

# Adherence to antiretroviral therapy, virologic failure and workload at the Rustenburg Provincial Hospital

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## Abstract

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**Background:** Adherence to antiretroviral therapy (ART) is a strong predictor of progression to AIDS and death. It remains the most important potentially alterable factor that determines treatment outcomes.

**Methods:** The study is a cross-sectional survey of self-reported adherence to ART and associated factors. It included a randomly selected sample of 100 adult patients who began ART between June 2006 and December 2007. A modified Adult AIDS Clinical Trials Group questionnaire was used. The analysis compared self-reported adherence levels by factor and viral load test results.

**Results:** Only 71% of patients had an adherence > 95%. Poor adherence was related to changes in daily routines (being away from home [21%] and busy with other things [17%]). All patients with symptoms suggestive of clinical depression had virologic failure. More unemployed patients (50.7%) had virologic failure than did employed patients (40%) ( $p < 0.05$ ). The clinic had a tenfold increase in patient enrolment and a ninefold decline in staff-to-patient ratio, and the proportion of patients lost to follow-up doubled in the preceding four years.

**Conclusion:** Adherence to ART was poor. The capacity of the clinic to manage patients adequately has declined significantly. Decentralisation of ART services to primary health care facilities should be considered.

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## Introduction

The backbone of the strategy to control the HIV/AIDS epidemic remains the prevention of HIV transmission. In generalised epidemics, the use of antiretroviral therapy (ART) is an additional component of HIV transmission prevention measures, as it reduces genital and plasma HIV-1 RNA.<sup>1-3</sup> This prevention benefit is lost when ART is interrupted, either through a structured process or through non-adherence.<sup>4,5</sup>

As an increasing number of people in developing countries are put on lifelong ART, adherence to therapy has become a major concern. Adherence to treatment is an unresolved, complex phenomenon in the management of chronic conditions such as hypertension.<sup>6-8</sup> Multiple doses and the side effects of medications are commonly cited factors associated with poor adherence.<sup>9</sup> With the advent of antiretrovirals (ARVs), it has become clear that HIV/AIDS is a chronic condition for which adherence to therapy is of public health relevance.<sup>10,11</sup>

Adherence to ART is the second strongest predictor of progression to AIDS and death after CD4 count and remains the most important potentially alterable factor that determines treatment outcomes for patients with HIV/AIDS.<sup>12-16</sup> Unlike treatment for most chronic conditions, ART requires very high levels of adherence for an indefinite period to achieve the desired results.<sup>17</sup> Near-perfect adherence levels of > 95% are required to optimise the outcomes of highly active antiretroviral therapy (HAART), such as minimised drug resistance, slowed disease progression, decreased hospitalisation and delayed death.<sup>18-21</sup>

At the beginning of the national ART programme implementation in South Africa, patients were screened to establish their ability to adhere to therapy prior to enrolment. Later, pressures to scale up the ART programme made this screening less stringent. The need for ART remains high in South Africa, a middle-income country with the second highest number of people living with HIV/AIDS (PLWHA) in the world (5.7 million by the middle of 2008).<sup>22</sup> By 2006,

764 000 PLWHA needed ART, of which less than half (353 945) were enrolled in the government ART programme and even fewer (273 400) received ARV.<sup>23</sup> As in many other sub-Saharan African countries, the South African ART programmes have improved. Of the 889 000 people in need of ART in 2007, 488 739 (55%) were enrolled and 371 731 (42%) were started on treatment.<sup>22</sup> The successes of the scale-up of ART programmes in South Africa make it imperative that the health system now invests in patient retention in treatment and care programmes.

The prevailing adherence levels in sub-Saharan Africa are far below the recommended 95%, with pooled estimates of 77%.<sup>24</sup> Adherence to ART entails more than simply remembering to take medication. There is an underlying amalgam of social, cultural, economic and personal factors.<sup>25</sup> In the South African context, the capacity of the weak public health system is an additional factor that adversely affects adherence.<sup>26</sup> Although reported barriers to adherence are consistent across multiple settings and countries, studies have also shown that adherence levels and the profile of factors that influence it differ by settings.<sup>27-29</sup> This study therefore proposes to assess the level of and validate (using viral load [VL] results) self-reported adherence among patients attending the HIV clinic of the Rustenburg Provincial Hospital (RPH), South Africa. It also describes the determining factors associated with poor adherence, including an assessment of workload at the clinic.

## Methods

### Setting

RPH serves a predominantly black population. Rustenburg is one of the fastest-growing cities in South Africa, home to large platinum mines with high unemployment rates. RPH serves as a referral hospital for three district hospitals, three community health centres and seven primary health clinics. Its wellness clinic provides ART services free of charge. When there are no complications, patients attend the clinic on a monthly basis for ARV refill and every six months for laboratory test monitoring.

### Study population and sample

RPH had 6 500 registered patients on its ART programme by the middle of 2008. To be included in the study, a patient had to be adult (18 years and above), be ARV naïve, be self-administering medication at home and have started treatment between 1 June 2006 and 31 December 2007. The patient had to have been on treatment for a period of between 12 and 18 months. The clinic register served

as the sampling frame. A sample size of 100 patients was established. A target of 10 randomly selected patients was set per day. Each morning, all the patients in the appointment diary who complied with the inclusion criteria were allocated a number. Coupons bearing these numbers were put in a hat and randomly drawn to make the selection of the 10 to participate in the study. These patients were approached for consent as they arrived at the clinic. Those who refused were replaced by another draw. Ethical approval was obtained from the Faculty of Health Sciences, University of Pretoria.

### Data sources, collection and management

The study used three sources of data: i) interview records of self-reported adherence levels, ii) the clients' clinical/hospital files for the VL test results and iii) the monthly/yearly statistics report of the clinic. Data were collected over three weeks during normal clinic hours. Prior to the interview, informed consent was sought. The patients were provided with an information sheet before consultation and afforded the opportunity to ask questions. It was made clear to them that refusal to participate would not jeopardise their access to services at the hospital. The interviews lasted about 20 minutes. After normal consultation, patients who consented to participate were taken to a designated private room within the clinic where the interviews were conducted. The patient brought along his or her hospital file. The principal researcher interviewed participants in English, using the self-report adherence questionnaire. When needed, a trained assistant fluent in the local language (Setswana) acted as an interpreter. The questionnaire was an abridged version of that developed by the Adult AIDS Clinical Trials Group.<sup>30</sup> Seven days was the time frame used to establish whether or not a patient had missed a dose as recall over a short time frame is more valid than over a longer time frame.<sup>31</sup>

The questionnaire had closed-ended questions grouped in three sections: the first for general demographics, the second for self-reported adherence (including the patient's latest VL) and the third for factors influencing adherence. The percentage adherence was calculated as the number of times the patient recalled to have taken medication (morning and evening doses) in the preceding week divided by the total number of doses prescribed for the week, multiplied by 100.

The VL test results were recorded from the patient's file immediately after the interview. The most recent VL results as recorded in the patient's file at the day of interview were recorded on the questionnaire. Clinicians are required to

staple laboratory test results on the patient files as well as transcribe the results in the clinical notes. The frequency and timing of VL measurement are determined by national guidelines<sup>32</sup> as well as the discretion of the clinician. Patients on ART undergo an initial baseline VL assessment followed by another VL test within 4–6 months of initiating treatment to ascertain good virologic response. Thereafter, VL testing is done six-monthly to ensure that virologic success is maintained. All VL testing is conducted by the hospital laboratory, which is part of the National Health Laboratory Service of South Africa.

### Operational definitions and outcome measures

- **Adherence:** With respect to HIV/AIDS care specifically, medication adherence has been defined as the ability of the PLWHA to be involved in choosing, starting, managing and maintaining a given therapeutic combination medication regimen to control viral (HIV) replication and improve immune function.<sup>20</sup>
- **Optimal adherence:** This is the level of adherence needed to maximally suppress viral replication in patients receiving HAART, estimated to be at least 95%.<sup>15</sup>
- **Virologic failure:** This is defined in the South African national guidelines as failure to achieve a VL < 400 copies/mL within 4–6 months of starting therapy.<sup>31</sup>
- **Capacity assessment:** The study used as norm the South African guidelines recommendation of an average of 12.5 staff to care for 500 patients on ART.<sup>31</sup>

### Data analysis and statistics

To validate the self-reported adherence levels elicited from the interviews, self-reports were compared to VL test result interpretation (virologic failure). Data were captured on Microsoft Excel and imported on STATA 8.0 for analysis. Frequency, percentage, cross-tables and histograms were used to summarise the data. The ARV adherence levels were expressed as a percentage. The Fischer exact test was used to compare the levels of agreement between the means of self-reported adherence level and virologic failure. The *p* value (< 0.05) from the Fischer and Chi-squared tests was used to assess whether differences were significant.

## Results

A response rate of 95.3% was achieved. Consent was sought from 105 patients at the wellness clinic during the study period; five patients declined to participate in the study. There were more female (73) than male respondents (27). There was no difference in the proportion of men and women with virologic failure (see Table I).

Table I: Gender distribution and virologic failure among study participants

	n	Virologic failure n (%)		p value
		Yes	No	
Men	27	13 (48.1)	14 (51.8)	0.78
Women	73	34 (46.6)	39 (53.4)	0.41

The majority (65%) of respondents were unemployed. Virologic failure was recorded in significantly higher proportions among unemployed patients (50.7%) compared to employed patients (40%) (*p* < 0.05) (see Table II). Slightly more than a third of patients (34%) reported psychological factors (feeling sad, unhappy or stressed) among the reasons affecting adherence. These factors correlated well with virologic failure. All patients (100%) feeling unhappy or sad and 85.7% of patients feeling stressed had virologic failure (*p* < 0.01).

Table II: Determinants of adherence and virologic failure among study participants

Determinants of adherence	n	Virologic failure n (%)		p value
		Yes	No	
Unemployed	65	33 (50.7)	32 (49.3)	0.86
Employed	35	14 (40.0)	21 (60.0)	0.09
Feeling unhappy or sad	13	13 (100.0)	0 (0.0)	0.001
Feeling stressed	21	18 (85.7)	3 (14.3)	0.001
Never forgot	37	0 (0.0)	37 (100.0)	0.001
Away from home	21	15 (71.4)	6 (28.6)	0.006
Busy with other things	17	15 (88.2)	2 (11.8)	0.001
Asleep when medication was due	22	18 (81.8)	4 (18.2)	0.001
Avoiding side effects	8	8 (100.0)	0 (0.0)	0.001

Being away from home and being busy were the most commonly reported contextual factors affecting adherence. Virologic failure among patients who reported these factors was high. Seventy-one per cent of patients who were away and 88% of those who were busy with other things had virologic failure. Regimen factors were also important. Virologic failure among patients who reported being “asleep when medication was due” and “avoiding side effects” was 81% and 100% respectively.

Virologic failure was present in slightly less than half of the respondents (47%). Virologic failure was higher among patients who reported low adherence levels (see Table III). There was alignment between self-reported adherence levels and virologic failure. Three-quarters (77.7%) of patients who reported < 90% adherence had virologic failure. Failure was much less (only 33.8%) among patients who reported > 95% adherence (*p* < 0.01).

The clinic has experienced considerable growth in the number of HIV-positive patients registered, from 1 373 patients in 2004 to 9 182 by 2007. By the end of 2004,

Table III: Self-reported adherence and virologic failure among study participants

		Adherence levels			Fisher's exact
		> 95%	90–95%	< 90%	
Self-reported adherence level (n = 100)		71/100 (71%)	11/100 (11%)	18/100 (18%)	< 0.01
Virologic failure within adherence level categories	Yes	24/71 (33.8%)	9/11 (81.8%)	14/18 (77.7%)	< 0.01
	No	(47/71) 66.2%	(2/11) 18.2%	(4/18) 22.3%	

571 HIV-positive patients were receiving ARV. This number increased to 5 800 patients receiving ARV in 2007 (see Figure 1).

Figure 1: Trends in patient enrolment at RPH's wellness clinic

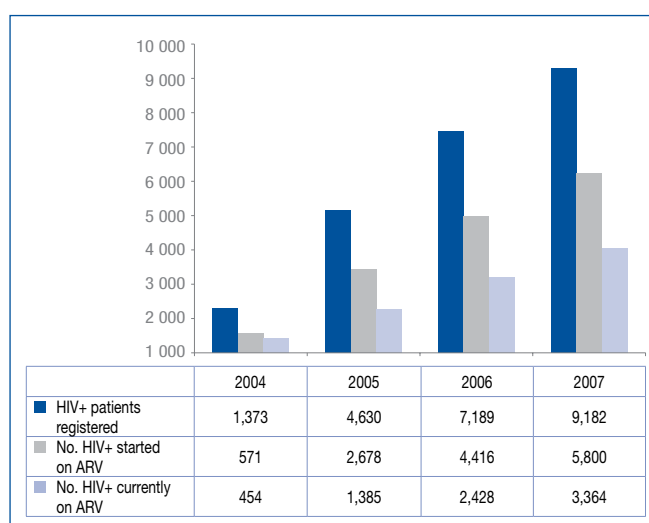
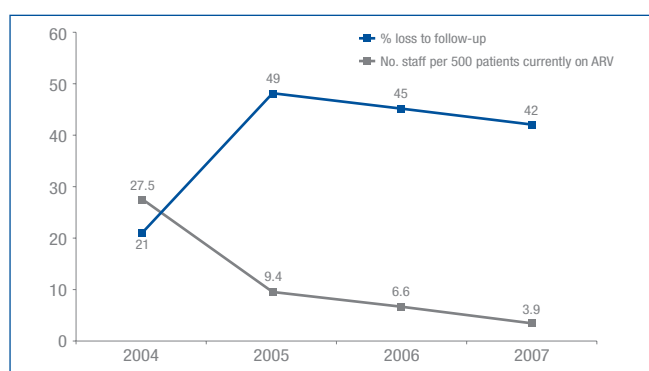


Figure 2: Trends in loss to follow-up and staffing norms at RPH's wellness clinic



The number of patients on ARV who were recorded as lost to follow-up (including known deaths, dropouts and transfers) was 117 in 2004, increasing steadily to 1 293, 1 988 and 2 436 in 2005, 2006 and 2007 respectively. In relative terms, the loss to follow-up had doubled in three years, from 21% in 2004 (117/571), reaching 42% in 2007 (2 436/5 800).

The increase in the number of staff, however, has not been proportional. Except for the year 2006 when the wellness clinic had 32 staff, the staffing level was kept relatively unchanged at 25 in 2004 and 26 in 2005 and 2007. When related to the number of patients currently receiving ARV at the wellness clinic, only in 2004 was the actual staff-to-patient ratio in compliance with the recommended norm of 12.5:500 of the national ART programme. There had been a steady decline in staff-to-patient ratio between 2004 and 2007 (see Figure 2).

## Discussion

This study reveals that 82% of respondents reported to have achieved at least 90% adherence to their ARV regimen in the week preceding the survey. This is, however, not optimal as a greater than 95% adherence level is required to sustain viral suppression and avoid resistance. Although 71% of respondents in this study reported > 95% adherence levels, this is lower than findings from similar local and African settings.<sup>32-34</sup> Not surprisingly, the proportion of patients with virologic failure was significantly higher among those with adherence levels less than 95%.

Overall, virologic failure was present in almost half (47%) the respondents, a much higher proportion than the average rate in South Africa, which ranges between 10% and 16%.<sup>26</sup> The poor results suggested by this study may be partly explained by the fact that the clinic has exceeded its optimal capacity for quality service delivery. Evidence suggests that good counselling at an HIV clinic is important in improving adherence.<sup>35</sup> This, however, requires more time for provider-client interaction,<sup>36</sup> which is not always possible in clinics with a high workload and staff shortage.

Staff shortage is a common problem faced by ART programmes that scale up rapidly, such as seen in Malawi, Uganda and Botswana where increase in staffing lagged behind the rates of enrolment of patients in the ART programmes.<sup>21,37</sup> Decentralisation of services and task shifting as practised in Lusikisiki and the Free State should be considered and rolled out nationally to alleviate the problems of capacity at major ART clinics.<sup>38-40</sup> There is now considerable evidence across Africa of the feasibility of integrated district-based approaches that achieve universal access while maintaining quality and outcomes.<sup>26,37,41,42</sup> Providing ART at the primary health care clinic level increases the number of entry points to care, while the greater proximity of services encourages retention in care.<sup>38</sup> However, a rapid transfer of large numbers of patients can overwhelm minimally staffed clinics if appropriate steps are not taken. In addition to the additional workload,

clinic staff may not feel confident enough to carry out their new responsibility, particularly if training and supervision mechanisms are not adequately provided.

In assessing the determinant of adherence, the limitations of this study are inherent to the use of a self-report questionnaire, namely social desirability bias and recall bias. To minimise the effect of these limitations, patients were assured of and provided with confidentiality of their answers on adherence. A seven-day recall time, an accepted time frame to minimise recall bias in research on ARV adherence, was used.

There is some evidence in South Africa that low socioeconomic status (an index composed of education, welfare, unemployment and overcrowding status with annual income) is not a barrier to successful ARV therapy.<sup>43</sup> Our study, however, suggests that unemployment was an important factor in adherence among study participants. The prevalence of virologic failure among unemployed patients was higher than among their employed counterparts.

The most common general factors were changes in daily routines, being away from home and being occupied at the time of having to take the ARV dose. The avoidance of side effects was a common regimen factor affecting adherence in our study, similar to findings elsewhere.<sup>25</sup> This reinforces the call for using combination ARVs and ARVs with fewer dosing frequencies and side effects.

The findings of our study suggest that a poor psychological state was associated with poor adherence. Other studies have also shown significant association between poor psychological states and non-adherence.<sup>25,44,45</sup> Randomised controlled trials in Europe and the United States have confirmed that dedicating time to individualised counselling and education increases patients' sense of self-worth and efficacy.<sup>46-48</sup> Although this may not be feasible in Africa given the current capacity challenges, patients should nevertheless be systematically screened for depressive diseases and treated accordingly.

In conclusion, the performance of the wellness clinic, in relation to adherence to ARV, was relatively poor. Unemployment, a complex non-health sector problem, was an important factor but cannot be resolved at clinic level. Drug-related factors can be remedied by the selection and procurement of ARVs with a better frequency-of-administration and side-effect profile. The alleviation of staff shortage will improve the quality of counselling and doctor-patient interaction. If the recruitment of additional staff is not possible, the capacity of large ART clinics, such as our study site, should be protected by decentralisation of ART services to smaller centres (primary health care centres and clinics).

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