UNIVERSITY OF TROMSØ, NORWAY

ADHERENCE TO ANTIRETROVIRAL (ARV) THERAPY IN MAUN, BOTSWANA

A STUDY OF 62 PATIENTS

THESIS FOR THE PROJECT:

"ADHERENCE TO ARV IN IN-PATIENTS IS ASSUMED TO BE EXCELLENT. CAN WE SAY THE SAME FOR OUT-PATIENTS?

IF NOT, WHAT ARE THE REASONS?"

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The collection of data was done in Maun, Botswana in April and May 2003

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AS PART OF STADIUM IV, 5TH YEAR OF MEDICAL STUDIES, UNIVERSITY OF TROMSØ

CONTENT

ACKNOWLEDGEMENTS

There are a lot of people who have helped med with this elective paper. First of all I want to thank Dr. Beltz and Dr. Mudiayi at Maun General Hospital for generous help in developing the questionnaire I have used and for counselling when I met problems in my work. I also want to thank the staff at the Resource Centre, especially Tebogo Beauty Modibati and Gopelomang Karome for all the practical help they have given me with the patients and with translation. And thanks to Gaeungwe Molefi for help with translation when the secretaries were busy and couldn't help me. And last, but not least, my supervisor in Tromsø, associate professor Bjørn Straume for great help with designing the project and writing the final paper.

RESUME

Background: 1/5 of the Botswana population has HIV and up till now little treatment has been available to the general public. MASA, the new ARV treatment programme in Botswana has now been run for about 1 year and is providing free HIV-treatment for everyone. An evaluation of adherence to ARV in Maun, Botswana was therefore a suitable project for writing an elective paper as part of my medical studies in Tromsø, Norway.

Method: All 62 patients filled in a questionnaire with 49 questions designed to assess different aspects of the ARV-programme in Maun including adherence assessed by pill-count and self-report. Most patients were consecutively picked out as they came to the Resource Centre in Maun (n=51) and the rest were called in (n=11).

Results: At 6 months, 93,8% of the patients with Viral Load (N=16) had non-detectable Viral Loads. By looking at pill-count, 6 patients (9,7%) had < 95% adherence and from self-report 12 patients (19,4%) admitted that they had missed one or more doses of medication. The main reason for this was forgetfulness (58,3%). More than 1/3 of all patients couldn't give a correct answer to 3 key issues from their counselling; significantly more males than females didn't know 2 side effects to their treatment.

The pharmacy had the greatest influence on 1/3 of the patient's adherence. Many patients had side effects and 35,4% of them indicated that GI-related side effects affected their adherence the most.

Conclusion: More males than females have < 95% adherence (p=0,04) and didn't know two side effects to their treatment (p=0,02). Based on this there has to be a better follow-up of the males on ARV therapy. Too few patients follow the guidelines for blood-test (CD4+ - cell count and Viral Load) and this need to be improved.

INTRODUCTION

Why do a project in Botswana?

As part of my medical studies in Norway I spent 1 month in Selebi-Phikwe, Botswana in April 2000. This sparked a genuine interest for Botswana in me and I was encouraged to come back and write my 5th year elective paper on a topic from Botswana. I used my contacts in Botswana and Dr. Beltz at Maun General Hospital helped me choose a topic and set up the project.

The HIV/AIDS-situation in Botswana and Sub-Saharan Africa

A sentinel report from 2001 on HIV prevalence in Botswana indicated a prevalence of around 30%. **[1]** Recent data from UNAIDS estimates that the national adult HIV prevalence in four southern African countries has risen higher than thought possible, exceeding 30%: Botswana (38.8%), Lesotho (31%), Swaziland (33.4%) and Zimbabwe (33.7%). Botswana's population is small (1.7 million people) and a disease like AIDS hits hard. Sub-Saharan Africa is now home to 29.4 million people living with HIV/AIDS. Approximately 3.5 million new infections occurred there in 2002, while the epidemic claimed the lives of an estimated 2.4 million Africans in the past year. There are almost 3 million children under 15 and 10 million young people (aged 15–24) are living with HIV. **[2]**

Fact box 1: **The *HIV/AIDS epidemic in Botswana* [3]**

- First AIDS-case in 1985.
- Prevalence among 15-49 year old pregnant women increased from 13,8% in 1992 to 35,4% in 2002.
- More than 1/3 of all Batswana's aged 15-49 are HIV-positive.
- In particular age-groups in some areas the prevalence is > 50%.
- More women than men are affected.
- There were 24,000 AIDS deaths in 2001; at the end of 2001 there were 69,000 AIDS orphans and 330,000 people living with HIV/AIDS. **[2]**
- Currently, life expectancy is 33.9 years, without AIDS it would be 72.4 years.
- One baby is infected with HIV approximately every hour in Botswana.

MASA [4]

MASA is the name Botswana's government has chosen for its ARV (Anti Retro Viral) Therapy Programme. "MASA" is a Setswana word meaning "new dawn" and symbolizes the renewed hope for Batswana's 330 000 HIV positive. With ARV therapy they can live longer, healthier lives and have time to nurture their families and build a future for Botswana as a nation. Through MASA, the Government of Botswana has taken a bold step to provide ARV therapy free of charge to all Batswana who need it. Behind the MASA ARV Therapy Programme is ACHAP. (See fact box 2)

It is estimated that over time 110 000 HIV-positive Batswana will require ARV therapy and the cost of implementing the program in the first year is approximately US$30 million. Government health officials have estimated that ARV costs P6 000 (about NOK 8 500) per patient per year. **[5]**

Through "MASA" Botswana has become the first African country to adopt a policy to ultimately make ARV therapy available to all citizens who need them. In addition, a handful of companies have announced schemes to provide ARV therapy to workers and some family members.

Public sites for HIV-testing, Tebelopole, are widely available throughout the country. After a patient has tested positive, he is referred to the nearest treatment-site. At present there are 4 such sites: Gaborone, Francistown, Serowe and Maun. In 2004 the ARV programme will expand to 4 new sites.

By February 2003 a total of 5201 people were enrolled in the programme and 3413 started on ARV (personal notification from Dr. Beltz, Maun). In Africa as a whole it's estimated that in 2001 between 150 000 and 200 000 of the about 40 million HIV-infected Africans were receiving antiviral treatment. **[6]**

Fact box 2: ACHAP (The African Comprehensive HIV/AIDS Partnerships) **[4]**

ACHAP was established in July 2000 and is a collaboration between the Government of Botswana (GOB), the Bill & Melinda Gates Foundation, and The Merck Company Foundation/Merck & Co., Inc.

The Bill & Melinda Gates Foundation and The Merck Company Foundation have each dedicated US$50 million over a 5 year period towards the project. Merck & Co. is also donating two anti-retroviral medicines for appropriate treatment programmes developed by the GOB for the duration of the initiative.

The treatment regimens in Botswana [7]

By national consensus, the criterion for starting ARV-treatment is:

A CD4+ - cell count of < 200 cells/mL and/or AIDS defined illness. Children are started at higher CD4+ - cell counts.

A patient with a positive HIV-test is referred from local clinics or public HIV-testing sites to one of the 4 treatment sites. At a treatment site an initial assessment of the patient will be done which includes talking to the social workers, blood test (CD4+ - cell count), seeing a nurse and have their medical history taken. Patients who fulfil the criteria for treatment are started up, the rest are observed until they fall in under the criteria referred above. As part of starting up a patient on ARV therapy, the patient will undergo both individual and group counselling by social worker, doctor, nurse and pharmacy (in this document, pharmacy is equivalent to any person working in the pharmacy, not just the pharmacists, but also the technicians) before treatment is started. This is to ensure that the patients have sufficient knowledge about their illness, the treatment they are about to start, the goals for the therapy, the most common side effects and the most important of all - the importance of 100% adherence!

Openness about HIV/AIDS is important for adherence and every patient has to choose one close person as his/her adherence partner. This partner will come with the patient to the Resource Centre every month and is responsible for encouraging and helping the patient taking all the medication. Once treatment is started the patient will be counselled at every contact with the health personnel. The pharmacy will have the most frequent contact since patients come every month for refill of pills. At these refills, the pharmacy will assess adherence by pill count and counsel according to this.

There are currently 15 antiretroviral drugs registered for use in Botswana. Patients are started on a first line regimen, 3 different drugs, and stay on this regimen unless there are signs of treatment failure (see fact box 3). Then the patient will move on to a second line regimen or a third line regimen if the second line regimen fails too.

Explanation of abbreviations: NRTI= Nucleoside Reverse Transcriptase Inhibitor. NNRTI= Non Nucleoside Reverse Transcriptase Inhibitor. PI= Protease Inhibitor.

First line regimen: 2 NRTI's plus 1 NNRTI

Adults:

- Zidovudine (ZDV) plus Lamivudine (3TC) plus Efavirenz (EFV) (for adult males and women in whom there is no reasonable risk of pregnancy)
- Zidovudine (ZDV) plus Lamivudine (3TC) plus Nevirapine (NVP) (for pregnant women in whom pregnancy is likely to occur)

Fact box 3: Criteria for treatment failure in Botswana [7]

- Viral Load rebound by 0,5 log.
- Viral Load becomes detectable again after being non-detectable.
- CD4+ - cell count.

Children:

- Under 5 yrs: Zidovudine (ZDV) plus Lamivudine (3TC) plus Nevirapine (NVP)
- Above 5 yrs: Zidovudine (ZDV) plus Lamivudine (3TC) plus Efavirenz (EFV)

Second line regimen: 2 NRTI's plus 1 PI: Both adult patients and children: Patients who fail the first line treatment will be referred for specialist advice. If there is no contraindication to using any of the drugs, Didanosine (ddI) plus Stavudine (d4T) plus Nelfinavir (NFV) is recommended.

Third line regimen: Both adult patients and children: Patients who fail the second line treatment will be referred for specialist advice and considered for the following third line regimen: Ritonavir (RTV) plus Saquinavir soft gel (SQV).

Recommended schedule for monitoring adult patients and children:

1. **Plasma HIV RNA (viral load):** At start of therapy, at 3 months to assess initial efficacy and every 6 months thereafter.
2. **CD4+ - cell counts:** Every 3-4 months.

3. **Blood chemistry and haematology:** At the start of therapy, at 2 weeks to assess toxicity from Nevirapine (NVP) and every 3 months thereafter.

4. **Clinical monitoring:** 1 week (doctor), 2 weeks for chemistry (doctor or other health worker), 1 months (doctor), 3 months (doctor) and every 3 months thereafter.

Adherence

Despite the importance of medication adherence - in HIV as well as other diseases - no universal definition of adherence have been developed. Instead of developing my own definition I will compare my understanding of adherence to the more well-known expression "compliance".

The classic definition of compliance is: "the extent to which a persons behaviour (in terms of taking medication, following diets or executing lifestyle changes) coincides with medical or health advice." [8] In compliance, the doctor tells the patient what to do, the patient has a passive role and if treatment fails it is the patient's fault. Adherence implies a more active and collaborative involvement of the patient working together with the clinician and the rest of the health team to plan and implement the treatment. There is a greater emphasis on the patient's role in deciding to carry out a particular treatment. Treatment failure is therefore not just the patient's fault; reasons can be numerous. Because of the complexity of HIV-treatment success, adherence has proved to be a more appropriate term to use than compliance.

Adherence-research in Botswana

Little research has been done on adherence to HAART (Highly Active Anti Retroviral Therapy) in an African context including Botswana. A search in Medline with the words Botswana, adherence and HIV only came up with one published article. I've only seen 1 study on adherence to HAART in Botswana presented internationally (Weiser et al. presented an abstract at the 14th International AIDS Conference in Barcelona 2002). In addition an unpublished study has been conducted at Maun General Hospital by Nwokike et al. Because there are few studies done on adherence to HAART in Botswana, my material is in many ways unique.

The study by Weiser et al. showed that only 53% of the patients were adherent by self-report [9]. Nwokike et al. showed that by using self-report and pill counts to assess adherence, the 176 patients reviewed had an average adherence per month of 83,16% and this is less than what's needed for sufficient viral suppression and the golden standard of 100% adherence to HAART (personal notification by JI Nwokike).

There are several projects in progress now and a search at http://www..hsph.harvard.edu came up with 16 research projects on AIDS in Botswana right now. The largest is the Tshepo study that will monitor the development of resistance to antiretroviral medications among HIV/AIDS patients in Botswana. In addition it seeks to determine how to improve patient adherence to complex drug regimens over the short and long term, comparing modified directly observed therapy (DOT) to Botswana's national standard of care. [10]

METHOD

This research is done on patients undergoing ARV therapy at Maun General Hospital's Resource Centre. A total of 62 patients were included. Some were consecutively selected as they came to the Resource Centre (N=51) and in addition some patients with review-dates in May-July 2003 were called in to enlarge the study population a bit (N=11). Inclusion criterion: Patients on ARV therapy longer than 1 month and still alive and on treatment.

The patients were divided into 2 groups:

1. Review by doctor (This group included both walk-in's who came because of problems and patients coming for scheduled appointments)

2. Refill (monthly refills)/Called in

These two groups were created because a lot of walk-in's came to the Resource Centre every day and I assumed that because of this that the review-group could be different from the other group in terms of adherence. This has not proven to be correct. In order to not make my paper too extensive, I haven't looked into greater details about these two groups in my paper since they were created by me and are not groups in everyday use in Maun.

Every patient filled out a questionnaire in English with 49 questions. Many patients needed the questions translated to Setswana and the secretaries or the driver at the Resource Centre provided translation. The following data was gathered and registered:

1. *Patient information:* Age, gender, marital status, number of children, education level, length of treatment and change of medication/dosage.

2. *Information from a patient's file:* CD4+ - cell count and Viral Load every 3 months, adherence from pharmacy record by pill-count done every month (>/< 95% adherence last 3 months or as long as they had been treated) and information about opportunistic infections. Pill-count is the most widely used objective measure of adherence. [11] Assessment of adherence from pill-count also overestimates adherence, but is regarded a better method than self-report. [12]

3. *Pre-adherence counselling:* Questions about the patients living situation, work, income and accessibility to Resource Centre. In addition they answered questions about adherence partner, if sharing HIV-status with closest family is important and why/why not, the pre-treatment counselling, 3 questions to test how much the patients remembered from their counselling and a question on who influenced them the most on the importance of adherence.

4. *Adherence:* This section included questions about pill-burden, if they had ever missed a dose of medication, if yes, why, side effects, side effects influencing their adherence the most, use of traditional medicine and how life was now after they had started ARV therapy. Self-report about non-adherence is a well established method of assessing adherence. It's cheap and easy though it's known to overestimate adherence. **[13]**

5. *Services offered by the Resource Centre*: Questions on how they were treated and what could be done to make improvements.

Evaluating all the data is beyond the scope of this paper, but the results/data not included in this paper will be provided separately as a service to the staff at the Resource Centre and be available to students from Tromsø doing a follow-up of this study.

The statistical calculations were done using Microsoft Excel. The Chi-square calculations were controlled with Epi Info.

RESULTS

A total of 62 patients, 16 males and 46 females were included in the study. Average age was 34,5 years (spread 9-55 years). 60% of the patients had been treated < 6 months. The majority of patients (83,9%) had been treated < 9 months. Over 1/6 (11 patients) had their medication/dosage changed, 8 because of a toxic reaction. As measurements of adherence I used pill-count and self-report. Six patients had < 95% adherence from pill-count and 12 patients admitted their non-adherence through self-report.

CD4+ - cell count and Viral Load

International research states that > 95% adherence is necessary to achieve therapeutic success (non-detectable virus load in plasma) in > 80% of treated patients. [14] For the lab in Botswana non-detectable levels are < 400 HIV RNA copies/mL. Effective treatment will give a 2,5 - 3 log fall in Viral Load after 8 weeks and 3,5 - 4 log fall after 12-16 weeks. [15] This normally gives a Viral Load of < 400 HIV RNA copies/mL after 8-12 weeks and < 50 HIV RNA copies after 24 weeks.

42 patients had been treated longer than 3 months. At 3 months 35 patients (83,3%) had a CD4+ - cell count registered and 29 patients (69,0%) had a Viral Load registered. At 6 months 4 of the patients that didn't have a CD4+ - cell count at 3 months had a CD4+ - cell count registered instead. Of the 13 patients with no Viral Load at 3 month, 7 had their first Viral Load registered at 6 months instead. A total of 4 patients treated 3 months or more didn't have ANY recording of Viral Load. In table 1 you

Table 1: Percentage of patients with treatment success at 3, 6 and 9 months of treatment
Treatment success is defined as < 400 HIV RNA copies/mL and can be seen as early as 3 months and needs to be present at 6 months in order to be classified as treatment success.

	At 3 months	*At 6 months*	*At 9 months*
Treated 3-6 months (N=17) [1]	83,3%	100,0%	-
Treated 6-9 months (N=15) [2]	63,7%	100,0%	100%
Treated more than 9 months (N=10) [3]	83,3%	85,7%	83,3%
Total for all patients treated > 3 months (N=42) [4]	73,3%	94,1%	85,7%

1: Viral Load recorded at 3 months: 12, at 6 months: 4
2: Viral Load recorded at 3 months: 11, at 6 months: 6, at 9 months: 1
3: Viral Load recorded at 3 months: 6, at 6 months: 7, at 9 months: 6
4: Viral Load recorded at 3 months: 29, at 6 months: 17, at 9 months: 7

can see how many patients that had a Viral Load < 400 HIV RNA copies/mL registered at 3, 6 and 9 months. At 3 and 6 months respectively 73,3% and 94,1% had non-detectable levels of virus.

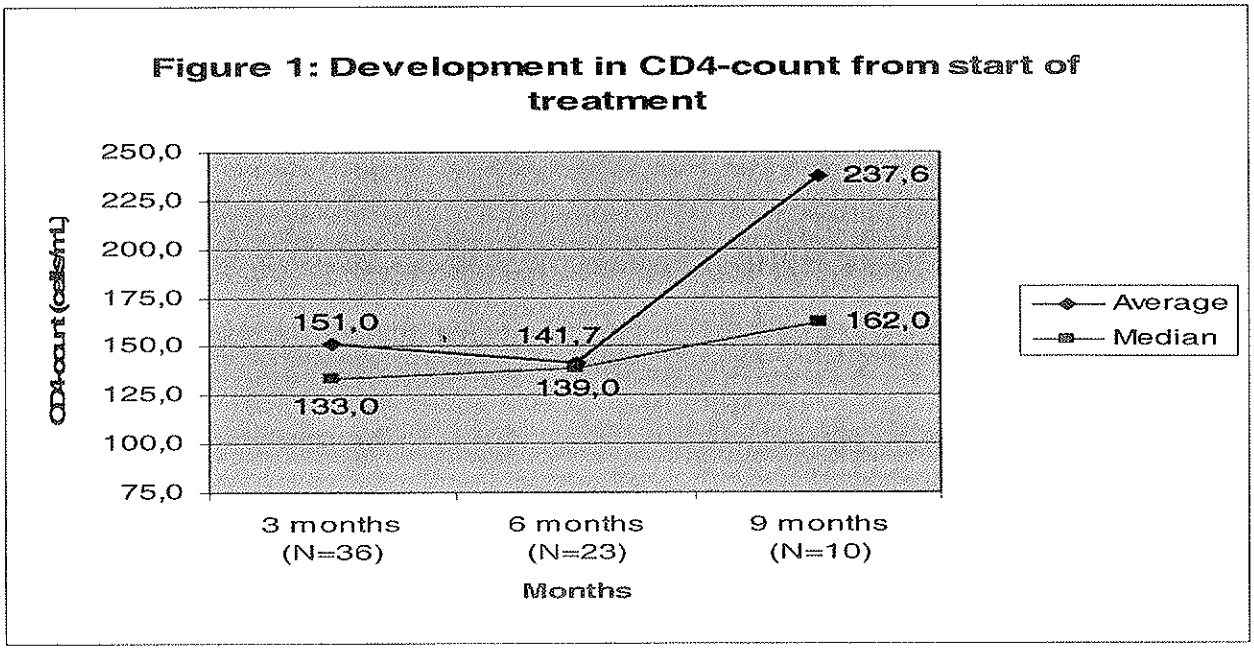
Eight patients had a follow-up Viral Load registered 3 or 6 months after their first Viral Load with non-detectable levels and 7 patients (87,5%) still had non-detectable levels of virus.

In the group with > 95% adherence (N=56), 26 patients had a Viral Load registered at 3 months and 21 of them (80,8%) had a Viral Load < 400 HIV RNA copies/mL already at 3 months. At 6 months 14 of the 15 patients (93,3%) had a Viral Load < 400 HIV RNA copies/mL.

By using Chi-square testing, I tested if there were significantly more males than females without CD4+ -cell count or Viral Load at 3 months. For CD4+ - cell count chi-square = 0,11 (p = 0,75 with 1 degree of freedom). For Viral Load chi-square = 0,19 (p = 0,67 with 1 degree of freedom).

I did a similar test for the group with more or less than 95% adherence to see if more patients with < 95% adherence missed their CD4+ - cell count and Viral Load at 3 months. For CD4+ - cell count chi-square = 0,13 (p = 0,72 with 1 degree of freedom). For Viral Load chi-square = 0,01 (p = 0,93 with 1 degree of freedom).

A steady rise in the quantity of CD4-cells is a good way to assess the effects of treatment and therefore also sufficient adherence. All patients but 1 had a CD4+ - cell count registered at start of



treatment. At start of treatment the CD4+ - cell count for all patients was in average 108 (spread 8-319). Most patients had a steady rise in CD4+ - cell count, but there were some declining figures, especially between 3rd and 6th month. Eight patients had a decline in CD4+ - cell count in this period, but only one of the patients had < 95% adherence last 3 months. The average/median CD4+ - cell count at 3, 6 and 9 months compared to initial levels is seen in figure 1.

Table 2: Adherence partners
(1 patient had more than 1 adherence partner)

	Total
Sister	21
Mother	18
Partner	7
Spouse	6
Other	6
Brother	2
Father	1
Best friend	1
Blank	1

Pre-adherence counselling

All the patients were counselled individually and in groups before treatment started and in the language they understood the best. Every patient has to have an adherence partner (see table 2) and 62,9% had mother or sister as adherence partner. Five patients (8,1%) didn't think it was important to share HIV-status with closest family/friends. They all had > 95% adherence.

Socioeconomic factors can influence a patient's adherence, but international research has never established a general clear connection between non-adherence and socioeconomic factors. **[16]** Questions 15-18 assessed 4 socioeconomic factors (permanent home, work, income and transportation) and the answers to these questions were very diverse: 5 patients had no permanent home (8,1%), 32 patients had no work (51,6%), 14 patients earned less than 500 pula/month (22,6%) and 10 patients needed help with transportation to the Resource Centre (16,1%). These 4 socioeconomic factors are compared to the two groups with non-adherence in table 3.

A few questions were designed to assess the effects of the pre-treatment counselling. Questions 25-

Table 3: Non-adherence according to socioeconomic factors
All 62 patients answered these 4 questions apart from question 17 about income were 16 patients left the question blank.
Number of patients with no home: 5, number of patients with no work: 32, number of patients with income < 500 pula/month: 14 and number of patients that need help with transport to Resource Centre: 10

	No home	*No work*	*Income < 500 pula/month*	*Need help with transport to Resource Centre*
< 95% adherence from pill-count (N=6)	2	2	1	0
Patients admitting to missed a dose of medication (N=12)	3	8	2	1

27 tested the patients on 3 key issues in their treatment (See table 4). A chi-square test was used on each question to see if there were significant gender differences: Question 25: Chi-square = 0,23 (p = 0,63 with 1 degree of freedom). Question 26: Chi-square = 4,14 (p = 0,04 with 1 degree of freedom) Question 27: Chi-square = 0,75 (p = 0,39 with 1 degree of freedom)

Question 28 assessed which profession had the greatest influence on a patient's adherence (see table 5). In total, the pharmacy had the greatest influence on a patient's adherence followed by the doctor and the social workers. When comparing the sexes, the pharmacy had the most influence on the females and the doctor had the most influence on males. Interestingly, the social workers influenced almost 2 times more females than males; 10% of the males were influenced by the nurses compared to 2% of the females.

Table 4: "Wrong" answers to question 25-27

Question 25: Can you tell me two of the goals we want to achieve for you through the ARV therapy?
Question 26: Can you give me two side effects of the drugs that you are using?
Question 27: Why should you take your pills at the same time every day for the rest of your life?

	Question 25 (%)	*Question 26 (%)*	*Question 27 (%)*
Males	7 (43,8%)	12 (75,0%)	6 (37,5%)
Females	17 (37,0%)	21 (45,7%)	23 (50%)
Total for all patients	**24 (38,7%)**	**33 (53,2%)**	**29 (46,8%)**
Patients with < 95% adherence (N=6)	4 (66,7%)	6 (100,0%)	4 (66,7%)
Patients admitting to have missed a dose of medication (N=12)	5 (41,7%)	6 (50,0%)	6 (50,0%)

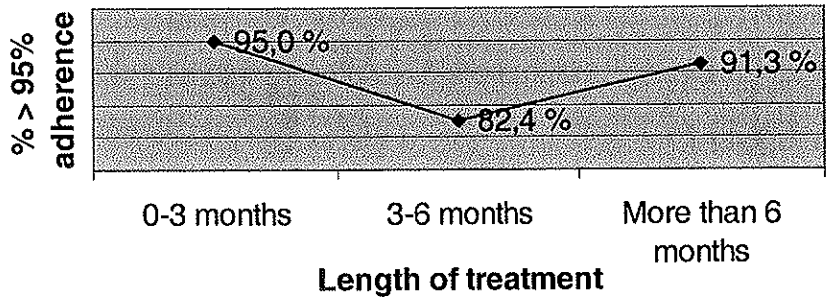
Table 5: Professions influencing a patients adherence

Every patient could tick more than 1 profession. All 62 patients answered and gave a total of 81 answers.

	The doctor	*The nurse*	*My adherence partner*	*The social workers*	*The Pharmacy*	*Blank*
Males	9 (31,0%)	3 (10,3%)	4 (13,8%)	4 (13,8%)	9 (31,0%)	-
Females	13 (25,0%)	1 (1,9%)	6 (11,5%)	13 (25,0%)	18 (34,6%)	1 (1,9%)
Total for all patients (N=81)	**22 (27,2%)**	**4 (4,9%)**	**10 (12,3%)**	**17 (21,0%)**	**27 (33,3%)**	**1 (1,2%)**
< 95% adherence from pill-count (N=6)	3 (42,9%)	-	2 (28,6%)	-	2 (28,6%)	-
Patients admitting to have missed a dose of medication (N=12)	4 (25%)	1 (6,3%)	2 (12,5%)	3 (18,8%)	5 (31,3%)	1 (6,3%)

Figure 2: > 95% adherence in 3 groups based on length of treatment:

All the patients are grouped according to how long they have been treated. This figure shows how many patients in each group that has > 95% adherence.



Adherence

An aim for the ARV programme in Botswana has been to design a simple treatment programme with a first line regimen with a small pill-burden (males take 5 pills/day and females take 4 pills/day) and as few serious side effects as possible. In average every patient in this study took 5 pills (spread 4-13). The pill-burden for 1 month will then be 150 pills for males and 120 pills for females. The patients got to categorize their pill-burden as good, fair or too much. 83,9% regarded their pill-burden as good.

A patient's adherence can be assessed in several ways. An easy and objective way is to look at pill-count. Every patient's pharmacy's record (pill-count the last 3 months or last month if the patient had been treated shorter) was reviewed. Six patients (9,7%), 4 males and 2 females, had < 95% adherence. A Chi-square test to see if significantly more males than females had < 95% adherence gave a chi-square

Table 6: Choice of adherence partner according to gender, patients with < 95% adherence from pill-count and patients admitting to forgetting dose of medication in self-report

61 patients answered. The missing patient had no information on adherence partner in the patient file. 1 patient had more than 1 adherence partner.

	Partner	*Spouse*	*Mother*	*Father*	*Sister*	*Brother*	*Best friend*	*Other*
Males	5 (31,3%)	3, (18,8%)	2 (12,5%)	0	2 (12,5%)	1 (6,25%)	1 (6,25%)	2 (12,5%)
Females	2 (4,3%)	3 (6,4%)	16 (34,0%)	1 (2,1%)	19 (40,4%)	1 (2,1%)	0	4 (8,5%)
Total for all patients (N=63)	**7 (11,1%)**	**6 (9,5%)**	**18 (28,6%)**	**1 (1,6%)**	**21 (33,3%)**	**2 (3,2%)**	**1 (1,6%)**	**6 (9,5%)**
< 95% adherence from pill-count	2 (33,3%)	-	1 (16,7%)	-	2 (33,3%)	-	-	1 (16,7%)
Patients admitting to have missed a dose of medication	1 (8,3%)	1 (8,3%)	5 (41,7%)	-	3 (25,0%)	1 (8,3%)	-	1 (8,3%)

= 5,79 (p = 0,02 with 1 degree of freedom). Figure 2 shows the percentage of patients with > 95% adherence depending on how long they have been treated.

Self-report is also a renowned way of assessing a patient's adherence and 12 patients (19,4%), 4 males and 8 females, admitted that they had missed one or more doses of medication. A Chi-square test too see if there were differences between the sexes gave a chi-square = 0,44 (p = 0,51 with 1 degree of freedom). The reasons given for missing doses were: Just forgot (58,3%), travelled and was without my drugs (16,7%) and other reasons like finished late from work and couldn't come for my refill. The 12

Table 7: Side effects affecting the patient's adherence the most
46 patients reported side effects and 34 of them reported that their side effects had influenced their adherence. Every patient could answer more than 1 side effect.

	Males	*Females*	*Total*	*Percentage*
GI-related side effects	1	16	17	35,4%
Skin rash	2	7	9	18,8%
Tiredness	1	8	9	18,8%
Peripheral neuropathy	2	4	6	12,5%
Sleep disturbance – vivid dreams	2	2	4	8,3%
Other side effect	1	2	3	6,3%
Total	9	39	48	100,1%

patients were also asked how often they forgot. Four answered during last 24 hrs, 4 answered once or several times a week and 4 answered once or several times a month.

Table 6 shows adherence partner compared to gender, patients with < 95% adherence from pill-count and patients admitting to forgetting a dose of medication in self-report. Of the patients with partner as adherence partner, 2 patients (28,5%) had < 95% adherence compared to 5,6% and 9,5% of the patients with mother and sister as adherence partner respectively. None of the patients with their spouse as adherence partner had < 95% adherence. Of the patients with mother as adherence partner, 5 patients (27,8%) had missed doses of medication compared to 3 patients (14,3%) with sister as adherence partner.

As many as 46 patients (74,2%) had experienced side effects and 71,3% of them experienced 2 or more side effects. Problems related to the Gastrointestinal (GI) - tract was the most common side effect (25,2%) followed by peripheral neuropathy (18,7%) and tiredness/skin rash (15,9%). Table 7 shows which side effects the patients felt influenced their adherence the most. Of the 46 patients with side

effects, 12 patients didn't feel their side effects influenced their adherence. 60 patients noted a clear improvement in their condition after starting ARV therapy.

Characteristics of the patients with less than perfect adherence (self-reported or by pill-count)

1. The 6 patients (9,7%) with < 95% adherence

The average age is 31,2 years (spread 19-46 years) and 4 are males and 2 are females. At start of treatment the CD4+ - cell count for this group was in average 138 (spread 64-195). Four patients had more than 1 CD4+ - cell count recorded and average increase to the last recorded CD4+ - cell count was 83,5. At 3 months 1 patient had < 400 HIV RNA copies/mL and 2 had the same at 6 months. (See-table 8)

Table 8: Development of CD4+ - cell count and Viral Load over time for 6 patients with < 95% adherence from pill-count

If a box is empty, this means that the patient has no recording of this blood test in the file. According to guidelines, CD4+ - cell count should be taken every 3-4 months and Viral Load at start of treatment, at 3 months to assess efficacy and every 6 months thereafter.

	Length of treatment (months)	*CD4+ - cell count*				*Viral Load*			
		Start of treatment	*3 months*	*6 months*	*9 months*	*Start of treatment*	*3 months*	*6 months*	*9 months*
Patient 1	0-3	195							
Patient 2	3-6	182				8810			
Patient 3	3-6	136	390				< 400		
Patient 4	3-6	130	275	292			1040	< 400	
Patient 5	6-9	65	393	405					
Patient 6	9-12	120	267	193	244	25300	633	< 400	24700

Looking at socioeconomic factors for this group, it's worth noting that 2 of the 5 patients with no permanent home had < 95% adherence. For all the other comparisons, see table 3.

Answers to questions 25-27 are see in table 4. In this group 3 patients (50%) didn't know the answer/answered "wrong" on all 3 questions. They were all males. The two patients with correct answers to question 25 and 27 were not the same on both questions.

Through self-report 4 of the patients in this group (66,7%) admitted their non-adherence and 3 of the 4 (75,0%) reported that they forgot once or several times a week.

Three patients reported side effects, 2 reported 2 side effects and 1 reported 4 side effects. They all had a different answer to which side effect that influenced their adherence the most (diarrhoea, tiredness and peripheral neuropathy). All 6 experienced improvement in their condition after they started ARV therapy. Five out of 6 patients were satisfied with the follow-up of their treatment.

2. The 12 patients (19,7%) who admitted to missing doses of medication through their self-report

The average age was 34,6 years (spread 19-46 years) and 4 patients were males and 8 were females.

CD4+ - cell count was on average 120 at start of treatment (spread 23-214) and 7 patients had recorded 2 or more CD4+ - cell counts. Their average increase in CD4+ - cell count after 3 months on

Table 9: Development of CD4+ - cell count and Viral Load over time for 12 patients who admitted to missing a dose of medication through self-report

If a box is empty, this means that the patient has no recording of this blood test in the file. According to guidelines, CD4+ - cell count should be taken every 3-4 months and Viral Load at start of treatment, at 3 months to assess efficacy and every 6 months thereafter.

	Length of treatment (months)	*CD4+ - cell count*				*Viral Load*			
		Start of treatment	*3 months*	*6 months*	*9 months*	*Start of treatment*	*3 months*	*6 months*	*9 months*
Patient 1	0-3	195							
Patient 2	0-3	54							
Patient 3	3-6	182				8810			
Patient 4	3-6	136	390				< 400		
Patient 5	3-6	130	275	292			1040	< 400	
Patient 6	3-6	23							
Patient 7	3-6	46	425				1490		
Patient 8	3-6	50	93						
Patient 9	3-6	182				8810			
Patient 10	6-9	65	393	405					
Patient 11	6-9	170	307	243			< 400	< 400	
Patient 12	9-12	120	267	193	244	25300	633	< 400	24700

treatment was 198,6 (spread 43-382). Of the 9 patients treated longer than 3 months, only 5 had CD4+ - cell count registered at 3 months. (See table 9). At 3 months 2 patients had a Viral Load < 400 HIV

RNA copies /mL (of the 5 patients with Viral Load registered) and all 3 with Viral Load registered at 6 months had < 400 HIV RNA copies /mL.

A Chi-square test to see if significantly more people with no work admitted to missing a dose of medication, gave chi-square = 1,34 (p = of 0,25 with 1 degree of freedom). Table 3 shows that 66,7% of the patients that had missed doses of medication had no work.

The results on questions 25-27 for this group are seen in table 4. Three patients had all 3 questions correct and 3 patients only had 1 of the 3 questions wrong. Two patients didn't know the answer/answered "wrong" on all 3 questions. 50% of the patients didn't know the answer/ answered "wrong" on each of the 3 questions.

Of the 12 patients, 10 reported side effects and the most common side effect was GI-related side effects (41,7%) followed by peripheral neuropathy (25,0%). The same two side effects influenced the patients' adherence the most. All 12 patients reported improvement in their condition after they started ARV therapy and 11 out of 12 patients were satisfied with the follow-up of their treatment.

Services offered by the Resource Centre

All patients were satisfied with how they were received at the Resource Centre. What made the patients feel most welcome were speed of attendance (males) and that they were offered help (females). 57 patients (91,9%) were satisfied with the follow-up of their treatment. By far the single most important factors that the patients reported could improve their adherence were more staff and reduced distances.

DISCUSSION

In Maun 454 patients have been enrolled in the ARV-programme and 427 have started ARV-treatment; 317 are still alive and on treatment. There is a discrepancy of 110 patients because some patients have defaulted, died or for some other reason left/been taken out of the programme. (Numbers by 27/4-03 – personal notification by Dr. Beltz, Maun). My initial goal was to include 100 patients in my material, but I quickly saw that to be difficult since a lot of new patients were enrolled every day and the more experienced patients didn't come that often to the Resource Centre. The 62 patients I did include are about a 5th of all the patients alive and on treatment right now. There are twice as many females as males in my material and that can be a bias because in the whole patient population it's more 60/40.

CD4+ - cell count and Viral Load

These two blood tests are in addition to the patient's clinical development crucial markers for treatment efficacy. The average development in CD4+ - cell count for all patients is very positive. Most patients show a steady increase in CD4+ - cell count (see figure 1), but especially between 3rd and 6th month there were some declines. Some were small and probably a sign of natural variation in CD4+ - cell count; others are signs of non-adherence. One of the 8 patients with declining CD4+ - cell counts had < 95% adherence and admitted his non-adherence through self-report. His non-adherence can clearly be seen with his Viral Load going from non-detectable to detectable levels between the 6th and 9th month of treatment. Also another of the 12 patients who admitted to missing a dose of medication had a declining CD4+ - cell count between 3rd and 6th month. His Viral Load stayed non-detectable and it can be argued why this is since this patient had declining CD4+ - cell count. It's probably a sign of natural variations or the patient might have been affected by something that reduce the CD4+ - cell count and with time will reduce his Viral Load. Often the reduction in Viral Load comes a bit after the reduction in CD4+ - cell count.

Cozzi et al's research [15] concluded that Viral Loads of < 400 HIV RNA copies/mL could be seen after 8-12 weeks of ARV therapy. At 3 months 73,3% of the patients with a Viral Load have non-detectable viral levels. At 6 and 9 months the percentage is 94,1% and 85,7% respectively. This is very

good. Since there are many patients with no Viral Load recorded at 3 and/or 6 months, I can only hope that this result is representative for them too.

Looking at the group with > 95% adherence, 80,2% had complete viral suppression at 3 months and 93,3% had this at 6 months and that's in line with Paterson's research and underlines the great need of excellent adherence in these patients in order to have sufficient viral suppression.

Long-term effectiveness of HAART is dependant upon achieving maximal and durable suppression of plasma Viral Load [17] In clinical practice this is achieved in as few as 40%-50% [18, 19] and the reason for this is mainly suboptimal adherence to medication. [20, 21]. In my material I only had 8 patients with a 2nd Viral Load registered 3 or 6 months after their 1st non-detectable Viral Load and 7 of them (87,5%) had non-detectable levels of virus. This is much better than what the larger international studies show. In addition, the international studies have measured viral suppression over years, I only had enough data to cover 6 months and that's a big difference and a weakness of this paper.

The statistical test to see if there were more males than females without CD4+ - cell count and Viral Load didn't give any significant gender differences. Neither did the tests on the patients with more or less than 95% adherence.

Since CD4+ - cell counts and Viral Loads are used to monitor treatment efficacy, it is worrying to see the number of patients in the group treated longer than 3 months with no CD4+ - cell count and/or Viral Load at 3 months. 83,3% and 69% respectively at 3 months aren't good enough. Looking at these figures I have to say there is a need for better follow-up of the patients blood testing. But there are some explanations for some of the missing results. One is that there was (still is?) a problem with delay of results from the lab in Gaborone and some recent results might have arrived after I left Maun. Another explanation is that some patients had their first CD4+ - cell count (4 patients) and Viral Load (7 patients) registered at 6 months instead.

Pre-adherence counselling

Lack of food is a source to non-adherence according to Weiser et al. [9] I have compared non-adherence to socioeconomic factors (See table 3).

Comparing the 6 patients with < 95% adherence I can see no clear pattern. Three patients (50%) have a permanent home, work, make more than 500 pula/month and have no problems with transport to the Resource Centre. Of the last 3, 1 patient has no permanent home, 1 has no work and the last patient has no permanent and no work.

The 12 patients who had missed doses of medication didn't show any clear pattern either. Only 2 patients with no work also had no home. Of the 8 who reported how much money they made, 6 had an income of more than 500 pula/month. Only 1 patient had problems with transport. When 2/3 of the patients who miss doses of medication have no work, this tells me that work is important for adherence and for a structured day. These 8 patients make up ¼ of the total amount of patients with no work. Patients are encouraged to link the time they take their medication to recurring events every day, like going to work in the morning, brushing teeth or watching the evening news. If you don't have work to go to every day, you lose some structure in your day and it's easier to forget to take your medication, both in the morning and in the evening. The patient's without work need to be identified and given a closer follow-up every time they meet the health personnel so that they can better equipped to remember to take their medication.

Every day the staff at the Resource Centre in Maun meet patients who struggle with their adherence because of socioeconomic factors like problems with transport and lack of food. I did not ask about lack of food and that is a weakness in my material since I discovered this to be a problem for some patients. Apart from work discussed above, my material shows few links between socioeconomic factors and non-adherence. My material might be biased since so few of the patients with less than perfect adherence had socioeconomic problems that could affect their adherence. It might also play a role that the majority of patients in my study are females. Females in general are more structured and used to remembering since they often are the "memory" in a family. Supported by international studies, [16, 22] I choose to believe that demographic factors like age, race, gender and socioeconomic factors don't predict non-adherence.

It was no surprise that the pharmacy had the greatest influence on a patient's adherence since they are in contact with the patients every month when they come for refill. The figures show that also the doctor and social workers have great influence on a patient's adherence. It is very interesting and also worrying that only 12,3 % of the answers (10 patients) implied that their adherence partner had influenced their adherence the most. Don't adherence partners have the desired effects on patients?

Seven of these patients had mother/sister as adherence partner. None mentioned their spouse. Only 4 patients mentioned the nurse as a person who influenced their adherence. There can be many reasons for this. There are few nurses working at the Resource Centre and their main task is translating for the doctors. These nurses aren't trained for this particular task of working with HIV-patients. The nurses do spend a lot of time with the patient's, preparing them for the doctor's review, but they have little time to counsel them. I think counselling done by nurses could be valuable since nurses might have other ways of addressing adherence problems, which can be a valuable addition to the adherence counselling given by doctors and pharmacists. In order to do this, there is a need for more nurses trained for this particular task at the Resource Centre.

Everyone involved in treating illnesses know that the cost of non-adherence is high and that non-adherence can play a significant part in the re-emergence of drug resistant organisms including tuberculosis. **[23, 24]** That's why so much effort is put into adherence counselling and follow-up of patients in Maun. But is the adherence counselling having an effect? The pre-adherence counselling is done by different professions, on a one on one basis and in groups. Very disappointingly more than 1/3 answered "wrong" on each of the 3 questions designed to test the patients on 3 key issues from counselling. Worst was the knowledge about side effects: Over 50% of the patients couldn't name two side effects of their medication and statistically there were more males than females that couldn't name two side effects (p=0,02). Close to 50% of the patients didn't know why it was important to take the pills at the same time every day for the rest of their life and 40% didn't know two of the goals that we want to achieve for the patients through providing ARV therapy free of charge. Some of these goals can be to live longer, be healthier, take care of family longer, go back to work etc.

In the group with < 95% adherence 2/3 or more answered every question wrong. All 6 patients answered wrong about side effects. Three of the 4 males in this group answered all 3 questions wrong.

The results were better in the group that had missed doses of medication, but 40-50% of the patients with wrong answer to each question aren't good enough. All these results are devastating and not good news to the personnel involved in the adherence counselling. Of course there are several reasons to these disappointing figures. Despite very good translation, in some cases the language barriers made it difficult to explain the questions and get across what kind of answers I was after. Another reason is probably that the messages on MASA-posters and in brochures about the ARV therapy aren't clear enough. These two reasons don't explain it all. There has to be a lack of knowledge

too. Knowledge disappears over time if the key issues aren't reinforced over and over again. Several studies clearly underline that counselling is an ongoing process and that adherence counselling needs to be a natural part of every meeting point health personnel have with patients on treatment [25, 26, 27]. A fourth reason is that the group counselling is done in English and translated to Setswana. I think adherence counselling needs to be given by a Batswana and in Setswana. Hearing a message in your mother tongue strengthens the message, makes it more personal and help stress the core of the counselling - the importance of prefect adherence. Speaking English is found to be an independent predictor for incomplete adherence (< 95%) and virologic failure (> 400 HIV RNA copies/mL)). [22]

Since significantly more males than females have < 95% adherence and 3 of these 4 males answered all 3 questions wrong, there seems to be a weak link between lack of knowledge and non-adherence and clearly the quality of the adherence counselling has to be improved and strengthened. By the time this paper is written group counselling's in Setswana might already be a reality; I know they are planned. If they haven't started yet, start them soon.

Adherence

In the general population around the world, the level of non-adherence varies between 15 and 93% depending on patient population, medical condition, form of treatment and the definition of adherence. [28] In average 1/3 of the patients fail to adhere properly. [29] Research examining patient adherence to medications given for treatment of chronic illnesses, particularly hypertension, found that most patients take about 50% of their prescribed doses. [16, 30] Several studies show that the average adherence to HAART is better than what's reported for other chronic illnesses. [31, 32, 33, 34] This gives us some hope, though an adherence to HAART of between 70-80%, as these 4 studies have shown, still isn't good enough. 100% adherence has to be the golden standard.

For most diseases an adherence of about 80% is equivalent to success. In treating HIV/AIDS, this is not enough. Paterson et al. showed that >95% adherence was needed to see complete viral suppression in >80% of the patients. If adherence fell below 80%, only 25% of the patients had complete viral suppression. The average adherence in that material was 74,7%. [14] Paterson et al. also did a prospective observational study in 81 patients, and only found 5 out of 23 patients (22%) with adherence rate of 95% or more to be suffering virologic failure (HIV RNA level >400 copies/mL). In

my material 3 out of 23 patients (13,0%) suffered virologic failure at 6 months. All 3 patients had Viral Loads close to 400 HIV RNA copies/mL (spread 402-532). By contrast the risk of virologic failure was over 80% in patients with adherence of less than 80%. [31] There are also more consequences to non-adherence beyond virologic failure. Singh et al. found that patients with less than 90% adherence experienced a median decrease in CD4 count of 5 cells/µl compared to a median increase in CD4-count of 78 cells/µl in patients whose adherence rates were 90% or higher. [35] Hogg et al. concluded that a 10% decrease in adherence was associated with a 16% increase in mortality. [36] These results clearly show that adherence has to be excellent or else there's an increasing risk of virologic failure, development of multiresistant HIV and thereby producing a potential public health consequence and ultimately increased mortality.

In my material 6 patients (9,7%) had < 95% adherence from pill-count and statistically there were significantly more males than females with insufficient adherence (p=0,02). This result is surprising and clearly indicates that male patients need to have a closer follow-up of their treatment in order to prevent development of resistance and increased morbidity and mortality. It would be interesting to see if this result is reproducible at one of the other treatment sites. If it is, this has to produce consequences for how the males are handled in the ARV-programme.

12 patients (19,4%) reported less than 100% adherence through self-report. Statistically there were not more males than females that reported that they missed their medication (p=0,51). If all patients were honest, you would expect similar statistically significant gender differences here as for the patients with < 95% adherence, but that's not the case. One explanation might be that more males than females are prone to under-report their non-adherence. If this is the case, pill-count is a better mean than self-report for assessing adherence amongst HIV-patients on ARV therapy in Maun, though you cannot rule out dishonesty in this method either. Regular estimations of adherence from pill-count need to be a pillar in the follow-up of patients on ARV, especially amongst the males. And cases of non-adherence need to be followed up closely by all health personnel involved with the patient.

4 of the patients (6,5%) that admitted that they had missed medication had forgotten during the last 24 hrs and that's lower than what international research has found. Hecht et al. found that ~20% of the patients had missed a dose of medication last 24 hrs [37] and Stone et al. found that ~30-35% of the patients have done the same over the past 3 days. [38] Assuming that my estimations of non-adherence

are representative for the rest of the patient population still alive and on ARV therapy, 31 patients (1/10 of the total patient population) have < 95% adherence and 62 patients (1/5) miss to take medication on a more or less regular basis. These patients can be a reservoir for development of resistance to the current therapies and that's worrying.

There are several reasons why patients tend to under-report their non-adherence: They try to deceive the researcher, they might not understand their regimen and therefore not know that they are not adhering and it's easy to forget instances of non-adherence. In Maun I think some patients didn't want to report their non-adherence in fear of making the doctor angry or being thrown out of the programme. As Roth and his colleagues wrote, it's easy to forget instances of non-adherence. Instead of asking if a patient had forgotten once or several times a week/month I probably should have asked in more detail about the last days (up to 3 or 5 days), patients tend to forget after that.

Pill-count is a good way of measuring adherence, but it does not give any indication if missing medication was thrown away or when during the day the medication was taken. [39] Based on this, there are probably more people with < 95% adherence from pill-count than what my review of the pharmacy records showed. The numbers are probably higher because of under-reporting, but still better than international studies. Knowing that both pill-count and self-report tend to underestimate adherence [12] [13]; continual improvement of the ARV programme is needed when the ARV-programme is expanding.

The patients that admitted missing medication reported forgetting (58,3%) followed by travelling (16,7%) as their main reason for missing doses of medication. These are the same two main reasons for missing medication as the AACTG (Adult AIDS Clinical Trials Group) study showed. In this study 66% reported that they simply forgot and 57% reported that they were away from home as their reason for missing medication. [40] Many trials try different kinds of reminders (calendars, different devices, alarms etc.) to help people remember. Since forgetfulness is a product of both cognitive and motivational issues, it cannot be assumed that reminders alone (focusing on the cognitive issue alone) can solve the issue of forgetting. In Botswana it's estimated that more than 110 000 patients will need ARV therapy in the future so equipping every patient with a device to help remembering will be expensive. But every 5th patient has trouble remembering to take his/her medication, so it is probably well worth both the time, effort and money to perfect the existing approaches and look into new ways

of helping people remember, device or no device. It could prevent an increase in viral failures in the future.

In Botswana, every patient has an adherence partner helping the patient remember to take his or her pills at the right time every day. Mother and sister are the most common adherence partners. They are also the most common adherence partners for the non-adherent patients. This is not surprising since 74,2% of the patients in my material are females. What's more interesting is that 28,5% of the patients with their partner (boyfriend/girlfriend/just living together) as adherence partner had < 95% adherence compared to 5,6% and 9,5% for the patients with mother and sister respectively. None of the 6 patients with their spouse as adherence partner had < 95% adherence. 27,8% of the patients with mother as adherence partner had missed doses of medication compared to 14,3% of the patients with sister as adherence partner. The numbers are small and adding or taking away 1 patient gives big changes in percentages. Statistically it is hard to draw the conclusion that spouses and sisters are better adherence partners than the rest ($p = 0,5$), but a marriage is a more long-term bond than just having a partner and I think the commitment is greater and a possible reason why spouses might to be better adherence partners than partners. It would be very interesting to see similar results from the other 3 treatment sites and see if they were comparable.

I also looked into side effects and their effect on adherence. More than 2/3 of the patients experienced side effects and 2/3 of the patients with side effects felt that one or more of their side effects influenced their adherence. The patients who missed doses or had < 95% adherence didn't have more side effects than the other patients. GI-related side effects (nausea/vomiting, stomach pain and diarrhoea) were the most common side effects and influenced the patient's adherence the most followed by skin rash/tiredness and peripheral neuropathy. When 2/3 of the patients with side effects (this is over 50% of my total patient population) feel that the side effects influence their adherence, this is serious. Side effects cannot be exterminated completely, but a more aggressive strategy for treating side effects; especially diarrhoea, vomiting/nausea and stomach can be beneficial.

In Weiser et al.'s study of adherence, the main reasons for non-adherence were financial constraints (44%), stigma (15%), travel/migration (10%), side effects (7%) and lack of food (7%). [9] Since the ARV therapy is provided for free now; financial constraints aren't a problem anymore.

People from Botswana travel a lot and at any time there are surprisingly many people on the move. My material came up with travel/migration as the 2nd most common reason for missing medication. Not only is it hard to remember to bring enough medication while travelling, but patients may miss appointments and therefore partly fall out of the treatment regimen they are in. Being on the move also increases the risk of spreading HIV and resistant strains of HIV. We can't stop people travelling, but only keep stressing the importance of perfect adherence and safe (-er) sex. A new computer system will be implemented over the coming years and this system will link all the treatment sites together in a common computer network. This network will help tracking the patients and prevent them from falling out of the treatment programme.

Having experienced Botswana culture and looking at the results from Weiser's study, I'm surprised that none in my material mentioned stigma as one reason for their non-adherence. Stigma is a big problem and officials and organisations in Botswana are addressing this and trying to create a society with greater openness. There are several reasons for this stigma, on is tradition which takes a lot of time and effort to turn around. The stigma is very noticeable just by looking at how many people go to the public testing sites (Tebelopele) compared to the percentage of people infected with HIV. Only a small proportion (about 8000 people) of the population have tested themselves there and those who are HIV-positive often postpone coming for treatment till it's almost too late. [41] The government and many different organisations working with HIV/AIDS relates issues have a great task in turning this around and making HIV nothing to be ashamed of.

International research has found that each patient's adherence declines with length of treatment. [25, 26, 27]. Figure 2 shows the percentage of patients with > 95% adherence grouped according to how long they have been treated. As we can see; the percentage of patients with > 95% adherence decline in the group treated 3-6 month for then to increase in the group on treatment longer than 6 month. This is interesting. My research said nothing of how each patient's adherence developed with time and is therefore not directly comparable to these international studies, but a comparable study from Senegal showed a similar pattern, though their limit for adherence was set to 80%. In this study the percentage of patients with adherence > 80% after 3 months was 90%, after 5 months: 87% and after 7 months: 95%. After 7 months there was a steady decrease. [42]

The increase in percentage of persons with > 95% adherence in the group treated longer than 6 months is very encouraging since this group included more than 1/3 of all patients. This small result

shows that it's possible to maintain a good adherence with time even though patients after some time on treatment may experience "treatment fatigue", lose their motivation or simply become complacent. The results should encourage further improvement of adherence counselling and better follow-up of patients rather than be a pillow to rest on.

Services offered by the Resource Centre

91% of the patients were satisfied with the follow-up of their treatment and that's good. This shows that the work that is being done is satisfactory to the majority of patients. By far the single most important factors that the patients reported could improve their adherence were more staff and reduced distances. More staff is a problem that it's hard to find a quick solution to, but reduced distances is already in place with the new co-location of doctor, pharmacy and social worker at the Resource Centre.

CONCLUSIONS

1. There were significantly more males than females with < 95% adherence, but not significantly more males than females that admitted their non-adherence through self-report. In general the adherence was better than comparable international research. Adherence, especially amongst male patients, needs to be closer followed up and monitored since 1/10 of the patients have < 95% adherence and 1/5 admit they miss doses of medication.

2. Significantly more males than females didn't know two side effects of their treatment. Three of the 4 males with < 95% adherence didn't know the answer to any of the 3 questions designed to test the effects of the adherence counselling. This shows, at least for the males, that there is a link between non-adherence and lack of knowledge. The work with adherence counselling needs to be improved and strengthened and the counselling needs to be given in Setswana by a Batswana.

3. At 3 months, 83,3% had a CD+ - cell count registered and 69,0% had a Viral Load registered. This is not in line with the 2002 Guidelines. There is great need for a better follow-up of all patients blood-test.

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APPENDIX 1

Registration form

Please answer all questions truthfully!

Patient information

1. ID-number	**2. Age**	**3. Gender:** ☐$_1$ Male ☐$_2$ Female
4. Marital status: ☐$_1$ Married ☐$_2$ Single ☐$_3$ Divorced ☐$_4$ Widow/-er	**5. Children:** ☐$_1$ Yes ☐$_2$ No If yes, how many?	**6. Education level:** ☐$_1$ Primary school ☐$_2$ High school ☐$_3$ University ☐$_4$ No school
7. How long on ARV therapy: ☐$_1$ 0-3 months ☐$_4$ 9-12 months ☐$_2$ 3-6 months ☐$_5$ > 12 months ☐$_3$ 6-9 months	**8. Has your medication/the dosage been changed while you've been treated?** ☐$_1$ Yes ☐$_2$ No	**9. Reason for this change?** ☐$_1$ Toxic reaction ☐$_2$ Failure of treatment ☐$_3$ Other: .....

Reason for ARV (to be filled in by the staff)

10. HIV-test date: (month/year)					
Date	**At start of treatment**	**After 3 months**	**After 6 months**	**After 9 months**	**After 12 months**
11. CD4-count					
12. Viral Load					

13. Opportunistic infections? ☐$_1$ Yes ☐$_2$ No

14. If yes, which one: ☐$_1$ Kaposi's sarcoma ☐$_2$ Candidasis ☐$_3$ Other: .....

Pre-adherence counselling:

15. Permanent home: ☐$_1$ Yes ☐$_2$ No

16. Work: ☐$_1$ Yes ☐$_2$ No

17. Your income: ☐$_1$ Less than 500 Pula per month ☐$_2$ More than 500 Pula per month

18. Geographical accessibility to resource centre:

☐$_1$ Independent ☐$_2$ Needs help to get to resource centre

19. Who is your adherence partner?

☐$_1$ Partner ☐$_2$ Spouse ☐$_3$ Mother ☐$_4$ Father ☐$_5$ Sister ☐$_6$ Brother ☐$_7$ Best friend ☐$_8$ Other

20. Do you think it is important to share your HIV-status with closest family/friends? ☐$_1$ Yes ☐$_2$ No

21. If you answered yes, what are the two most important reasons for you?

1. 2.

22. If you answered no, what were the two most important reasons?

1. 2.

23. Were you counselled before you started treatment? ☐$_1$ Yes ☐$_2$ No

24. Were you counselled in the language that you understand best? ☐$_1$ Yes ☐$_2$ No

25. Can you tell me two of the goals we want to achieve <u>for you</u> through the ARV therapy? ☐$_1$ Yes ☐$_2$ No

1. 2.

26. Can you give me two side effects of the drugs that you are using? ☐$_1$ Yes ☐$_2$ No

1. 2.

APPENDIX 1

27. Why should you take your pills at the same time every day for the rest of your life? ☐$_1$ Yes ☐$_2$ No
1. 2.

28. Who influenced you most on the importance of taking your pills at the same time every day for the rest of your life?
☐$_1$ The doctor ☐$_2$ The nurse ☐$_3$ Your adherence partner ☐$_4$ The social workers
☐$_5$ The pharmacy

29. Who chose when, during the day, to take your pills?
☐$_1$ I did ☐$_2$ The pharmacist ☐$_3$ Other

Adherence

30. How many pills do you take a day? .....

31. Is the amount of tablets: ☐$_1$ Good ☐$_2$ Fair ☐$_3$ Too much

32. Honestly, have you ever missed a dose of medication? ☐$_1$ Yes ☐$_2$ No

33. Have you missed a dose of medication.....
- during the last 24 hours? ☐$_1$ Yes ☐$_2$ No
- once or several times during a week? ☐$_1$ Yes ☐$_2$ No
- once or several times during a month? ☐$_1$ Yes ☐$_2$ No

34. If you answered yes, why did you miss 1 or more of your doses?
☐$_1$ Travelled and was not with my drugs ☐$_2$ I had problems taking my medication in public
☐$_3$ Fear of stigmatisation ☐$_4$ I just forgot
☐$_5$ I had been drinking ☐$_6$ I felt too sick to take pills
☐$_7$ Misplaced my drugs ☐$_8$ Change of routines
☐$_9$ No good reason ☐$_9$ Other reason: .....

35. Have you ever skipped a dose because you felt well? ☐$_1$ Yes ☐$_2$ No

36. If you answered yes, do you know the possible consequences of doing so? ☐$_1$ Yes ☐$_2$ No

37. Have you experienced side effects? ☐$_1$ Yes ☐$_2$ No

38. If you answered yes, indicate one or more side effects
☐$_1$ Painful stomach ☐$_2$ Nausea/vomiting
☐$_3$ Diarrhoea ☐$_4$ Skin rash
☐$_5$ Tiredness ☐$_6$ Tingling in feet/fingers
☐$_7$ Sleep disturbance – vivid dreams ☐$_8$ Other side effect What:.....

39. Which side effect has influenced your adherence (taking your pills at the same time every day) the most?
☐$_1$ Painful stomach ☐$_2$ Nausea/vomiting
☐$_3$ Diarrhoea ☐$_4$ Skin rash
☐$_5$ Tiredness ☐$_6$ Tingling in feet/fingers
☐$_7$ Sleep disturbance – vivid dreams ☐$_8$ Other side effect What:.....

40. Have you noticed any change in your life with ARV?
☐$_1$ Improvement ☐$_2$ Worsening

41. Do you use traditional medicine together with your ARV? ☐$_1$ Yes ☐$_2$ No

42. If you answered yes, Why?
State 1 reason.....

APPENDIX 1

43. Are you aware of the dangers of traditional medicine together with ARV? ☐$_1$ Yes ☐$_2$ No

Services offered by the resource centre

44. When you arrive at the resource centre, what makes you most welcome? Name one reason
☐$_1$ I'm greeted ☐$_2$ I'm offered help ☐$_3$ The speed of attendance
☐$_4$ Tidiness of centre ☐$_5$ Confidentiality ☐$_6$ Other reason: .....

45. In general, are you satisfied with how you are received at the resource centre?
☐$_1$ Yes ☐$_2$ No

46. Name the person whom you feel is the most helpful at the resource centre?
☐$_1$ Doctor ☐$_2$ Nurse ☐$_3$ Secretary ☐$_4$ Social worker ☐$_5$ Cleaner ☐$_6$ Driver

47. How do you feel about the location of the Resource centre, lab, pharmacy and social worker?
☐$_1$ Satisfactory ☐$_2$ Too long distance between locations

48. Are you satisfied with the follow-up of your treatment?
☐$_1$ Yes ☐$_2$ No

49. What single factor can improve the follow-up of your ARV?
☐$_1$ More staff ☐$_2$ Improved staff behaviour ☐$_3$ Reduced distances ☐$_4$ Increased privacy
☐$_5$ Other factor: .....

APPENDIX 2

FILE NUMBER:

Why are you here:

☐ Review by doctor
☐ Refill of pills
☐ We called you in

Consent form

About me

My name is Thomas Rolfsen and I'm a 5th year medical student at the University of Tromsø, Norway. As part of my medical training I have to write an elective paper during our 5th year. I've been encouraged to do a project with a topic from Botswana. The reason for this is that I in April 2000 spent 1 month in Selebi-Phikwe, Botswana, also that as part of my medical studies. As a follow-up of this it was suggested that a topic from Botswana could be suitable for a 5th year elective paper.

About the project

Recent data from UNAIDS has acknowledged the high prevalence of HIV in Botswana and southern Africa in general. Treating HIV is very expensive. The government of Botswana has in cooperation with some organisations lunched it's Anti RetroViral-therapy (ARV) - programme MASA. Through this programme HIV-patients now receive free treatment. ARV is a tough and life long therapy. Research from all over the world has proven that sticking to the treatment, which is called adherence, is the pillar of the success of ARV. I want to meet 100 patients from Maun who are on the ARV-programme, go through their medical records and see what factors influence adherence the most.

Project title:
Adherence to Anti RetroViral (ARV) therapy in Maun, Botswana. A study of 100 HIV-patients.

Thesis for the project:
"*Adherence to ARV in in-patients is assumed to be excellent. Can we say the same for out-patients?*
If not, what are the reasons?"

All patient information will be anonymized and treated with confidentiality and respect

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Consent form

I hereby give Thomas Rolfsen permission to access my patient file and use my answers on the registration form as part of his research-project.

_____ _____

Date **Name**