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**State of the ART: Clinical efficacy and improved quality-of-life in the public anti-retroviral therapy program, Free State Province, South Africa**

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## **State of the ART: Clinical efficacy and improved quality of life in the public antiretroviral therapy program, Free State Province, South Africa**

### **Abstract**

The South African public-sector antiretroviral treatment (ART) program has yielded promising early results. To extend and reinforce these preliminary findings, we undertook a detailed assessment of the clinical efficacy and outcomes over two years of ART. The primary objective was to assess the clinical outcomes and adverse effects of two years of ART, while identifying the possible effects of baseline health and patient characteristics. A secondary objective was to address the interplay between positive and negative outcomes (clinical benefits versus adverse effects) in terms of the patients' physical and emotional quality of life (QoL). Clinical outcome, baseline characteristics, health status, and physical and emotional QoL scores were determined from clinical files and interviews with 268 patients enrolled in the Free State ART program at three time points (six, 12, and 24 months of ART). Age, sex, education, and baseline health (CD4 cell count and viral load) were all independently associated with the ART outcome in the early stages of treatment, but their impact diminished as the treatment progressed. The number of patients classified as treatment successes increased over the first two years of ART, whereas the proportion of patients experiencing adverse effects diminished. Importantly, our findings show that ART had strong and stable positive effects on physical and emotional QoL. These favorable results demonstrate that a well-managed public-sector ART program can be very successful within a high-HIV-prevalence resource-limited setting. This finding emphasizes the need to adopt treatment scale-up as a key policy priority, while at the same time ensuring that the highest standards of healthcare provision are maintained. Healthcare services should also target vulnerable groups (males, less-educated patients, those with low baseline CD4 cell counts and high baseline viral loads) who are most likely to experience treatment failure.

## Introduction

An estimated 5.4 million South Africans are currently infected with HIV, making the South Africa HIV/AIDS epidemic one of the most challenging in the world (Day et al., 2007; R. Wood et al., 2008). Despite the government adoption of the *Comprehensive HIV and AIDS Care, Management and Treatment Programme* in 2003, which incorporated antiretroviral treatment (ART) into public-sector healthcare, ART coverage in 2007 was estimated to be only 28% among patients with advanced infection (Department of Health, 2003; UNAIDS et al., 2008). It was recently suggested that efforts to expand the provision of ART in sub-Saharan Africa are constrained by the concern that inadequate health services and poor treatment adherence will reduce the effectiveness of ART (Fairall et al., 2008; Paredes et al., 2008). Others claim that ART effectiveness in sub-Saharan Africa is hampered by severe shortages of human resources for healthcare, which seriously curtail ART implementation and scale-up (Dal Poz et al., 2008; Mukherjee et al., 2003; Nixon et al., 2008; Rosen et al., 2005; Schneider et al., 2006; Van Damme et al., 2008; Van Damme et al., 2006; Van Oosterhout et al., 2007).

Since the launch of the *Comprehensive Plan*, significant resources have been allocated to the treatment, care, and support of people with HIV/AIDS. However, the treatment outcomes for this large-scale public ART program, although promising, are still preliminary (Baggaley, 2006; Baggaley et al., 2005; Fairall et al., 2008; Larson et al., 2008; Wouters et al., 2008). To assess the effectiveness of the South African public-sector ART program, research is required into the long-term immunological and virological outcomes of patients enrolled in the program.

There have been impressive gains in survival following the introduction of ART into public-sector healthcare. Even so, the clinical benefits can be offset by the toxicity and adverse effects associated with long-term ART use (Ahdieh Grant et al., 2001; Calmy et al., 2007; Gatti et al., 1999; Mutimura et al., 2007). Therefore, the adverse effects of treatment

must be taken into account when assessing the outcomes of the South African public ART program (Park-Wyllie et al., 2007).

One approach to evaluating the balance between the potential positive and adverse consequences of treatment is to monitor the quality of life (QoL) of people living with HIV/AIDS who are receiving treatment (Jelsma et al., 2005; Park-Wyllie et al., 2007; Rosen et al., 2008). Improvements in their functional status and well-being can be considered essential determinants of the balance between the clinical benefits and potential adverse effects.

QoL is a multidimensional construct with two aspects, the physical and emotional (Aaronson et al., 1991; Burgess et al., 2000; Burgess et al., 1993; Cella et al., 2005; Hays et al., 1995; Hays et al., 1990; Lenderking et al., 1997; Vickrey et al., 1992; Ware et al., 1994). We measured the impact of the disease on physical QoL by assessing physical and functional limitations. We also assessed changes in the emotional state, with an emphasis on mood, depression, and life satisfaction (Revicki et al., 1998; Ware et al., 1998). Most studies have focused on clinical and physical outcomes, and little is known about how ART affects emotional QoL, especially in patients living in resource-poor settings (Berzon et al., 1997; Bloom et al., 2006; Cella et al., 1998; Holmes et al., 1998; O'Connell et al., 2004; Préau et al., 2004; Skevington et al., 2003).

Previous reports have suggested that baseline health (baseline CD4 cell count and baseline viral load) and individual characteristics (age, sex, education) correlate with ART outcome and the associated improvement in QoL among public-sector the ART patients in resource-poor settings (Jelsma et al., 2005; Jia et al., 2005; Jia et al., 2007; WHOQOL HIV Group, 2004). Therefore, these parameters must be taken into account when assessing the outcomes of public-sector ART.

This study had two central objectives. The first was to evaluate the clinical outcomes and adverse effects of ART, measured at three time points (after six, 12, and 24 months of ART), in a sample of 268 patients enrolled in the Free State public-sector ART program,

while controlling for the possible effects of baseline health and patient characteristics. The second was to examine the impact of those 24 months of ART and the associated positive and negative outcomes (clinical benefits and adverse effects) on the physical and emotional QoL measured in the same sample of patients.

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## Materials & methods

### *Study population*

The sampling frame consisted of a list of names, obtained from the Provincial Department of Health, of adult patients certified as medically ready to commence ART (CD4 < 200 cells/ $\mu$ L and/or WHO stage IV), within two months of the first patient commencing therapy. To detect a 5% difference in this population at the 95% confidence level, 268 patients on ART were randomly selected, in proportion to the number of patients per clinic.

### *Data collection and study variables*

'Baseline' was defined as the date of ART initiation (time 0 or after 0 days of ART). We subsequently gathered three waves of panel data to examine the impact of public-sector ART on clinical parameters and QoL outcomes. At time 1 (<6 months of ART), trained enumerators conducted face-to-face interviews with the 268 study participants using a standard questionnaire, after the written consent of all the patients had been obtained. Approximately six months later (time 2 or <12 months of ART), 232 patients from the original cohort were interviewed again using an updated version of the questionnaire. One year later, 183 of the original study participants were interviewed yet again (time 3).

Because patient characteristics may influence both ARV treatment outcomes and the associated QoL benefits, data on age, sex, and educational levels were collected. To assess educational levels, five educational categories were established based on the patient responses: no education, primary schooling only, some secondary education, grade 12, and tertiary education. CD4 cell counts and plasma HIV RNA levels (viral load), measured immediately before the commencement of ART (time 0), were used as the baseline measures of CD4 cell counts and viral loads.

In accordance with previous studies, we measured the treatment outcomes as a combination of virological and immunological measures (Bratt et al., 1998; Brigido et al., 2004; Ferradini et al., 2007; E. Wood et al., 2006). Virological status was measured as the

level of plasma HIV RNA at times 1, 2, and 3 and was categorized dichotomously as undetectable ( $\leq 400$  copies/mL) or detectable ( $> 400$  copies/mL) (Bratt et al., 1998; Monforte et al., 1998). Immunological outcomes were assessed at times 1, 2, and 3, with a distinction made between nonresponders ( $CD4 \leq 200$  cells/ $\mu$ L) and responders ( $CD4 > 200$  cells/ $\mu$ L). A summation score categorized the patients as treatment successes (patients with undetectable viral load and  $CD4 > 200$  cells/ $\mu$ L), partial successes (patients with undetectable viral load or  $CD4 > 200$  cells/ $\mu$ L), and treatment failures (patients with detectable viral load and  $CD4 \leq 200$  cells/ $\mu$ L) (Brigido et al., 2004; Ferradini et al., 2007; Monforte et al., 1998; E. Wood et al., 2006). All clinical data were collected directly from the patient files<sup>1</sup> after the written consent of all the patients had been obtained and with the authorization of the provincial Department of Health.

We measured the adverse effects of ART using a construct that categorized patients as having no adverse effects, mild adverse effects, or disruptive adverse effects. The severity of any adverse effects is an important consideration because many adverse effects relate to mild toxicities that can be treated easily.

To assess physical QoL in our study, a latent variable<sup>2</sup> was constructed using EuroQoL 5D (EQ-5D). This is a standardized, widely validated and tested instrument developed by the EuroQoL Group to cover five generic aspects of current health: mobility, self-care, limitation of activities, pain, and mood<sup>3</sup>. However, in this study, a distinction was drawn between the physical and emotional outcomes of ART. The mood item in the EQ-5D assesses an aspect of emotional health and was not included as an indicator of physical QoL.

Measures of overall emotional or psychological well-being are generally based on self-reports. This is called subjective well-being (SWB) (Bookwalter et al., 2004; Diener et al., 1997; Ormel et al., 1999). There is a current consensus that SWB consists of three primary components: life satisfaction, pleasant affect, and low levels of unpleasant affect (Busseri et al., 2006; Diener et al., 2003; Diener et al., 1997; Eid et al., 2004; Kashdan, 2004). Patient responses to a standard five-point-scaled item regarding overall life satisfaction are used to



measure the cognitive part of SWB. An item asking about global happiness is used as a measure of positive emotions. The fifth EuroQoL item, measuring anxiety and depression, is used to measure the third component of SWB, the lack of unpleasant affect. This instrument has shown good reliability and construct validity in earlier studies of QoL among ART patients in South Africa (Wouters et al., 2007).

#### *Statistical analysis*

We used structural equation modeling to analyze the clinical outcomes, adverse effects, and associated physical and emotional QoL scores over 24 months of public-sector ART.

FIGURE 1

## Results

### *Sample description*

The demographic characteristics of the 268 ART patients are presented in Table I. The table also records their clinical outcomes, adverse effects of treatment, and emotional and physical QoL scores.

TABLE 1

### *Attrition analysis*

The attrition rate of 13% (34 patients) between the first two interviews was mainly attributed to patient death (n=15), patient refusal to be interviewed (n=8), and our failure to trace the patients (n=6). The primary reasons for nonresponse at time 3 (21%, 51 patients) were similar: death (n=19), refusal to be interviewed (n=13), and failure to determine current patient whereabouts (n=7). A series of bivariate analyses showed no statistically significant differences in the study variables (age, sex, physical and emotional QoL, and adverse effects of treatment) between the responders and the nonresponders at time 2. However, one year later, the physical and emotional QoL of the nonresponders was significantly lower than that of the responders ( $P<0.05$ ). The differences in the other study variables (age, sex, and adverse effects of treatment) were not significant. When we studied the clinical parameters, the results showed that the patients lost to death had a significantly lower mean baseline CD4 cell count (mean difference =32 cells/ $\mu$ L,  $P<0.05$ ) than that of the surviving patients.

### *The measurement model*

Table 2 presents the final measurement model, with acceptable practical fit indices. The findings support the reliability and validity of the two constructs and their indicators over time.

TABLE 2

### *Structural model*

The model fitting results are shown in Table 3. The root mean square error of approximation indicates a close fit of the overall model, with reasonable errors of approximation in the population.

*Impact of baseline health and patient characteristics on ART outcomes*

The treatment outcome after six months of ART was not strongly associated with the patient characteristics. The clinical outcome was weakly associated with patient age ( $\beta=0.09$ ,  $P<0.05$ ). Older patients also experienced more adverse affects than did younger patients ( $\beta=0.11$ ,  $P<0.05$ ). Educational level contributed significantly but weakly to the explanation of the variance in ART outcomes: higher education was associated with a better ART response ( $\beta=0.07$ ,  $P<0.05$ ) and with fewer adverse treatment effects ( $\beta=-0.08$ ,  $P<0.05$ ). Sex had no significant impact on the clinical outcomes or adverse treatment effects at the first time point. Six months later, there was no significant association between patient age and clinical outcome. Sex ( $\beta=0.05$ ,  $P<0.05$ ) and education ( $\beta=0.07$ ,  $P<0.05$ ) significantly affected the clinical outcome: among our sample of patients, female or highly educated patients had more favorable ART outcomes at 12 months than male or less educated patients. Age ( $\beta=0.10$ ,  $P<0.05$ ), sex ( $\beta=0.09$ ,  $P<0.05$ ), and education ( $\beta=-0.07$ ,  $P<0.05$ ) significantly influenced the adverse effects of ART. Finally, after two years of ART, only the sex of the patient ( $\beta=0.02$ ,  $P<0.05$ ) was significantly but weakly associated with the clinical outcome. At this stage of treatment, age ( $\beta=0.09$ ,  $P<0.05$ ) was the only characteristic that correlated with adverse treatment effects.

During the first six months of ART, clinical outcomes and adverse effects were strongly influenced by baseline health. Patients with low baseline CD4 cell counts had a greater risk of treatment failure ( $\beta=0.26$ ,  $P<0.001$ ) and disruptive adverse effects ( $\beta=-0.16$ ,  $P<0.001$ ) compared with patients with a higher baseline CD4 count. Similar results were observed among patients with low baseline viral loads, insofar as baseline viral suppression increased the patient's chance of treatment success by 0.18 standard deviations ( $P<0.001$ ) and

reduced his/her chance of severe adverse effects by 0.12 standard deviations ( $P<0.01$ ). Approximately six months later, the baseline CD4 cell values and baseline viral loads continued to influence the treatment outcome. However, pre-ART health had a much weaker impact on antiviral efficacy and adverse treatment effects at this stage of treatment. After two years of ART, the impact of baseline health on the ART response became even weaker. The baseline CD4 cell count ( $\beta=0.06$ ,  $P<0.05$ ) was significantly associated with the clinical outcome at this stage of treatment but there was no significant association between the baseline viral load and the ART response. Baseline health also did not predict the adverse effects of ART at this stage of treatment.

*Impact of clinical outcomes and adverse ART effects on physical and emotional QoL*

The model also tested the impact of the positive and negative outcomes of ART (clinical benefits and adverse effects) on physical and emotional QoL. After six months, an improved clinical outcome was significantly associated with improved physical ( $\beta=0.14$ ,  $P<0.01$ ) and emotional QoL ( $\beta=0.13$ ,  $P<0.05$ ). At this stage of treatment, improvement in QoL was significantly constrained by the adverse effects of ART. Physical QoL decreased by 0.19 standard deviations ( $P<0.01$ ) and emotional QoL decreased by 0.15 standard deviations ( $P<0.01$ ) when the patient reported adverse effects ( $P<0.01$ ). There was also a strong positive association between physical and emotional QoL ( $\beta=0.29$ ,  $P<0.001$ ). After six months, improved clinical parameters were strongly associated with improvements in physical ( $\beta=0.21$ ,  $P<0.001$ ) and emotional QoL ( $\beta=0.20$ ,  $P<0.01$ ). The impact of adverse treatment effects decreased slightly but remained significant, and the adverse effects of ART negatively affected both physical ( $\beta=-0.10$ ,  $P<0.05$ ) and emotional QoL ( $\beta=-0.11$ ,  $P<0.05$ ). As before, physical QoL strongly and significantly predicted emotional QoL ( $\beta=0.30$ ,  $P<0.001$ ). Finally, after two years of ART, improved clinical parameters were again positively associated with improvements in QoL. Patients who responded well to treatment reported significantly better physical ( $\beta=0.14$ ,  $P<0.01$ ) and emotional well-being ( $\beta=0.13$ ,  $P<0.05$ ) than did patients with less favorable treatment outcomes. At this stage of treatment, adverse effects did not

significantly predict the patients' physical or emotional QoL. However, physical QoL remained the most important predictor of emotional well-being among our sample of ART patients ( $\beta=0.29$ ,  $P<0.001$ ).

TABLE 3

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## Discussion

In this analysis of 268 patients followed over the first two years of public-sector ART in one South African province, three of every four patients could be classified as treatment successes (CD4 cell count  $\geq 200$  cells/ $\mu\text{L}$  and viral load  $< 400$  copies/mL) after 24 months of ART. Strikingly, the overall survival rate was 87.3% during the first 24 months of treatment. Most deaths were associated with low baseline CD4 cell counts (in this subsample of patients, the mean CD4 cell count was 77 cells/ $\mu\text{L}$ ). Patients reported significantly fewer adverse effects as the duration of the treatment increased. The most cited adverse effects (dizziness, nausea, and skin problems) related to mild toxicities that did not require discontinuation of the therapy or drug substitution, but could be overcome by symptomatic treatment (WHO, 2006). Overall, the success rate was similar if not superior to rates reported in industrialized societies (Braithwaite et al., 2007; Ferradini et al., 2007). Therefore, this longitudinal study provides strong evidence that the South African public-sector ART program is effective in delivering sustained viral suppression, and confirms universal access to ART as a key policy priority.

Among the factors predicting a favorable ART outcome, patient characteristics did not have an important impact on treatment outcomes. The patient's education only weakly influenced the treatment response during the first six months of ART. An increase in the patient's educational level of one standard deviation resulted in an improvement in ART outcome of 0.07 standard deviations. In contrast, baseline health was the most important predictor of the clinical outcome of ART and of the adverse effects suffered during the first six months of ART. Patients with low baseline CD4 cell counts and/or high baseline viral loads had a significantly increased risk of treatment failure during the introductory months of treatment. Delayed ART initiation (very low CD4 cell count and high viral load) also predicted an increased severity of adverse effects. However, baseline health became less important as a predictive factor as the duration of ART increased. Although our understanding of the factors predicting ART outcomes in resource-limited high-prevalence settings is still preliminary, these observations are similar to those reported by Murphy et al. (2004), Bisson

et al. (2006), and Wood et al. (2006) (Bisson et al., 2006; Murphy et al., 2004; E. Wood et al., 2006).

This study emphasizes that ART can have both positive and negative outcomes for the patient. Therefore, the central question remains: how do the two opposing factors (clinical benefit versus adverse effects) balance each other in determining the overall outcome, the patient's QoL? Our findings show a strong and stable positive effect of ART on both physical and emotional QoL. Patients with favorable treatment outcomes reported less pain or discomfort and significantly fewer problems with self-care, daily activities, and general mobility. Patients who responded well to treatment also reported higher levels of emotional QoL, with less anxiety and depression, than those of nonresponders. A favorable clinical outcome was also associated with improvements in happiness and life satisfaction. However, at the initiation of ART, adverse effects dramatically reduced the improvement in QoL produced by ART. Drug toxicity negatively affected physical and emotional well-being. However, the impact of the adverse drug effects on QoL diminished with time and eventually became insignificant. This may be attributable to the skewed distribution of the adverse effects and QoL scales, leading to ceiling effects (Jelsma et al., 2005; Skevington et al., 2003). Overall, our findings demonstrate that the virological and immunological improvements produced by ART translated into progressive improvement in both physical and emotional QoL over the first two years of public-sector ART.

The strengths of this study include its longitudinal character and the availability of information on an understudied population. First, differences between the patients lost to attrition and the retained patients could potentially lead to an overestimation of the impact of ART on the clinical parameters and QoL, because it is expected that patients experiencing adverse effects of treatment and/or with a lower QoL are more likely to drop out of care. Therefore, our findings are more appropriately interpreted as being conditional on remaining in care for two years. Second, although the analysis focused on clinical ART outcomes and adverse effects as they related to physical and emotional QoL, the structural equation model

offers an incomplete explanation of the QoL scores. Other potentially relevant predictors of QoL (e.g., ART adherence, opportunistic infections) were not available in the dataset.

The study findings have clear practical implications. This study demonstrates that a well-managed public-sector ART program can be very successful within a high-HIV-prevalence resource-limited setting. Despite some early adverse drug effects, the public-sector treatment achieved important improvements in the clinical parameters and associated physical and emotional well-being of patients. However, complacency is not warranted. First, our findings indicate that the delayed initiation of ART significantly reduces the treatment response. Healthcare services should target vulnerable groups most likely to fail treatment, i.e., those patients with low baseline CD4 counts and high baseline viral loads. Second, recent studies suggest that many patients eligible for enrolment in South Africa's public-sector ART program die before starting ART (Fairall et al., 2008). Our findings demonstrate that the ART provided by the South African public-sector health services dramatically improves both survival rates and QoL of people living with HIV/AIDS. This should encourage policy makers to take radical measures to expand the access to and reduce the waiting times for these services, while at the same ensuring that the highest standards of healthcare provision are maintained.



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**Notes**

1. Almost all patients (97.8%) received a regimen consisting either stavudine, lamivudine, and efavirenz, or stavudine, lamivudine, and nevirapine. Bivariate analysis showed no statistical differences in the study variables (ART outcomes, adverse effects, physical and emotional QoL) between the two regimens.
2. A patient's physical QoL cannot be directly and reliably measured by asking one question. This is called a "latent concept". Such constructs can only be measured indirectly by observable indicators, such as questionnaire items designed to measure various physical capacities of the patient. We can then compile one construct expressing the patient's physical QoL from these items.
3. EuroQoL also includes a 'thermometer' of overall health, the visual analogue scale. The visual analogue scale is a measure of generic health and was therefore omitted from the analysis.

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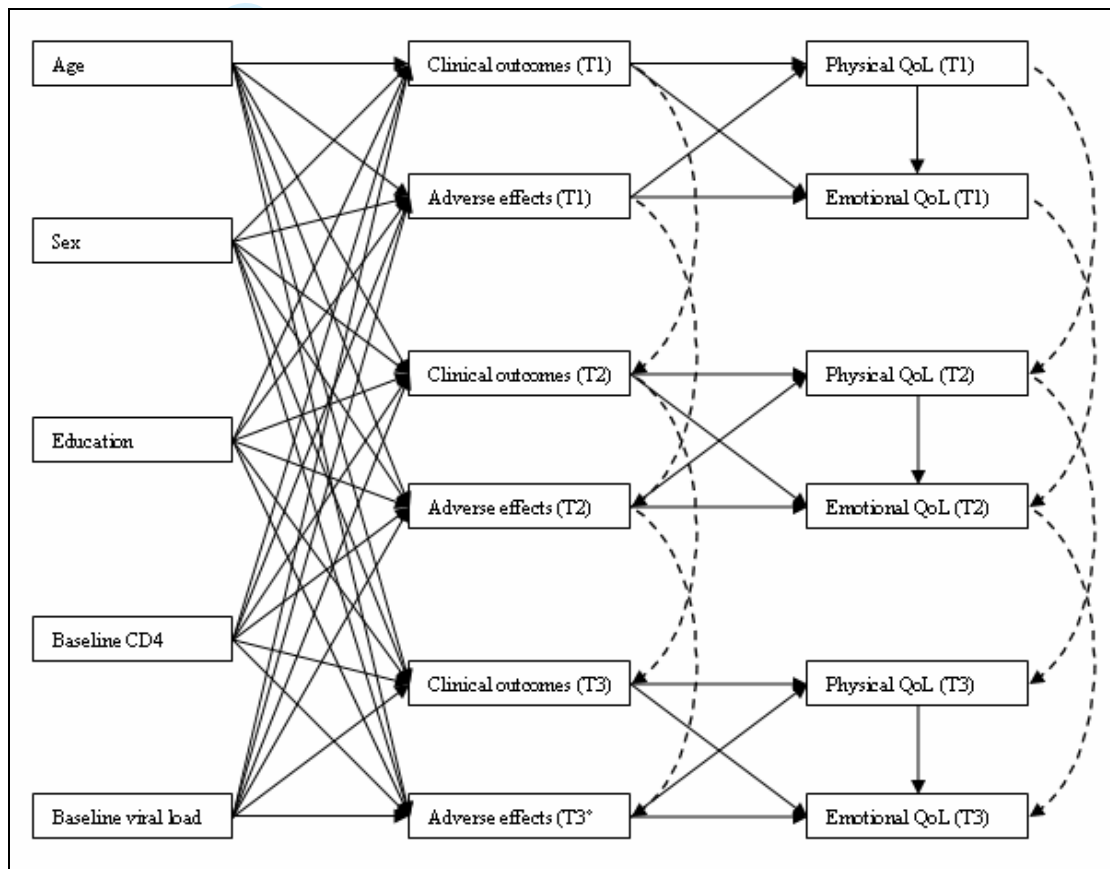
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**Figure 1.** The structural equation model with the hypothesized relationships between patient characteristics (age, sex and education), baseline health (CD4 and viral load), clinical outcome, adverse effects of treatment and physical and emotional quality of life (QoL) outcomes across three time-points. Dashed arrows connecting like-variables over time represent within-variable regression paths, estimating the relative stability of each variable. Solid lines show regression paths, first from patient characteristics to ART outcomes (clinical outcomes and adverse effects of ART), second from ART outcomes to physical and emotional QoL, and finally paths measuring the impact of physical QoL on emotional QoL.



**State of the ART: Clinical efficacy and improved quality-of-life in the public anti-retroviral therapy program, Free State Province, South Africa**

**Table 1.** Baseline characteristics, baseline health, clinical outcomes and physical and emotional quality of life (QoL) in a sample of ART patients (n = 268)

	Baseline	Time 1	Time 2	Time 3
<b>Demography</b>				
Male, %	34.7			
Age, mean (SD)	37.9 (8.6)			
Education, %				
No education	3.7			
Primary education	28.7			
Some secondary education	47.8			
Grade 12	15.3			
Tertiary education	4.5			
<b>Clinical response</b>				
CD4 count (cells/ $\mu$ l), mean (SD)	109 (68)	236 (158)	275 (140)	393 (207)
CD4 gain (cells/ $\mu$ l), mean (SD)	—	+ 127 (130)	+ 39 (101)	+ 118 (259)
< 200 cells/ $\mu$ l, %	—	44.8	30.3	17.3
$\geq$ 200 cells/ $\mu$ l, %	—	55.2	69.7	82.7
Viral load (copies/ml), mean (SD)	299,090 (628,028)	34,488 (221,029)	5,833 (36,128)	8,855 (42,976)
< 400 copies/ml, %	—	83.5	84.7	85.6
$\geq$ 400 copies/ml, %	—	16.5	15.3	14.4
Treatment outcome				
Treatment failure, %	—	9.6	8.5	7.5
Partial treatment success, %	—	44.3	27.4	16.1
Treatment success, %	—	46.1	64.1	76.4
<b>Adverse effects of treatment</b>				
No adverse effects, %		44.9	72.7	91.3
Mild adverse effects, %		20.0	9.1	3.3
Disruptive adverse effects <sup>1</sup> , %		35.1	18.2	4.4
Skin problems / rash, %		26.7	19.4	1.6
Nausea, %		18.2	3.9	0.0
Dizziness, %		16.9	5.2	2.2
Swollen/painful joints/limbs, %		13.8	8.2	3.8
Diarrhea, %		8.4	3.0	1.6
Fatigue, %		2.7	4.3	3.3
<b>Quality of Life</b>				
Physical QoL				
Mobility, mean (SD) <sup>2</sup>	—	1.80 (0.41)	1.83 (0.39)	1.90 (0.31)
Self-care, mean (SD) <sup>2</sup>	—	1.92 (0.30)	1.95 (0.22)	1.97 (0.18)
Usual activities, mean (SD) <sup>2</sup>	—	1.77 (0.49)	1.84 (0.40)	1.93 (0.25)
Pain/discomfort, mean (SD) <sup>2</sup>	—	1.55 (0.59)	1.59 (0.57)	1.74 (0.49)
Emotional QoL				
Life satisfaction, mean (SD) <sup>3</sup>	—	2.36 (1.20)	2.39 (1.14)	2.58 (1.18)
Positive affect, mean (SD) <sup>3</sup>	—	3.02 (0.96)	2.87 (1.02)	2.79 (1.05)
Lack of neg. affect, mean (SD) <sup>2</sup>	—	1.63 (0.61)	1.71 (0.52)	1.80 (0.45)

<sup>1</sup> Patients had to state whether the reported adverse effects of treatment disrupted their daily lives.

<sup>2</sup> Minimum = 0 (severe problems), maximum = 2 (no problems)

<sup>3</sup> Minimum = 0 (very unsatisfied), maximum = 4 (very satisfied)



**Table 2.** Item analysis, goodness-of-fit and reliability assessment of the measurement model (n = 364)

Scale	Standardised loadings		
	Time 1	Time 2	Time 3
<b>Physical QoL</b>			
Mobility	0.792***	0.758***	0.752***
Usual activities	0.976***	0.966***	0.967***
Pain	0.952***	0.874***	0.892***
Self-Care	0.836***	0.789***	0.873***
<b>Emotional QoL</b>			
Satisfaction with life	0.693***	0.679***	0.861***
Pleasant affect	0.879***	0.703***	0.825***
Absence of unpleasant affect	0.794***	0.881***	0.816***
<b>Test for fit</b>	<b>Measurement model</b>	<b>Criteria for good fit</b>	
RMSEA	0.0000	< 0.05	
NFI	0.992	> 0.9	
NNFI	1.000	> 0.9	
CFI	1.000	> 0.9	
<b>Reliability</b>	<b>Composite Reliability</b>	<b>Criteria for reliability</b>	
Physical QoL (Time 1)	0.841	> 0.7	
Physical QoL (Time 2)	0.821	> 0.7	
Physical QoL (Time 3)	0.827	> 0.7	
Emotional QoL (Time 1)	0.720	> 0.7	
Emotional QoL (Time 2)	0.733	> 0.7	
Emotional QoL (Time 3)	0.763	> 0.7	
<b>Validity</b>	<b>Extracted variance test</b>	<b>Criteria for validity</b>	
Physical QoL (Time 1)	0.572	> 0.5	
Physical QoL (Time 2)	0.537	> 0.5	
Physical QoL (Time 3)	0.546	> 0.5	
Emotional QoL (Time 1)	0.509	> 0.5	
Emotional QoL (Time 2)	0.522	> 0.5	
Emotional QoL (Time 3)	0.517	> 0.5	

\*\*\* p < 0.001

**Table 3.** Standardized LISREL coefficients (minus relative stability paths) and model summary of the structural model (n = 268).

Path		Path coefficient	t-value	P-value
Age	→ Treatment outcome (T1)	0.089	2.447	< 0.05
Gender	→ Treatment outcome (T1)	0.034	1.933	NS
Education	→ Treatment outcome (T1)	0.073	2.208	< 0.05
Baseline CD4 cell count (T0)	→ Treatment outcome (T1)	0.260	7.032	< 0.001
Baseline viral load (T0)	→ Treatment outcome (T1)	-0.177	-5.293	< 0.001
Age	→ Adverse effects (T1)	0.106	2.839	< 0.01
Gender	→ Adverse effects (T1)	0.112	1.839	NS
Education	→ Adverse effects (T1)	-0.082	-1.998	< 0.05
Baseline CD4 cell count (T0)	→ Adverse effects (T1)	-0.159	-4.998	< 0.001
Baseline viral load (T0)	→ Adverse effects (T1)	0.123	2.782	< 0.01
Treatment outcome (T1)	→ Physical QoL (T1)	0.142	3.012	< 0.01
Treatment outcome (T1)	→ Emotional QoL (T1)	0.132	2.488	< 0.05
Adverse effects (T1)	→ Physical QoL (T1)	-0.192	-2.837	< 0.01
Adverse effects (T1)	→ Emotional QoL (T1)	-0.152	-3.192	< 0.01
Physical QoL (T1)	→ Emotional QoL (T1)	0.291	4.893	< 0.001
Age	→ Treatment outcome (T2)	0.043	1.544	NS
Gender	→ Treatment outcome (T2)	0.048	2.374	< 0.05
Education	→ Treatment outcome (T2)	0.067	2.293	< 0.05
Baseline CD4 cell count (T0)	→ Treatment outcome (T2)	0.072	2.299	< 0.05
Baseline viral load (T0)	→ Treatment outcome (T2)	-0.069	-2.289	< 0.05
Age	→ Adverse effects (T2)	0.103	2.288	< 0.05
Gender	→ Adverse effects (T2)	0.088	2.112	< 0.05
Education	→ Adverse effects (T2)	-0.072	-2.098	< 0.05
Baseline CD4 cell count (T0)	→ Adverse effects (T2)	-0.111	-2.676	< 0.01
Baseline viral load (T0)	→ Adverse effects (T2)	0.101	2.579	< 0.01
Treatment outcome (T2)	→ Physical QoL (T2)	0.211	4.362	< 0.001
Treatment outcome (T2)	→ Emotional QoL (T2)	0.199	3.021	< 0.01
Adverse effects (T2)	→ Physical QoL (T2)	-0.098	-2.403	< 0.05
Adverse effects (T2)	→ Emotional QoL (T2)	-0.114	-2.102	< 0.05
Physical QoL (T2)	→ Emotional QoL (T2)	0.301	5.003	< 0.001
Age	→ Treatment outcome (T3)	0.098	0.839	NS
Gender	→ Treatment outcome (T3)	0.023	2.054	< 0.05
Education	→ Treatment outcome (T3)	0.032	1.839	NS
Baseline CD4 cell count (T0)	→ Treatment outcome (T3)	0.055	1.997	< 0.05
Baseline viral load (T0)	→ Treatment outcome (T3)	-0.082	-1.224	NS
Age	→ Adverse effects (T3)	0.093	1.989	< 0.05
Gender	→ Adverse effects (T3)	0.040	0.983	NS
Education	→ Adverse effects (T3)	-0.038	-1.038	NS
Baseline CD4 cell count (T0)	→ Adverse effects (T3)	-0.079	-1.832	NS
Baseline viral load (T0)	→ Adverse effects (T3)	0.029	1.029	NS
Treatment outcome (T3)	→ Physical QoL (T3)	0.143	2.738	< 0.01
Treatment outcome (T3)	→ Emotional QoL (T3)	0.127	2.382	< 0.05
Adverse effects (T3)	→ Physical QoL (T3)	-0.056	-1.793	NS
Adverse effects (T3)	→ Emotional QoL (T3)	-0.043	-1.829	NS
Physical QoL (T3)	→ Emotional QoL (T3)	0.289	4.828	< 0.001
<b>Test for fit</b>		<b>Model</b>	<b>Criteria for good fit</b>	
RMSEA		0.0446	< 0.05	
Normed Fit Index (NFI)		0.943	> 0.90	
Non-Normed Fit Index (NNFI)		0.911	> 0.90	
Comparative Fit Index		0.963	> 0.90	
Parsimony Normed Fit Index (PNFI)		0.601		

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