

# NON-ADHERENCE TO HIV ANTIRETROVIRAL MEDICATIONS: 'THE DRUGS ARE WORKING AND I'M A CONTINUING SUCCESS STORY'

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## ABSTRACT

**Non-adherence to antiretroviral (ARV) regimens has been associated with HIV drug resistance. Anecdotal evidence in our client group, people living with HIV/AIDS infection in Central Sydney Area Health Service (CSAHS), suggested that non-adherence was an issue. Eighty three participants completed an anonymous questionnaire; with a 98% response rate. The mean age of respondents was 44 years with 68% over age 40 years. 68% of respondents missed doses of ARV, 54% because they forgot. 54% stated they did not report the non-adherence to their doctor. They were more likely to miss the lunch time dosage (n=49, p<0.05). The results demonstrate that non-adherence with medications is a significant issue and further research into strategies for interventions to aid adherence is required.**

## INTRODUCTION

Antiretroviral drug resistance has emerged as a result of Human Immunodeficiency Virus (HIV) gene mutations. Multi-drug resistance HIV (MDRHIV) has drawn attention to the issue of adherence to antiretroviral (ARV) regimes. HIV can rapidly mutate at the reverse transcriptase gene and protease gene and develop resistance to standard medication. It has been stated that a 95% compliance to drug regimens results in a viralogic failure rate of 20%, with the failure rate increasing even further as compliance rates decrease (Patterson et al 1998). The development of resistance to one ARV drug can lead to cross resistance with other ARV medications or the class of medications, therefore greatly limiting the future choice of effective treatment. For those with HIV, non-adherence may result in deterioration in health and lead to an increase in opportunistic diseases resulting in hospitalisation.

Although it would be reasonable to assume patients with a potentially fatal condition would be compliant with medication, previous research has shown this is not the case. For example, Rovel and colleagues (cited in Cramer 1996) found that the leading cause of organ rejection and failure in transplant patients was non-compliance with immunosuppressant medications. It seems that regardless of the illness or disease that is diagnosed - acute, chronic or terminal - it cannot be assumed that the client will be adherent to their prescribed medication regimen (Cramer 1996).

Anecdotal evidence in our client group, people living with HIV/AIDS infection in the CSAHS, suggests that non-adherence is a common problem. We therefore aimed to investigate the frequency and cause of non-adherence in our population. To this end, we surveyed patients with HIV/AIDS who accessed the outpatients' clinic at the Royal Prince Alfred Hospital, Sydney, NSW, and those who were seen by the HIV/AIDS Community Health Service (CSAHS).

## METHOD

### Setting and sample

The study was conducted within the CSAHS and was approved by the Institutional Ethics Review Committee. All clients living with HIV/AIDS and attending the outpatient department of the Royal Prince Alfred Hospital, a major teaching hospital, and those accessing the services of the HIV/AIDS Community Health Service over a two-month period were considered for this study. Inclusion criteria included that the subject be at least 17 years of age, be receiving related care within CSAHS, have a diagnosis of HIV/AIDS but were not newly HIV/AIDS diagnosed and did not have a known diagnosis of an HIV related dementia.

### Instrument

A questionnaire was developed by the researchers that took into consideration factors found to be related to non-adherence in previous research in order to determine patient self reported adherence to medication as well as reasons for non-adherence. Although the questionnaire collected information from all clients, this study only reports on those currently prescribed ARV medications. The Likert score system was used for the subject to rate their confidence in taking medication as prescribed, confidence that the medication was working, drug and alcohol intake, social activity and educational issues regarding HIV and adherence.

### Study design

Clients were approached to participate in this study during their outpatient visit or during a community visit. The anonymous self-administered questionnaire was completed voluntarily by the clients and returned to the researchers at that or subsequent visits. A total of 85 questionnaires were distributed.

### Statistical methods

Statistical analysis was performed using the SPSS-X version 9.0 number and Number Crunching Statistical System 6.0 software package. Attempts were made to normalise non-parametric data. Where this was not possible, non-parametric tests were used. Continuous data were analysed by t-test and Mann Whitney tests. Categorical data was analysed by c2 test. Logistic regression was performed to determine independent predictors of non-adherence, eliminating non-significant variables for a base model, which included all variables with a significance of 0.1 on initial analysis. Results were regarded as significant at the 0.05 level (two-tailed). Results are expressed as mean and standard deviation (SD) for parametric data and frequency and percent, median and inter-quartile range (IQR) for non-parametric data.

## RESULTS

Eighty-three questionnaires were completed, representing a 98% response rate. Five respondents were community based and were excluded from further analysis

as this group was underrepresented in the sample. Ten respondents who were not prescribed ARV medications were also excluded from analysis. Therefore the following results refer to the remaining 68 respondents taking ARV medication at the time of the survey.

The respondents were predominantly male (97.1%). The mean age of respondents was 44 (SD: 9 yrs), which is much older than other studies on HIV adherence (Singh et al 1996). The majority of respondents (68%) were over age 40.

Overall, 68% of subjects reported missing medications at some time. Those in the 36-45 age group were more likely to miss medications than other age groups (72.7% vs 27.3%, 32.83%;  $c2(df-2) = 1$ ;  $p=0.044$ ). The majority (77%) of respondents taking 10 pills or less reported missing pills at least occasionally. Adherence was greater in individuals prescribed more medication (between 11-30 pills per day), with only 58% of this group reporting missing medication ( $c2(df-1)=1$ ;  $p<0.05$ ).

The timing of the dose of medication was found to be a significant determinant of missed medication, with 62% of individuals reporting missing their lunchtime dose ( $c2(df-1) = 1$ ;  $p=0.007$ ). Respondents were also more likely to miss medication if they had consumed alcohol (40% vs 4%, 75.75%;  $c2(df-1) = 1$ ;  $p=0.042$ ).

The most frequently cited reason for missing medication was because the respondent forgot (82%). Logistic regression found that forgetting was the only independent predictor associated with non-adherence, ( $p=0.00002$ ), accounting for 25% of the variance.

Factors considered, but found not to be statistically significant ( $p\geq 0.05$ ) in influencing adherence include age, the use of a protease inhibitor (PI) regimen versus a PI sparing regime, confidence in the medications working, education concerning medication issues, HIV/AIDS virological status, number of HIV/AIDS related hospitalisations, use of other substances including recreational drugs.

The majority of respondents (65%) had difficulty telling their doctors about missing medications. Reasons cited for not reporting missed medication are listed in Table 1.

| Reasons   | No. of respondents |
|---|--------------------|
| 'did not think it was important because only a few doses were missed' | 18                 |
| 'thought the doctor would lecture me'                                 | 8                  |
| 'I don't want the doctor to think I don't care'                       | 6                  |
| 'there were more important things to discuss'                         | 4                  |
| 'I was concerned it would affect how I'm treated'                     | 3                  |
| 'I don't want to upset the doctor'                                    | 3                  |
| Other   | 2                  |

## DISCUSSION

This study used a questionnaire design that was based upon findings from a number of previous adherence/compliance studies and the researchers experiences within this clinic (Holzemer et al 1999; Chesney 1997; Cramer 1996). This cohort includes people at different stages and duration of their HIV or AIDS process. Accordingly, this study has captured the diverse experiences these people face daily with taking their ARV medications. The results of this study have identified a number of issues that have been previously shown to be associated with non-adherence.

It has been previously found that the complexity of the medication regimen may affect adherence (Atlice and Friedland 1998; Gathe 1998; Levine 1998; Chesney 1997; Crespo-Fierro 1997; Deyo et al 1981). Regimens that contain a PI usually introduces changes in the number of pills taken per day, increase in frequency of medication and dietary restrictions. In this study, when specifically looking at individual PI medication, the majority of individuals who had soft gel saquinavir (Fortovase Roche®) as part of their regime admitted to missing doses, this figure was approaching statistical significance. We speculated that this could be attributed to the number of soft gel saquinavir pills, as the current recommended dose is 18 pills divided into three times a day. Given that this is possibly a fraction of the pill burden per day, the number of saquinavir may be enough to tip the scales in favour of non-adherence.

Adherence has been shown to be affected by the number of daily medications a person is prescribed. While Cramer (1996) questioned why many women fail to take their daily oral contraceptive pill, others concluded that fewer pills aid adherence (Rabkin and Chesney 1998; Chesney 1997). We identified that individuals taking between 11-30 pills per day were less likely to miss pills. Why this number of pills per day would incur a lesser degree of non-adherence is difficult to identify. For those taking more than 30 pills per day, perhaps the more complex regimens, greater than three types of ARV medications, incur a greater number of pills and may require a more focused approach to the medication regimen.

Individuals were most likely to miss their lunchtime dose, while a lesser percentage was missing their evening ARV doses. Possible reasons for this include commitments - if going out for the day a person may forget to take medications with them or may anticipate getting home in time to take medications but get held up and so miss this dose; a need for privacy -colleagues at work may not know the person is HIV positive and they may have some difficulty taking the medications in private; or forgetting - people become involved in daily events and simply forget their medications. Adherence to medication regimen can also impact on lifestyles and routines and require considerable adjustment of these. Lifestyle and daily routines are issues that should be incorporated into prescribing medication and discussing adherence.

We propose that the client should be encouraged to discuss lifestyle and routines when being prescribed ARV medication. In short, health care providers need at times to be flexible and creative in their education regarding medication adherence.

It has previously been found that a positive effect on adherence could be attributed to a client having confidence in that ARV medication is working (Cadman 1998; Levine 1998; Rabkin and Chesney 1998; Bundura 1982). The more confident the respondents considered they were in being able to take their medication as prescribed the more adherent they were. Future educational strategies need to include empowering the individual to have the confidence in themselves and improving the person's perception that they have the ability to take medications as prescribed.

Education concerning the effects of HIV on the immune system and its implication for disease progression, information on ARV medication including side effect profile, resistance and cross-resistance has been shown to have a positive effect on adherence (Cadman 1998). Ninety eight of the respondents considered they had been well educated by health care workers and believed they had a good to excellent knowledge of side effect profiles, a good understanding of viral load and CD4 levels and of resistance. Yet, 68% stated they missed ARV medication some of the time.

While previous studies have shown that regular medical follow up and support may possibly influence adherence, this was not found to be the case in our population (Levine 1998; Crespo-Fierro 1997; Williams 1997). However, a number of respondents in this study reported experiencing difficulty telling their doctors about missing medications. The main reason for not telling the doctor was that the subject 'did not think it was important because only a few doses were missed'. We have postulated that some people visit their doctors for specific concerns. Therefore, a multidisciplinary team approach may provide more avenues for the client to feel able to disclose and discuss issues concerning adherence.

'Partying' or taking recreational drugs was not found to have any effect on adherence. Alcohol was significant when assessing subjects missing their medication, although it was not an independent predictor to missing medication. Past experiences in our clinic have illustrated that some clients make an informed decision to omit medication when planning a night out that would involve drinking alcohol and/or recreational drugs, so as to avoid undesirable side effects.

In our cohort, 55 people were over 36 years of age, with those in the 36-45 age group more likely to miss medications than other age groups. While age has not been identified in this study as significantly affecting adherence, age has been identified in other research as having some affect on adherence with medication (Holzemer et al 1999; Cramer 1996; Singh et al 1996; Lee and Tam 1979). We did not identify any contributing factor, such as full-time work, as to why this age group

would be more likely to miss medication. On the basis that this population will continue to grow older it is important to identify the reasons for this age group missing medications, as with ageing the development of co-morbidities could incur an increase in the number of medications to be taken.

As shown in this study, forgetting accounts for 25% of the variance. Forty-one clients reported forgetting to take a drug some of the time. Forgetting medication has been highlighted in other studies on adherence; in this study we have identified forgetting as a major contributing factor for non-adherence (Weidle et al 1999; Gallant and Block 1998; Levine 1998; Nissele 1998; Crespo-Fierro 1997; Ungvarski 1997).

We are aware that some of the respondents use reminder devices such as diaries, watch alarms, notes around the house and dosette boxes. When respondents were asked to share experiences regarding HIV and medication, a number of subjects commented on the usefulness of dosette boxes and the need for alarms/watches, preferably those that could be set to alarm a number of times during the day.

There were several limitations to this study including the low number of female respondents thus possibly giving results some gender bias. Community clients were recruited to the study but we were unable to overcome this gender bias. An age bias may also be considered, as 68% of respondents were over 40 years of age. Issues pertaining to medications may be different in women and a younger age group. Newly diagnosed individuals were excluded from this study and may have specific needs initially when taking medications. Further research is warranted for these issues.

## CONCLUSION

Non-adherence is individual, it is not disease specific. While this study has illustrated some important aspects associated with non-adherence, it has also highlighted some possible strategies for assisting adherence. Adherence patterns need to be assessed in those who do not frequent specialist clinics for example: community based clients, women and women with children. As a consequence of the findings from this study, nurses have implemented changes in our clinic. We have increased our focus on assessing the clients' daily routine and suggesting memory aids for the individual to assist with adherence. This process also enables staff to support and follow-up adherence and other issues that may be important to the client. This follow-up is carried out in both the outpatient department and in the individual's home. While our education initiatives are more individually focused we need also to develop initiatives for the 35-44 age group

The future holds a number of concerns relating to adherence by people who are HIV positive. It had previously been stated that the risk associated with old age might not be an issue with HIV positive people (Metha et

al 1998), we believe this not to be the case. The consumption of more medication for illnesses such as hypertension and diabetes could open a Pandora's box of issues relating to non-adherence, not to mention drug interactions. Based on this premise, future compatibility of medications, number of medications and medication regimes could become an increasing dilemma for both the patients and health care providers. To assist our clients in obtaining and maintaining the quality of life they are aiming for, the need to assist them with adherence is of paramount concern for the health care provider if we are to make a positive impact on the clients' future.

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