Factors Affecting Adherence to Highly Active Antiretroviral Therapy among Patients Attending Public Healthcare Facility

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Abstract: The research focused on factors associated with poor adherence to HAART (highly active antiretroviral therapy) among HIV/AIDS. A descriptive cross sectional study was conducted using a standardized questionnaire and face-to-face exit interviews to collect data. Pill-counts were performed and computed adherence rate of $\geq 95\%$ was considered acceptable. Data were analyzed using SPSS 21.0. Univariate factors associated with poor adherence to HAART were assessed with ANOVA (analysis of variance) and logistic regression model excluded confounders determining independent predictors of poor adherence. A $P \leq 0.05$ was statistical significant. Of 102 HIV-infected on HAART for 24.68 ± 20.5 months, 83.3% were females and 16.7% males. The mean age ($\pm$ SD) was 35.09 ± 9.3 years. Univariate factors associated with poor adherence to HAART were: CD4 count > 350 cells/mm³ ($\chi^2 = 46$; $P = 0.05$), age > 35 years ($\chi^2 = 28.75$; $P = 0.011$), primary educational background ($\chi^2 = 9.18$; $P = 0.027$), HAART regimen 1A-TDF ($\chi^2 = 14.37$; $P = 0.003$), and > 4 combined tablets ($\chi^2 = 11.87$; $P = 0.001$). There was a linear correlation between age and primary educational background ($r = 0.538$; $P < 0.001$). After adjusting for univariate confounders, primary educational background ($P = 0.020$) and > 4 combined tablets ($P = 0.026$) were identified as independent predictors of poor adherence to HAART. Although there is an increase number of HIV-infected receiving HAART, these findings have shown that many of these will not adhere to their treatment once they improve clinically. This could be due to lack of education and complexity of combined ARVs with other drugs.

Key words: Adherence, highly active antiretroviral therapy, HIV/AIDS, public sector.

1. Introduction

The introduction of HAART (highly active antiretroviral therapy) especially the new and more potent ARV (antiretroviral) agents, resulted from the advances in the knowledge of HIV (human immunodeficiency virus) pathogenesis and viral load monitoring. HAART treatment regimens modified HIV infection and AIDS (acquired immune deficiency syndrome) thus affecting HIV/AIDS patient's clinical care [1]. This also according to Spire and others [2] produced an impact in reducing morbidity and mortality associated with HIV infection. According to

various authors [3-5], the use of three-drug regimens that include a PI (protease inhibitor) in combination with nucleoside analogues, have become the standard treatment approach to HIV/AIDS in that they produce a greatly increased level and long-term suppression of HIV replication, decreasing the viral load, that is associated with a slowdown of illness progression and significant decrease of mortality rates.

According to the UNAIDS (United Nations Programme for HIV/AIDS), an estimated 5.6 million people were living with HIV/AIDS in SA in 2011, the highest number of people in any country. It is also reported that 270,190 South Africans died of HIV/AIDS-related causes, though many lives have been saved through a massive scale-up of treatment in

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the last few years [6]. South Africa has recently had one of the largest increases in treatment access in the world, with a scale of 75% between 2009 and 2011. In October 2012, SA reached the target of universal access to treatment as the total number of people receiving treatment reached 2 million (or 80% of all in need of ART (antiretroviral therapy)) [7].

The long-term effectiveness of the prescribed ART combinations is dependent upon strict adherence since HIV-drug resistance to these drugs can develop with sub therapeutic doses. Sustaining successful ART scale-up in resource-limited settings depends largely upon the ability of ART programs to deliver ART in a way that supports optimal patient adherence, thereby maximizing durability of first- and second-line regimens. The full and sustained benefits of ART can only be obtained from high levels of adherence to ARV regimens. Peterson and colleagues [8] established in their study conducted in the United States and Europe that adherence above 95% is required for viral suppression, with 80% of near perfect adherence maintaining an undetectable viral load over six months.

Low adherence to ART is a predictor of virologic suppression [9], emergence of HIV drug resistance [10, 11], disease progression [12], premature morbidity and death [13]. Low adherence is the second strongest determinant for disease deterioration, and death after CD4 count [14]. Non-adherence to ART allows for inconsistent drug levels and persistent viral replication, increasing the likelihood of the formation of viral variants resistant to the currently prescribed regimens [15]. This was also emphasised by Edlin [16], that consequences of poor adherence to ART not only include diminished patient care outcome, but is also a public health threat in that it leads to multidrug-resistant HIV, and widespread transmission of drug-resistant virus, similar to that seen in multidrug-resistant tuberculosis. This also has an impact on the economy of any country in that it leads to higher hospitalization rates, productivity loss, disease progression, and death in both high-income

and resource-limited settings [17].

Specific data on possible barriers for poor ART adherence in the Eastern Cape have not been reported. Therefore, the objective of this study was to determine factors affecting adherence rates to HAART in HIV-infected patients attending a primary health care centre in Mthatha, Eastern Cape, South Africa.

2. Materials and Methods

2.1 Study Design, Population and Data Collection

This was a descriptive cross-sectional study that was conducted in June 2013 among a convenience sample of HIV-infected patients attending at an ARV clinic. A convenience sampling was used on patients who had been on ART for a period of six months and were eligible to participate in the study. The cut-off point of six months was chosen to allow the researchers to use viral load and CD4 count as an endpoints, because it can take up to six months for individuals to achieve virologic suppression on ART.

Data were collected by trained interviewers using face-to-face exit interviews using a standardized questionnaire to collect variables of interest like socio-demographic information as well as other variables of interest. In addition, other data like CD4 count and viral loads were retrieved in patient record reviews. Pill count data were used to assess adherence to ART over the previous month, as ARVs are dispensed on a monthly basis. The adherence rate was calculated as follows: the numerator was the total number of tablets provided at the previous visit minus the number of tablets remaining, and the denominator was the number of tablets required per day the number of days since the last visit; this ratio was multiplied by 100. Adherence to ART was considered acceptable when the pill count was $\geq 95\%$ of prescribed doses.

This study questionnaire has been initially tested for validity and reliability. Validity was established by a panel of experts and following a field test that determined whether the questionnaire measured what it intended to measure, whether it represented the

appropriate content, whether it was appropriate for the study population and whether it was comprehensive enough to collect the needed information. Reliability was computed after a pilot field test to indicate the accuracy of the measuring questionnaire using test-retest approach.

2.2 Data Analysis

Data were captured in the computer using MS Excel® and analysis was performed using SPSS® statistical software version 21.0 (SPSS Inc; Chicago, IL, USA). Categorical data were expressed as proportions (percentages). ANOVA (analysis of variance) was performed to assess poor adherence to HAART. Chi-square test was used to test the degree of association of categorical variables. Multiple logistic regression models were used to evaluate the prediction capacity of each independent variable in the occurrence of the expected outcome. Unadjusted ORs (odds ratios) were initially calculated to screen for inclusion in multivariate models; variables that exhibited at least moderate association ($P < 0.20$) with the outcome were considered for inclusion in the final models. Multivariate ORs (95% CI) were computed after adjusting for confounding univariate factors and to determine independent predictors of poor adherence. All tests were two-sided and a p value of ≤ 0.05 was considered as statistical significant.

2.3 Ethical Considerations

Permission to conduct the study was obtained from both the Scientific and Ethical Committee of the Faculty of Health Sciences, Walter Sisulu University as well as from the Eastern Cape department of Health. The Ethical Clearance number issued was 015/012. Each study participant signed an informed consent.

3. Results

A total of 102 HIV-infected patients on HAART were recruited, of which 85 (83.3%) were females and 17 (16.7%) males. The mean age ($\pm$ SD) of

participants was 35.09 ($\pm$ 9.3) years. Patients were on HAART for 24.68 ($\pm$ 20.5) months. Univariate factors associated with poor adherence rates to HAART were: CD4+ T count > 350 cells/mm³ ($\chi^2 = 46$; $P = 0.05$), age > 35 years ($\chi^2 = 28.75$; $P = 0.011$), primary educational background ($\chi^2 = 9.18$; $P = 0.027$), HAART regimen 1A-TDF ($\chi^2 = 14.37$; $P = 0.003$), and > 4 combined tablets (including ARV tablets) received per dose ($\chi^2 = 11.87$; $P = 0.001$) as demonstrated in Table 1.

There was a linear correlation between age > 35 years and primary educational background ($r = 0.538$; $P < 0.001$). After adjusting for univariate confounders, primary educational background ($P = 0.020$) and > 4 combined pills (including ART tablets) received per dose ($P = 0.026$) were identified as independent predictors of poor adherence to HAART among the study participants as shown in Table 2.

4. Discussion

Results from this study revealed that 83% females attended the ARV clinic as compared to 16.7% males. In this facility, females access the health care facility more than men. Results from this study indicated that 26 (89.7%) of females had acceptable adherence rates as compared to 3 (10.3%) males and 59 (80.8%) of males had poor adherence rates as compared to 14 (19.2%) females. These results concur with those obtained by Kigozi et al. [18], in his study done in SA. He reported that women who accessed HAART services were more than men by a ratio of 3: 1 and 20% of the women were more likely to adhere to HAART as compared to men. This could be explained that the large numbers of women were more familiar with the health care services as compared to men and especially women interacted with the clinics when accessing other services like antenatal, maternity and family planning as this was also supported by Muala and colleagues [19]. The authors further explained men were thought to be slower in uptake of HAART services due to the stigma acquired with it.

Table 1 Univariate associations between factors of interest and poor adherence to HAART in HIV-infected.

Factors of interest	Acceptable adherence rate $\geq 95\%$	Poor adherence rate $< 95\%$	P-value
Age (years)			0.011
≤ 35	23 (79.3)	36 (49.3)	
> 35	6 (20.7)	37 (50.7)	
Gender			0.22
Male	3 (10.3)	14 (19.20)	
Female	26 (89.7)	59 (80.8)	
Marital status			0.17
Married	7 (24.1)	23 (31.5)	
Single	22 (75.9)	44 (60.3)	
Widowed	0 (0)		
Salary scale (ZA rands)			0.7
< 2000	2 (66.7)	5 (41.7)	
2000-4000	1 (33.3)	6 (50)	
> 4000	0 (0)	1 (8.3)	
Educational level			0.027
Primary	2 (6.9)	22 (31.4)	
High school	19 (65.5)	26 (37.1)	
Matric	8 (27.6)	21 (30)	
Tertiary	0 (0)	1 (1.4)	
Employment status			0.32
Employed	3 (11.1)	12 (17.9)	
Unemployed	24 (88.9)	55 (82.1)	
Total No. of pills taken due to AIDS			0.037
< 4	8 (27.5)	7 (9.7)	
≥ 4	21 (72.4)	65 (90.3)	
CD4+ T cell count (cells/mm ³)			0.048
≤ 350	7 (24.1)	12 (16.4)	
> 350	22 (75.9)	61 (83.6)	
HARRT regimen			0.04
1A (Lamivudine, Stavudine, Efav)	1 (3.6)	5 (7)	
1A-TDF (3TC, TDF, EFV)	20 (71.4)	60 (84.5)	
1B (3TC, D4T, NVP)	0 (0)	1 (1.4)	
1B-TDF (3TC, TDF, NVP)	0 (0)	2 (2.8)	
1A-AZT (3TC, AZT, EFV)	1 (3.6)	0 (0)	
1B-AZT (3TC, AZT, NVP)	1 (3.6)	1 (1.4)	
Other regimens	5 (17.9)	2 (2.8)	

TDF = Tenofovir, 3TC = Lamivudine, EFV = Efavirenz, D4T = Stavudine, NVP = Nevirapine, AZT = Zidovudine.

Table 2 Independent determinants of poor adherence to HAART in HIV-infected patients ($n = 102$).

Variables	Beta-coefficient	SE	Wald χ^2	OR (95% CI)	P-value
Age (years)					
> 35	0.023	0.008	2.81	1.6 (1.2-1.9)	0.021
≤ 35			Reference	1	
CD4+ T cell count (cells/mm ³)					
> 350	0.001	0.0001	1.88	1.8 (1.4-2.3)	0.05
≤ 350			Reference	1	
Constant	0.331	0.54	2.79		0.039

Adjust for gender, marital status, educational level, ART regimen, and total number of pills taken by the patient. There was a linear correlation between age > 35 years and primary educational background ($r = 0.538$; $P < 0.0001$).

Acceptable adherence rate in this study was considered as $\geq 95\%$ while $\leq 95\%$ was unacceptable. A study conducted in USA [8] established that adherence at or above 95% is required for viral suppression with 80% of near-perfect adherence maintaining an undetectable viral load over six months.

Patient factors that were analyzed in this study included demographic, psychosocial, socioeconomic, and/or clinical in nature. Results revealed that age was among the univariate factor associated with poor adherence to HAART in that patients ≥ 35 years correlated with higher adherence rates as compared to patients of age < 35 years and this was statistically significant with a p value of 0.011. These results concurred with results obtained by Nachega and others [20] in South Africa who found that adolescents as compared to adults were less adherent to HAART, and had lower rates of virologic suppression and immunologic recovery, and had higher rates of virologic rebound after initial response. Therefore, there is an urgent need to determine the specific barriers in this age group and develop appropriate interventions.

Other demographic patient factors such as gender seemed to be associated with poor adherence. Results of this study revealed that 59 (80.8%) women had poor adherence rates as compared to 14 (15.2%) males. Gender had been associated with variations in drug levels, efficacy, and in susceptibility to adverse effects of ART, which in turn may affect adherence to treatment. This was confirmed in one study by Bersoff-Matcha and colleagues [21] who reported that women were seven times more likely to develop a severe rash from the common NNRTI (non-nucleoside reverse transcriptase inhibitor) nevirapine, than men and this resulted to women likely to discontinue treatment. However, another study [22] suggested that there are gender-specific differences in outcomes and may be explained by worse adherence in males. The authors continue to argue that there is a growing body

of evidence indicating that adult men face important challenges in accessing HIV/AIDS services as often as their female counterparts and this leads to them experiencing worse treatment outcomes including mortality. A case in point in this study was that few men 17 (16.79%) as compared to females 85 (83.3%) attended the HIV/AIDS clinics. So, more intensive monitoring and adherence interventions in men are necessary.

Other factors observed in this study having an effect on adherence were unemployment as supported by Small and others [23] in their study. In this study, 88.9% of the unemployed had $\geq 95\%$ of the accepted adherence rates as compared to 27.5% who were employed. Kalichman and other investigators [24] also reported that illiteracy and a low level of education can also lead to an adequate understanding about the effectiveness of medications, and this result in reduced adherence to treatment. Results obtained in this study concur with the same statement in that those with higher education had accepted adherence rates as compared with those with unacceptable adherence rates and the values obtained were of statistical significance.

Results in this study also revealed that primary education background was an independent predictor for low adherence and was statistically significant. Kissinger and colleagues [25] in a study on compliance in HIV/AIDS medical care found out that patients with lower socioeconomic status associated with decreased adherence were unstable or poor housing, low income and low level of education. In case of low level education patients need to be educated about the importance of drug compliance. More so low level education patients do not understand the disease and its treatment and health care professionals may not verify patient's understanding of information.

In this study, marital status was one of the factors of interest associated with low adherence rates especially the single married patients. Spire and co-authors [2] in

their investigation on adherence to HAART in HIV-infected patients established that younger, unmarried patients living in poor socio-economic environment were more likely to be non-adherent.

The total number of tablets taken by the HIV/AIDS in this study was also statistically significant with poor adherence. These results correlated with those of authors [26] who did investigated antiretroviral therapy adherence in Brazil and reported that the number of pills taken by patients and the time taken on treatment showed a linear trend for non-adherence ($P < 0.01$). The higher the number of tablets, the higher is the non-adherence. In this study, the logistic regression model observed a higher chance for non-adherence associated with the number of tablets. The number of tablets is a global treatment predictor because it involves the regimens the patients are taking, in terms of the number, the frequency and the time that the tablets must be taken. In their study, performed in Brazil, Bonolo and others [26] pointed out that adverse reactions and the number of pills constitute obstacles that challenge the patients' ability to organize their everyday activities and work task. This could potentially lead to the interruptions of treatment.

HAART regimen 1A-TDF (Lamivudine, Efavirenz and Tenofovir) was also one of the univariate factors associated with poor adherence to HAART with a $P = 0.04$ that is statically significant. Authors reported in their study [27] on medication taking behaviors, that as the complexity of the prescribed regimen increases, so do rates of non-adherence. As a prescribed regimen becomes more complex, it also becomes more inconvenient and difficult to incorporate into daily living. Although a medication timer is suggested as one of the possible solutions to compliance [27], patients who are less motivated with low social reinforcement, or with disordered lives like the alcoholics, regimen complexity may be a barrier to compliance.

In this study, it was established that the majority 66

(84.5%) of the patients were on HAART regimen 1A-TDF (3TC, Tenofovir and Efavirenz) and were none adherent. The recommended ART guidelines do suggest triple therapy because it has a significant advance in the treatment of HIV/AIDS disease as opposed to monotherapy. Triple therapy delays the disease progression to AIDS, thus decreasing the number of opportunistic infections leading to the improving the quality of life of patients. Little and colleagues [28] reported that the potent and effective new combinations have proven to be efficacious in reducing viral loads and improving clinical outcomes of patients. But the challenge faced by the patients is the large number of drugs these patients have to take plus the tolerability that leads them to be non-adherent.

Higher CD4+ T cell count (> 350 cells/mm³) was also another univariate factor associated with poor adherence to HAART with a P of 0.048 that was statistically significant. A study [29] done on self-reported adherence to ARV identified several psychosocial predictors of acceptable levels of adherence. Patient's knowledge and beliefs about the disease had an influence on adherence. Patients need to understand the relationship between adherence, CD4+ T counts, viral loads and disease progression. As observed in this study, patients seemed to have stopped adhering to their ARVs, once they started to improve clinically (CD4+ T count > 350 cells/mm³).

5. Conclusions

Although there are recently an increase number of HIV-infected on receiving HAART, findings from this study have shown that many will not adhere to their ARV treatments, once they start to improve clinically (CD4 + T count > 350 cells/mm³). The underlying assumption remain the lack of education and complexity of combined ARV regimens prescribed to these patients (the triple therapy plus other drugs taken by the HIV/AIDS patients).

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References

- [1] Abellán, J., Garrote, M., Pulido, F., Rubio, R., and Costa, R. J. 1999. "Evaluation of Adherence to a Triple Antiretroviral Therapy in HIV-Positive Patients." *Eur. J. Intern. Med.* 10: 202-5.
- [2] Spire, B., Duran, S., Souville, M., Leport, C., Raffi, F., and Moatti, J. P.; APROCO cohort study group. 2002. "Adherence to Highly Active Antiretroviral Therapies (HAART) in HIV-Infected Patients: From a Predictive to a Dynamic Approach." *Social Science Medicine* 54 (10):1481-96.
- [3] Carpenter, C. C., Fischl, M. A., Hammer, S. M., Hirsch M. S., Jacobsen, D. M., Katzenstein, D. A., Montaner, J. S., Richman D. D., Saag, M. S., Schooley, R. T., Thompson, M. A., Vella, S., Yeni, P. G., and Volberding, P. A. 1998. "Antiretroviral Therapy for HIV Infection in 1998: Updated Recommendations of the International AIDS Society-USA Panel." *JAMA* 280: 78-86.
- [4] Mocroft, A., Vella, S., Benfield, T. L., Chiesi, A., Miller, V., Gargalianos, P., d'Arminio Monforte, A., Yust, I., Bruun, J. N., Phillips, A. N., and Lundgren, J. D. 1998. "Changing Patterns of Mortality across Europe in Patients Infected with HIV-1." *Lancet* 352 (9142): 1725-30.
- [5] Mehta, S., Moore, R. D., and Graham, N. M. H. 1997. "Potential Factors Affecting Adherence with HIV Therapy." *AIDS* 11 (14): 1665-70.
- [6] UNAIDS (2011) World AIDS Day report-Results. Accessed October 10, 2013. <http://www.unaids.org/en/resources/campaigns/worldaidsdayreport/index.html>.
- [7] UNAIDS (2012). Together We Will End AIDS. Accessed October 20, 2013. <http://www.unaids.org/en/resources/campaigns/togetherweillenddaids/index.html>.
- [8] Paterson, D. L., Swindells, S., Mohr, J., Brester, M., Vergis, E. N., Squier, C., Wagener, M. M., and Singh, N. 2000. "Adherence to Protease Inhibitor Therapy and Outcomes in Patients with HIV Infection." *Ann. Intern. Med.* 133 (1): 21-30.
- [9] Martin, M., Del Cacho, E., Codina, C., Tuset, M., De Lazzari, E., Mallolas, J., Miró, J. M., Gatell, J. M., and Ribas, J. 2008. Relationship between Adherence Level, Type of Antiretroviral Regimen, and Plasma HIV Type 1 RNA Viral Load: A Prospective Cohort Study." *AIDS Res. Hum. Retroviruses* 24 (10): 1263-8.
- [10] Bangsberg, D. R., Acosta, E. P., Gupta, R., Guzman, D., Riley, E. D., Harrigan, P. R., Parkin, N., and Deeks, S. G. 2006. "Adherence-Resistance Relationship for Protease and Non-nucleoside Reverse Transcriptase Inhibitors Explained by Virological Fitness." *AIDS* 20 (2): 223-31. doi: 10.1097/01.aids.000011999825.34241.49.
- [11] Harrigan, P. R., Hogg, R. S., Dong W. W., Yip, B., Wynhoven, B., Woodward, J., Brumme, C. J., Brumme, Z. L., Mo, T., Alexander, C. S., and Montaner, J. S. 2005. "Predictors of HIV Drug-Resistance Mutations in a Large Antiretroviral-Naïve Cohort Initiating Triple Antiretroviral Therapy." *J. Infect. Dis.* 191 (3): 339-47.
- [12] Bangsberg, D. R., Perry, S., Charlebois, E. D., Clark, R. A., Roberston, M., Zolopa, A. R., and Moss, A. 2001. "Non-Adherence to Highly Active Antiretroviral Therapy Predicts Progression to Aids." *AIDS* 15 (9):1181-3.
- [13] Wood, E., Hogg, R. S., Yip, B., Moore, D., Harrigan, P. R., and Montaner, J. S. 2006. "Impact of Baseline Viral Load and Adherence on Survival of HIV-Infected Adults with Baseline CD4 Cell Count > OR = 200 Cells/Microl." *AIDS* 20 (8): 1117-23.
- [14] Unge, C., Sodergard, B., Marrone, G., Thorson, A., Lukhwaro, A., Carter, J., Ilako, F., and Ekström, A. M. 2010. "Long-Term Adherence to Antiretroviral Treatment and Program Drop-Out in a High-Risk Urban Setting in Sub-Saharan Africa: A Prospective Cohort Study." *PLoS one* 5 (10): e13613. Accessed November, 2013. <http://www.plosone.org/article/Info%3Adoi%2F10.1371>.
- [15] Kozal, M. J., Hullsiek, K. H., MaCarthur, R. D., Berg-Wolf, M., Peng, G., Xiang, Y., Baxter, J. D., Uy, J., Telzak, E. E., and Novak, R. M.; Terry Bein Community Programs for Clinical Research on AIDS (CPCRA). 2007. "The Incidence of HIV Drug Resistance and Its Impact on Progression of HIV Disease among Antiretroviral-Naïve Participants Started on Three Different Antiretroviral Therapy Strategies." *HIV Clin. Trials.* 8 (6): 357-70.
- [16] Edlin, B. R., Toakrs, J. I., Grieco, M. H., Crawford, J. T., Williams, J., Sordillo, E. M., Ong, K. R., Kilburn, J. O., Dooley, S. W., Castro, K. G., Jarvis, W. R., and Holmberg, S. D. 1992. "An Outbreak of Multidrug-Resistant Tuberculosis among Hospitalised Patients with the Acquired Immunodeficiency Syndrome." *N. Engl. J. Med.* 326 (23): 1514-21.
- [17] Bajunirwe, F., Arts, E. J., Tisch, D. J., King, C. H., Debanne, S. M., and Sethi, A. K. 2009. "Adherence and

- Treatment Response among HIV-1-Infected Adults Receiving Antiretroviral Therapy in a Rural Government Hospital in South Western Uganda.” *J. Intern. Assoc. Physicians in AIDS Care* 8 (2): 139-47.
- [18] Kigozi, L. J. 2008. “Client Factors Determining ARV Adherence in Natalspruit Hospital and Empilisweni CHC in Gauteng Province in 2006.” Master thesis, University of the Witwatersrand.
- [19] Muula, A. S., Ngulube, T. J., Siziya, S., Makupe, C. M., Umar, E., Prozesky, H. W., Wiysonge, C. S., and Mataya, R. H. 2007. “Gender Distribution of Adult Patients on HAART in Southern Africa: A Systematic Review.” *BMC Public Health* 7: 63. doi: 10.1186/1471-2458-7-63.
- [20] Nachega, J. B., Mills, E. J., and Schechter, M. 2010. “Antiretroviral Adherence and Retention in Care in Middle-Income and Low-Income Countries: Current Status of Knowledge and Research Priorities.” *Curr. Opin. HIV AIDS* 5: 70-7.
- [21] Bersoff-Matcha, S. J., Miller, W. C., Aberg, J. A., van Der Horst, C., Hamrick, Jr. H. J., Powderly, W. G., and Mundy, L. M. 2001. “Sex Differences in Nevirapine Rash.” *Clin. Infect. Dis.* 32 (1): 124-9.
- [22] Druyts, E., Dybul, M., Kanfers, S., Nachega, J., Birungi, J., Ford, N., Thorlund, K., Negin, J., Lester, R., Yaya, S., and Mills, E. J. 2013. “Male Sex and the Risk of Mortality among Individuals Enrolled in Antiretroviral Therapy Programs in Africa: A Systematic Review and Meta-analysis.” *AIDS* 27 (3): 417-25.
- [23] Small, W., Wood, E., Betteridge, G., Montaner, J., and Kerr, T. 2009. “The Impact of Incarceration upon Adherence to HIV Treatment among HIV-Positive Injection Drug Users: A Quantitative Study.” *AIDS Care* 21 (6):708-14.
- [24] Kalichman, S. C., Ramachandran, B., and Catz, S. 1999. “Adherence to Combination Antiretroviral Therapies in HIV Patients of Low Health Literacy.” *J. Intern. Med.* 14 (5): 267-72.
- [25] Kissinger, P., Cohen, D., Brandon, W., Rice, J., Morse, A., and Clark, R. 1995. “Compliance with Public Sector HIV Medical Care.” *J. Natl. Med. Assoc.* 87 (1): 19-24.
- [26] Bonolo, P. F., Cesar, C. C., Acurcio, F. A., Ceccato, Md., de P álua, C. A., Alvares, J., Campos, L. N., Carmo, R. A., and Guimar ães, M. D. 2005. “Non-adherence among Patients Initiating Antiretroviral Therapy: A Challenge for Health Professionals in Brazil.” *AIDS* 19 (suppl. 4): S5-S13.
- [27] Wallisten, S. M. 1995. “Functioning Elderly: MacArthur Field Studies of Successful Adding.” *Ann Pharmacother* 29: 359-64.
- [28] Little, S. J., Daar, E. S., D’Aquila, R. T., Keiser, P. H., Connick, E., Whitcomb, J. M., Hellmann, N. S., Petropoulos, C. J., Sutton, L., Pitt, J. A., Rosenberg, E. S., Koup, R. A., Walker, B. D., and Richman, D. D. 1999. “Reduced Antiretroviral Drug Susceptibility among Patients with Primary HIV Infection.” *JAMA* 282 (12): 1142-9.
- [29] Chesney, M. A., Ickovics, J. R., Chambers, D. B., Gifford, A. L., Neidig, J., Zwickl, B., and Wu, A. W. 2000. “Self-reported Adherence to Antiretroviral Medication among Participants in HIV Clinical Trials: The AACTG Adherence Instruments. Patient Care Committee and Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG).” *AIDS Care* 12 (3): 255-66.