantitative review of the literature. *Journal of the International Neuropsychological Society*, *17*(06), 956-969.

Amberbir, A., Woldemichael, K., Getachew, S., Girma, B., & Deribe, K. (2008). Predictors of adherence to antiretroviral therapy among HIV-infected persons: a prospective study in Southwest Ethiopia. *BMC Public Health*, *8*(1), 265.

Baldewicz, T. T., Leserman, J., Silva, S. G., Petitto, J. M., Golden, R. N., Perkins, D. O., ... & Evans, D. L. (2004). Changes in neuropsychological functioning with progression of HIV-1 infection: results of an 8-year longitudinal investigation. *AIDS and Behavior*, *8*(3), 345-355.

Bonolo, P., César, C. C., Acúrcio, F. A., Maria das Graças, B. C., de Pádua, C. A. M., Álvares, J., ... & Guimarães, M. D. (2005). Non-adherence among patients initiating antiretroviral therapy: a challenge for health professionals in Brazil. *Aids*, *19*, S5-S13.

Campbell JI, Ruano AL, Samayoa B, EstradoMuy DL, Arathoon E, Young B. Adherence to antiretroviral therapy in an urban, free-care HIV clinic in Guatemala city, Guatemala. J Int Asso Phy AIDS Care. 2010;9(6):390–395

Carr, R. L., & Gramling, L. F. (2004). Stigma: A health barrier for women with HIV/AIDS. *Journal of the Association of Nurses in AIDS Care*, *15*(5), 30-39.

Chesney, M. A. (2006). The elusive gold standard: future perspectives for HIV adherence assessment and intervention. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *43*, S149-S155.

Ciccarelli, N., Fabbiani, M., Di Giambenedetto, S., Fanti, I., Baldonero, E., Bracciale, L., ... & Silveri, M. C. (2011). Efavirenz associated with cognitive disorders in otherwise asymptomatic HIV-infected patients. *Neurology*, *76*(16), 1403-1409.

Claypoole, K. H., Elliott, A. J., Uldall, K. K., Russo, J., Dugbartey, A. T., Bergam, K., & Roy-Byrne, P. P. (1998). Cognitive functions and complaints in HIV-1 individuals treated for depression. *Applied neuropsychology*, *5*(2), 74-84.

Cohen, M. S., Chen, Y. Q., McCauley, M., Gamble, T., Hosseinipour, M. C., Kumarasamy, N., & Fleming, T. R. (2011). Prevention of HIV-1 infection with early antiretroviral therapy. *New England journal of medicine*, *365*(6), 493-505.

Endrias M, Alemayehu W, Gail D. Adherence to ART in PLWHA at Yirgalem Hosptial, South Ethiopia. Ethio J Health Dev. 2008;22(2):174–179.

Fisher, J. D., Fisher, W. A., Amico, K. R., & Harman, J. J. (2006). An information-motivation-behavioral skills model of adherence to antiretroviral therapy. *Health Psychology*, *25*(4), 462.

Gill, C. J., Hamer, D. H., Simon, J. L., Thea, D. M., & Sabin, L. L. (2005). No room for complacency about adherence to antiretroviral therapy in sub-Saharan Africa. *Aids*, *19*(12), 1243-1249.

Habtamu M, Tekabe A, Zelalem T. Factors Affecting Adherence to Antiretroviral Treatment in Harari National Regional State. Vol. 2013. Eastern Ethiopia: ISRN AIDS; 2013. p. 7

Halkitis, P. N., Shrem, M. T., Zade, D. D., & Wilton, L. (2005). The physical, emotional and interpersonal impact of HAART: exploring the realities of HIV seropositive individuals on combination therapy. *Journal of Health Psychology*, *10*(3), 345-358.

Haubrich, R. H., Little, S. J., Currier, J. S., Forthal, D. N., Kemper, C. A., Beall, G. N., ... & California Collaborative Treatment Group. (1999). The value of patient-reported adherence to antiretroviral therapy in predicting virologic and immunologic response. *Aids*, *13*(9), 1099-1107.

Heaton, R. K., Clifford, D. B., Franklin, D. R., Woods, S. P., Ake, C., Vaida, F., & CHARTER Group. (2010). HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy CHARTER Study. *Neurology*, *75*(23), 2087-2096.

Kenya AIDS Indicator Survey (KAIS, 2012). A report on Adults and adolescents aged 15–64 years who self-reported HIV-infected currently taking ART who have missed taking a ARVs in the past 30 days.

Koopmans, P. P., Ellis, R., Best, B. M., & Letendre, S. (2009). Should antiretroviral therapy for HIV infection be tailored for intracerebral penetration?.

Lentz MR, Kim WK, Kim H, Soulas C, Lee V, Venna N, González RG. Alterations in brain metabolism during the first year of HIV infection.Journal of Neurovirology. 2011;17(3):220–229.

Letendre, S., Marquie-Beck, J., Capparelli, E., Best, B., Clifford, D., Collier, A. C., ... & Ellis, R. J. (2008). Validation of the CNS Penetration-Effectiveness rank for quantifying antiretroviral penetration into the central nervous system. *Archives of neurology*, *65*(1), 65-70.

Iliyasu I, Kabir M, Abubakar I, Babashani M, Zubair Z: Compliance to antiretroviral therapy among AIDS patients in Amino Kano Teaching Hospital, Kano. Niger J Med 2005,14(3):290–294.PubMedMehta, S., Moore, R. D., & Graham, N. M. (1997). Potential factors affecting adherence with HIV therapy. Aids, 11(14), 1665-1670.

Maqutu D, Zewotir T, North D, Naidoo K, Grobler A. Factors affecting first-month adherence to antiretroviral therapy among HIV-positive adults in South Africa. Afr J AIDS Res. 2010;9(2):117–124.

Mills E, Nachega J, Bangsberg D, Singh S, Rachlis B, et al. (2006) Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators. *PLoS Med* 3: e438.

Neuroplasticity and Cognitive Reserve in Aging with HIV: Recommendations for Protection and Rehabilitation. *The Journal of neuroscience nursing: journal of the American Association of Neuroscience Nurses*, *45*(5), 306.

Nieuwkerk, P. T., Sprangers, M. A., Burger, D. M., Hoetelmans, R. M., Hugen, P. W., Danner, S. A., ... & Lange, J. M. (2001). Limited patient adherence to highly active antiretroviral therapy for HIV-1 infection in an observational cohort study. *Archives of Internal Medicine*, *161*(16), 1962-1968.

Parsons, T. D., Braaten, A. J., Hall, C. D., & Robertson, K. R. (2006). Better quality of life with neuropsychological improvement on HAART. *Health and quality of life outcomes*, *4*(11), d0i110.

Salami, A. K., Fadeyi, A., Ogunmodede, J. A., & Desalu, O. (2010). Factors influencing adherence to antiretroviral medication in Ilorin, Nigeria. *Journal of the International Association of Physicians in AIDS Care (JIAPAC)*, *9*(3), 191-195.

Simioni, S., Cavassini, M., Annoni, J. M., Abraham, A. R., Bourquin, I., Schiffer, V., ... & Du Pasquier, R. A.

(2010). Cognitive dysfunction in HIV patients despite long-standing suppression of viremia. *Aids*, *24*(9), 1243-1250.

Stirratt, M. J., Remien, R. H., Smith, A., Copeland, O. Q., Dolezal, C., Krieger, D., & SMART Couples Study Team. (2006). The role of HIV serostatus disclosure in antiretroviral medication adherence. *AIDS and Behavior*, *10*(5), 483-493.

Tessema B, Biadglegne F, Mulu A, Getachew A, Emmrich F, Sack U. Magnitude and determinants of non-adherence and non-readiness to highly active antiretroviral therapy among people living with HIV/AIDS in Northwest Ethiopia: a cross-sectional study. AIDS Res Ther. 2010;7:2.

Thames, A. D., Becker, B. W., Marcotte, T. D., Hines, L. J., Foley, J. M., Ramezani, A., ... & Hinkin, C. H. (2011). Depression, cognition, and self-appraisal of functional abilities in HIV: An examination of subjective appraisal versus objective performance. *The Clinical Neuropsychologist*, *25*(2), 224-243.

Thompson, M. A., Mugavero, M. J., Amico, K. R., Cargill, V. A., Chang, L. W., Gross, R., ... & Nachega, J. B. (2012). 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. *Annals of Internal Medicine*, *156*(11), 817-833.

Vance, D. E., Eagerton, G., Harnish, B., McKie, P., & Fazeli, P. L. (2011). Cognitive prescriptions. *Journal of Gerontological Nursing*, *37*(4), 22-9.

Vance, D. E., Webb, N. M., Marceaux, J. C., Viamonte, S. M., Foote, A. W., & Ball, K. K. (2008). Mental stimulation, neural plasticity, and aging: directions for nursing research and practice. *Journal of Neuroscience Nursing*, *40*(4), 241-249.

Wenger N, Gifford A, Liu H, et al. Patient characteristics and attitudes associated with antiretroviral (AR) adherence. In: Program and abstracts of the 6th Conference on Retroviruses and Opportunistic Infections; January 31-February 4, 1999; Chicago. Abstract 98. Golin C, Kaplan A, Liu HH, et al. Patient factors associated .

Weiser, S., Wolfe, W., Bangsberg, D., Thior, I., Gilbert, P., Makhema, J., ... & Marlink, R. (2003). Barriers to antiretroviral adherence for patients living with HIV infection and AIDS in Botswana. *JAIDS-HAGERSTOWN MD-*, *34*(3), 281-288.

Woods, S. P., Carey, C. L., Moran, L. M., Dawson, M. S., Letendre, S. L., Grant, I., & HIV Neurobehavioral Research Center (HNRC) Group. (2007). Frequency and predictors of self-reported prospective memory complaints in individuals infected with HIV. *Archives of Clinical Neuropsychology*, *22*(2), 187-195.

World Health Organization (WHO). Adherence to long term therapies—evidence for action. 2003.