AIDS Care

The influence of symptom experiences and attributions on adherence to highly active anti-retroviral therapy (HAART): a six-month prospective, follow-up study

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The influence of symptom experiences and attributions on adherence to highly active anti-retroviral therapy (HAART): a six-month prospective, follow-up study

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Objective. To examine changes in individuals' experiences of symptoms over the first six months of taking highly active anti-retroviral therapy (HAART) and to assess the impact of symptom experiences and attributions on adherence to HAART. *Methods*. A prospective study where consecutive HIV positive individuals initiating HAART completed validated questionnaires assessing their experiences of symptoms, depression, beliefs about HAART and adherence, before starting treatment and after one, three and six months of treatment. *Results*. Rates of low ($<95\%$) adherence to HAART increased over time ($p<0.001$). Overall, the number of HIV or HAART-related symptoms reported did not change significantly over follow-up. However, symptom experiences differed between those reporting high ($\geq95\%$) adherence and those reporting low adherence. Individuals reporting high adherence experienced a decrease in symptoms they attributed to HIV ($p<0.05$), and a decrease in the symptoms they attributed to HAART-side effects ($p<0.05$) over time. This decrease in symptoms over time was not seen among individuals reporting low adherence. A lack of symptomatic improvement was associated with increasing doubts about the continued necessity for HAART ($p<0.05$). *Conclusions*. The findings suggest that adherence to HAART is influenced by individuals' experiences of both HIV and HAART-related symptoms. Patients who experience persistent symptoms while on HAART may begin to doubt their continued need for treatment and respond by missing doses. These findings have implications for the development of evidence-based interventions to increase adherence.

Keywords: adherence; HIV; HAART; symptoms; side effects; treatment perceptions

Introduction

Highly active anti-retroviral therapy (HAART) has greatly reduced morbidity and mortality associated with HIV (Mocroft et al., 2003) however, low adherence seriously compromises the efficacy of this treatment (Paterson et al., 2000; Wood et al., 2003). Maintaining high levels of adherence over long-term often proves difficult (Golin et al., 2002; Gross, Bilker, Friedman, & Strom, 2001). Identifying antecedents of non-adherence is crucial in order to develop effective strategies to help people to achieve maximum benefit from HAART. While recent developments in the formulation of antiretroviral medicines have addressed some of the practical barriers to adherence, HAART continues to carry the risk of unpleasant or intolerable side effects. Even the most simple drug regimen may pose problems for adherence if it makes the individual feel worse or does not improve symptoms.

Symptoms are common among individuals receiving HAART (Bonfanti et al., 2000; Lucas, Chaisson, & Moore, 1999) and have been associated with both non-adherence (Ammassari et al., 2001; Chesney et al., 2000) and discontinuation of HAART (Mocroft et al., 2001; O'Brien, Clark, Besch, Myers, & Kissinger, 2003). In order to develop appropriate interventions, several methodological issues need to be addressed. Most studies to date have been cross-sectional and therefore it was not possible to determine the direction of associations between symptoms and non-adherence. Little is known about how symptoms change over time or what impact such changes have on adherence. Most studies failed to distinguish between treatment side effects and disease-related symptoms. We need to understand the subjective distinction between symptoms of disease and side effects of treatment in order to inform efforts to help individuals cope with symptoms and improve the management of side effects. Studies have not adjusted for the possible influence of depression in their analyses, yet depression is common among people with HIV (Ciesla & Roberts, 2001) and may impact on both symptom experiences (Watson & Pennebaker, 1989) and adherence (Ammassari et al.,

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2004). Finally, the mechanisms by which symptoms impact on adherence have not been adequately explored.

The self-regulatory model (SRM) (Leventhal & Cameron, 1987; Leventhal, Nerenz & Sraus, 1992) proposes that illness-related behaviours are influenced by the way in which individuals interpret their symptom experiences. Within this model, non-adherence is viewed as a "common sense" response to a lack of coherence between individuals' beliefs about the illness, their experience of symptoms and the doctor's instructions. A qualitative study provided support for this model (Siegel, Schrimshaw, & Dean, 1999), with individuals reporting that they missed doses of their antiretroviral treatment in order to avoid side effects, and were prepared to accept the consequence of reduced clinical benefit.

Horne (1997, 2003) proposed a method for operationalising the SRM to explain variations in adherence to medication. He suggests that adherence is influenced by the way in which the individuals judge their personal need for treatment relative to their concerns about potential adverse effects. These judgements are influenced by the individual's perception of their illness and their interpretation of symptom experiences. Previous research in a range of conditions including HIV (Aikens, Nease, Nau, Klinkman & Schwenk, 2005; Brown et al., 2005, Horne & Weimnan, 2002; Horne et al., 2004, 2007; Llewellyn, Miners, Lee, Harrington & Weinman, 2003; Neame & Hammond, 2005) has provided support for the necessity-concerns framework (NCF) in relation to adherence, however, little is known about how patients' experiences of symptoms impact on their beliefs about HAART.

The aims of this study were to (1) explore individuals' differential attributions of symptoms to HIV or HAART; (2) explore changes in subjective experiences of HIV and HAART-related symptoms over time; and (3) examine associations between symptoms and beliefs about HAART over time.

Methods

Design

Patients attending an outpatient HIV clinic in Brighton, UK, completed validated questionnaires assessing their adherence, experiences of symptoms and beliefs about HAART before initiating treatment (0M) and after one (1M), three (3M) and six months (6M). Data was collected between January 2000 and May 2004.

Participants

Patients were eligible for the study if they were *not* currently taking antiretroviral medication. Participants were followed up over a year, and those who subsequently accepted a clinically indicated offer of HAART formed the sample for this study. Exclusion criteria included having insufficient understanding of English or being too ill to complete the study questionnaires.

Procedure

Consecutive study-eligible individuals were referred by their HIV physician to a research assistant. Standard procedures for consent were followed. Researchers attended weekly clinical meetings to identify participants who were eligible for a HAART recommendation on the basis of contemporaneous guidelines (British HIV Association, 1997, 2001, 2003). Following a treatment recommendation, participants were given a questionnaire booklet to complete along with a stamped addressed envelope. Medical files and pharmacy records were consulted to identify those who initiated HAART. These participants were sent follow-up questionnaires one month (1M), three months (3M) and six months (6M) after initiating treatment. Telephone reminders were administered to optimise response rates.

Measures

Adherence

Adherence to HAART was measured using the Medication Adherence Self Report Inventory (MASRI) (Walsh, Mandalia & Gazard, 2002). Participants were asked to estimate on a visual analogue scale of 0–100 the percentage of medication they had taken as prescribed over the previous month. Participants who reported taking less than 95% of HAART medicines were allocated to a "low adherence" group, and those taking 95% or more of their medication as prescribed allocated to a "high adherence" group (Paterson et al., 2000).

Symptom experiences and attributions

Symptom experiences were assessed using the *Identity* subscale of the Illness Perceptions Questionnaire (IPQ) (Moss-Morris et al., 2002; Weinman, Petrie, Moss-Morris & Horne, 1996) comprising 11 "core" symptoms common to a variety of illnesses and modified by the addition of 12 common HIV/HAART-related symptoms. There were two symptom scales, each comprising the same 23 symptoms. On one list, participants were asked to rate only those

symptoms they believed to result from HIV. On a second list, participants were asked to rate only those symptoms they associated with HAART. The scoring was conducted by first asking whether the person was experiencing the symptom (yes/no) and second, by asking the participants to rate the severity of each symptom they experienced on a scale of 1–5, where 1 = very mild, 2 = mild, 3 = moderate, 4 = severe, 5 = very severe. To ensure that only symptoms that were troublesome to the individual were included, only scores rated 3–5 were used in the analyses, thereby excluding symptoms rated as "mild" or "very mild". Possible scores ranged from 0 to 23, representing the number of symptoms the patient perceived to be moderate, severe or very severe.

Beliefs about HAART

Beliefs about HAART were assessed using the Beliefs about Medicines Questionnaire-HAART specific version (BMQ-HAART) (Horne, Weinman & Hankins, 1999; Horne et al., 2004, 2007). The BMQ-HAART comprises two scales: a HAART-*necessity* scale assessing individuals' perceptions of their personal need for HAART for controlling HIV and maintaining health, and a HAART-*concerns* scale, assessing concerns about potential adverse effects of HAART (e.g. worries about short and long-term side effects and concerns about the disruptive effects of the HAART regimen on daily life). These were derived from studies of patients' perceptions of HAART (Cooper et al., 2002; Horne et al, 2004).

Participants were presented with a series of statements and asked to rate their level of agreement with each item on a scale, where responses ranged from strongly agree (scored 5) to strongly disagree (scored 1). Scores for individual items within each scale were summed. A mean score was computed by dividing each total by the number of items, giving a range of one to five for both necessity and concerns scales.

Depression

The depression subscale of the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983) was used to measure patients' experience of depressive symptoms over the previous month. Possible total scores range from 0 to 21, with higher scores indicating greater depression.

Clinical and demographic data

Clinical and demographic information, including age, sex, employment status, HIV acquisition risk, number of years since first HIV diagnosis, symptom classification (asymptomatic HIV, symptomatic HIV or AIDS), whether the person had previously been prescribed antiretroviral treatment, CD4 count and viral load (log_{10}), was extracted from participants' medical files.

Statistical methods

Data were analysed using SPSS® 12.0 (SPSS Inc, Chicago, Ill). Clinical and demographic characteristics were compared between those who completed the study and those with missing data, using chi-square tests for categorical data and independent samples *t*-tests for continuous variables. Clinical and demographic associations with adherence were also examined in this way. NcNemar's test was used to compare the number of patients reporting low adherence at 1M and 6M. The frequency of individual symptoms was compared between high and low adherence groups using chi-square tests. Repeated measures ANCOVA was used to assess changes in symptom experiences over time and the impact of these changes on adherence at 6M, controlling for clinical variables that were associated with adherence in the univariate analyses (prior antiretroviral use and time since HIV diagnosis), baseline depression and adherence at 1M and 3M. Estimated marginal means (EMMs) were plotted. Associations between changes in symptoms and medication beliefs were assessed using Pearson's correlations and residualised change scores between baseline and six months measures (Cohen & Cohen, 1983).

Results

Subjects

One hundred and twenty participants initiated HAART. Over the follow-up, 10 participants stopped treatment, two died, 10 were lost to follow up and 18 missed one or more follow-up assessment or returned questionnaires with missing data (Figure 1). Eighty participants (66.7%) provided the data for this study.

Clinical and demographic characteristics of the sample are shown in Table 1.

Validity of adherence measure

Fifty-nine (96.7%) of those reporting high adherence at one month had an undetectable viral load (< 50 copies/ml) at six months compared to 16 (84.2%) of those reporting low adherence ($\chi^2 = 3.87$, $p < 0.05$).

Predictors of adherence

The number of participants reporting low adherence increased from 5 (6.3%) at 1M to 17 (21.3%) at 6M (McNemar's test: $p < 0.001$). Low adherence at 6M was associated with having been diagnosed for a
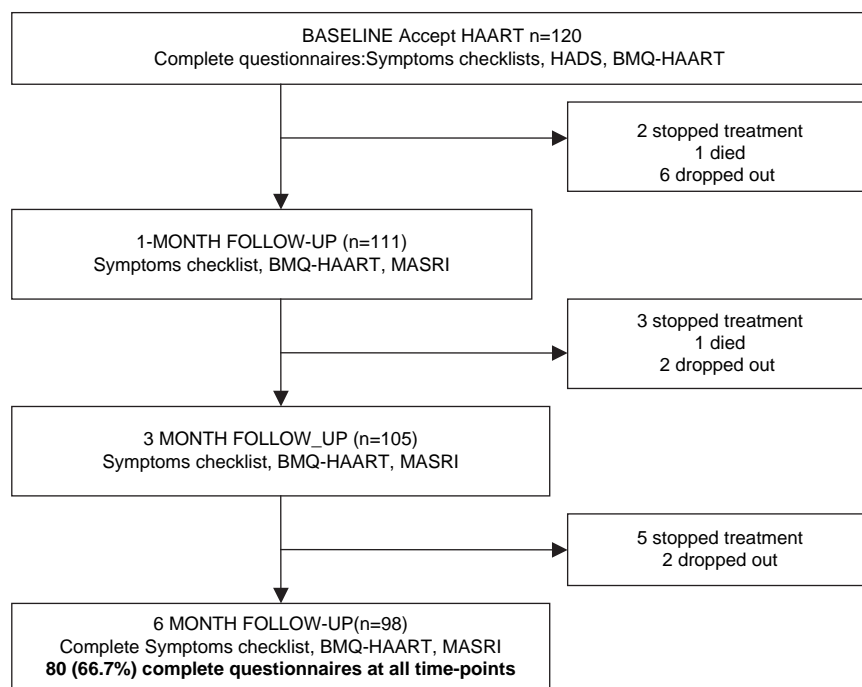
Figure 1. Study design and attrition.

longer time (F (1,79) = 5.94, $p < 0.05$) and having previously been prescribed antiretroviral medication ($\chi^2 = 10.6$, $p < 0.001$).

Symptom attributions and impact on adherence

The 12 symptoms (rated moderate-severe) most commonly attributed to HIV and HAART at 6M are shown in Figure 2. No individual symptoms were

more frequently attributed to HIV or HAART (McNemar's test, all $p > 0.05$).

Symptoms attributed to HIV

At baseline, 66 (82.5%) participants reported ≥ 1 moderate-severe symptom they attributed to HIV. The number of symptoms reported ranged from 0 to 21 (mean = 5.1, SD = 4.5). At 6M, 42 (58.8%) participants reported ≥ 1 moderate to severe symptom

Table 1. Sample demographics and clinical characteristics.

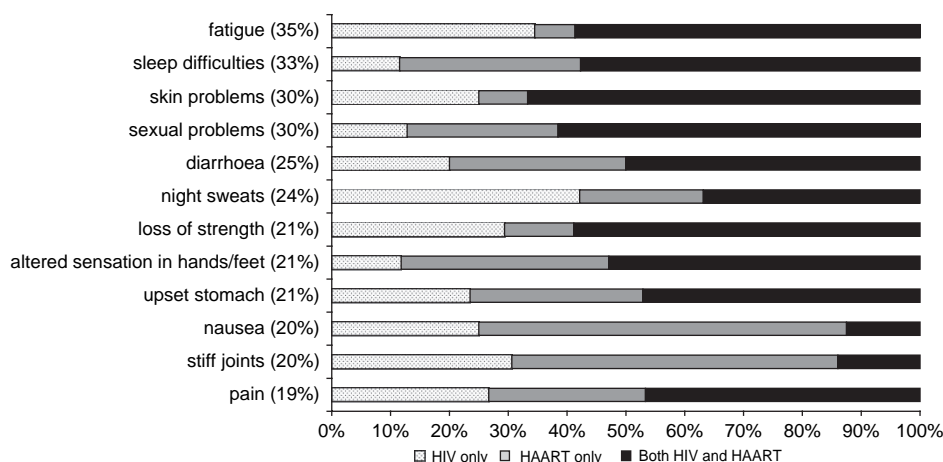| Baseline clinical/demographic feature		Completed study $n = 80$	Missing data $n = 40$	P
Age (years)	**Mean (SD)**	**40.0 (8.7)**	**34.0 (6.1)**	**< 0.001**
Transmission risk: gay man	n (%)	74 (92.5)	34 (85.0)	> 0.1
White British	n (%)	70 (87.5)	27 (77.1)	> 0.1
Years since HIV diagnosis	Mean (SD)	4.1 (4.2)	4.5 (5.0)	> 0.1
Asymptomatic HIV	n (%)	25 (31.3)	12 (30.0)	> 0.1
Symptomatic HIV	n (%)	36 (45.0)	15 (37.5)	> 0.1
AIDS	n (%)	19 (23.8)	13 (32.5)	> 0.1
Prior experience of ART	***n* (%)**	**22 (27.5)**	**22 (55.0)**	**< 0.005**
CD4 count (mm^{-3}/L)	Mean (SD)	204 (131)	176 (124)	> 0.1
Viral load ($\log_{10}$ copies/ml)	Mean (SD)	5.3 (0.5)	5.3 (0.5)	> 0.1
Moderate-severe symptoms (HIV)	Mean (SD)	5.1 (4.6)	5.6 (5.0)	> 0.1
HAART-necessity	**Mean (SD)**	**4.0 (0.5)**	**3.6 (0.6)**	**< 0.001**
HAART-concerns	Mean (SD)	3.0 (0.6)	3.2 (0.6)	> 0.05
HADS-depression	**Means (SD)**	**5.2 (4.3)**	**7.5 (4.7)**	**< 0.01**

Figure 2. Causal attribution of moderate-severe symptoms to HIV, HAART or both at six months.

they attributed to HIV, the number ranged from 0 to 17 (mean = 3.0, SD = 4.2).

Symptoms attributed to HAART-side effects

At 1M, 59 (73.8%) participants reported ≥1 moderate to severe symptom they attributed to HAART. The number of symptoms reported ranged from 0 to 17 (mean = 3.8, SD = 4.3). At 6M, 47 (58.8%) of participants reported ≥1 moderate to severe symptom they attributed to HAART. The number of symptoms ranged from 0 to 17 (mean = 3.2, SD = 4.4).

Relationships between symptom experiences and adherence

In cross-sectional analyses assessing the relationships between symptom experiences and adherence at six months, a greater number of symptoms associated with both HIV ($t(78) = 2.249$, $p < 0.05$) and HAART ($t(78) = 2.490$, $p < 0.05$) were associated with low adherence. Individual HAART-related symptoms associated with low adherence were night-sweats ($p < 0.01$) and sexual problems ($p < 0.001$). Individual HIV-related symptoms associated with low adherence were: fatigue ($p < 0.01$), sleep difficulties and altered sensation in hands or feet (all $p < 0.05$).

In repeated measures analysis, there was no significant main effect of time ($F(1,66) = 0.17$, $p > 0.1$) or group ($F(1,66) = 0.11$, $p > 0.1$) on HIV-related symptoms. There was, a significant group by time interaction ($F(1,66) = 5.0$, $p < 0.05$). Figure 3 shows the main effects and interaction (also reported in Table 2).

There was no significant main effect of time ($F(1,66) = 0.03$, $p > 0.1$) or group ($F(1,66) = 1.07$, $p > 0.1$) on HAART-side effects. There was a significant group by time interaction ($F(1,66) = 4.1$,

$p < 0.05$). Figure 4 shows the main effects and interaction (also reported in Table 2).

Associations between symptoms and beliefs about HAART

There was a significant inverse correlation between changes in symptom experiences and changes in necessity scores over time (HIV-symptoms $r = -0.22$, $p < 0.05$; HAART symptoms $r = -0.22$, $p < 0.05$), consistent with an increase in symptoms being associated with a decrease in perceived necessity for HAART. Neither the change in HIV symptoms ($r = 0.09$, $p > 0.1$) nor change in HAART symptoms ($r = 0.14$, $p > 0.1$) had a significant impact on individuals' concerns about HAART.
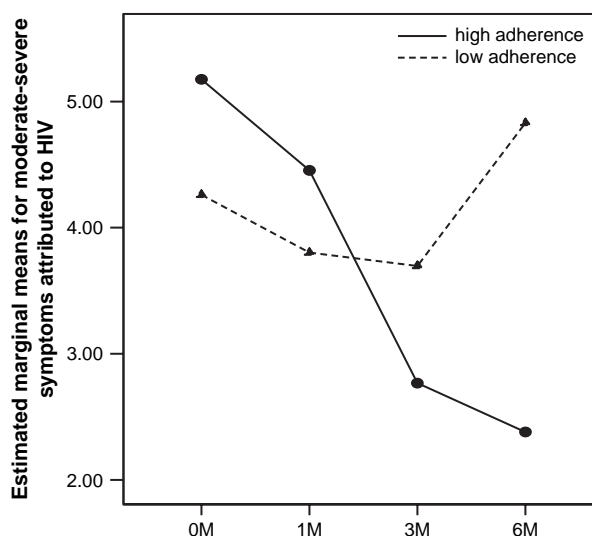

Figure 3. Adjusted means for number of HIV symptoms reported.

Table 2. Adjusted means for number of HIV and HAART symptoms reported. The adjusted mean is the value of the group mean adjusted for prior treatment experience, time since diagnosis, baseline depression and adherence at 1M and 3M.

Moderate-severe HIV-related symptoms

Adherence group	Follow-up	Mean	95% CI
High	baseline	5.1	4.0–6.2
High	one month	4.3	3.0–5.6
High	three months	2.7	1.8–3.7
High	six months	2.4	1.4–3.4
Low	baseline	4.3	1.4–7.1
Low	one month	3.9	0.7–7.0
Low	three months	3.7	1.3–7.2
Low	six months	4.9	2.3–7.4

Moderate-severe HAART-related symptoms

Adherence group	Follow-up	Mean	95% CI
High	one month	3.8	2.9–4.8
High	three months	2.5	1.5–3.4
High	six months	2.6	1.6–3.6
Low	one month	4.0	1.6–6.3
Low	three months	3.8	1.5–6.1
Low	six months	5.0	2.6–7.4

Discussion

Low adherence to HAART was associated with changes in individuals' subjective experiences of symptoms over time. People who experienced a lack of improvement in either the symptoms they attributed to

Figure 4. Adjusted means for number of HAART symptoms reported.

HIV or to HAART over the first six months of treatment were more likely to report low adherence.

The results are consistent with previous findings linking symptoms to non-adherence to HAART (Ammassari et al., 2001, Carrieri et al., 2001; Chesney et al., 2000; Duran et al., 2001; Gifford et al., 2000) and provide further insight into the nature of these relationships. First, they show that the pattern of relationships between symptom experiences and adherence was similar with respect to both HIV and HAART-related symptoms. This finding is consistent with the SRM (Leventhal et al., 1982, 1987) suggesting that low adherence results from a lack of coherence between patients' expectations of treatment and their experience of symptoms. Second, the findings suggest a possible pathway through which symptom experiences may impact on adherence. In line with the model proposed by Horne (1997, 2003), they suggest that individuals who experience persistent symptoms after initiating HAART may begin to doubt their need for HAART and respond with low adherence. Third, we showed that the results were unlikely to be an artefact due to depressed mood. Finally, the fact that relationships between symptoms and adherence remained statistically significant when earlier adherence was controlled for in the analysis is consistent with the experience of persistent side effects leading to non-adherence, rather than symptoms being the result of earlier non-adherence.

This study has several limitations. The sample consisted of predominately gay men. In order to be representative of the wider HIV positive population in the UK, the study should be replicated among other groups. Those who provided data were significantly older and more likely to be antiretroviral naïve than the overall study sample. Since younger age (Carrieri et al., 2001; Moatti et al., 2000) and having prior experience of antiretroviral treatment (Duran et al., 2001; Mannheimer, Friedland, Matts, Child & Chesney, 2002) have previously been associated with non-adherence, it is likely that non-adherence was underestimated in this study. The symptom measure did not encompass the wide spectrum of symptoms that may be experienced by people living with HIV and those using HAART (e.g. CNS disturbance). It is therefore possible that some participants could have been experiencing one or more severe symptom that was not covered by the measure. Furthermore, we did not explore experiences of side effects that occur with longer-term use of HAART, such as lipodystrophy. Depressed mood was measured only at baseline. In order to fully control for the possible influence of depression on self-reported symptoms and adherence, future studies should control for depression at every time-point.
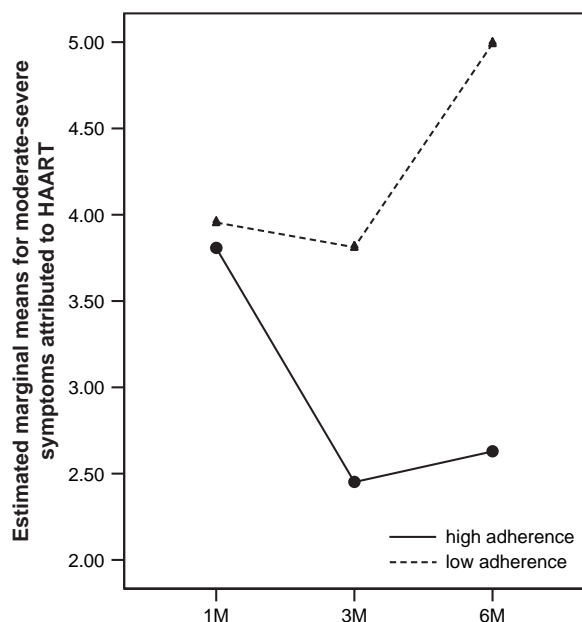
The study relied heavily on self-report measures, including a self-report measure of adherence, which may be subject to a positive bias. Future studies, using objective measures of adherence are required.

The results of this study only represent two thirds of the participants originally recruited; those who remained in the study and on treatment for six months, and who provided complete data at every follow-up. It is therefore likely that the sample was biased in terms of high adherence.

Although our adherence categorisation was significantly related to viral suppression, with almost all (97%) of those in the high adherence group attaining a viral load <50 copies/ml at the six month follow-up, 84% of those in the low adherence group also had an undetectable viral load. In setting our cut-off point for high adherence we adopted the convention of 95%, current at the time the study was conducted (Paterson et al., 2000). More recent studies suggest that viral suppression may be achieved at lower rates of adherence to boosted protease inhibitor (Gross et al., 2006) and NNRTI-based regimens (Bangsberg, 2006).

Despite these limitations, our findings support the idea that non-adherence stems from incongruence between individuals' expectations and experiences of HAART and are consistent with the theory that symptom experiences influence beliefs about treatment (Horne, 1997, 2003). Specifically, they suggest that experiencing persistent symptoms attributed to HIV or developing persistent symptoms related to HAART leads individuals to doubt their continued need for HAART and this has been previously associated with non-adherence (Horne et al., 2007). Furthermore studies, with larger samples, are required in order to fully test possible mediational relationships between symptoms, beliefs about HAART and adherence.

Our findings are relevant to clinical practice and the design of interventions to promote adherence to HAART. Intervening to alleviate symptoms may be an economical and clinically relevant way to optimise adherence. Siegel, Schrimshaw, and Dean (1999) found that individuals tended to resort to non-adherence before discussing symptoms with their clinicians. Clinicians should encourage patients to report any new symptoms so that the likely cause, duration and possible treatment of each can be discussed. It should be noted that symptoms are subjective experiences, and those that are not considered to be clinically significant may be perceived as severe by the patient. Indeed, previous studies found that low adherence was associated with patients' perceptions of symptoms, but not by physician estimates of symptoms (Carrieri et al., 2001; Duran et al., 2001) and that providers underestimated the presence and intensity of symptoms (Justice, Rabeneck, Hays, Wu & Bozzette, 1999). Furthermore, adherence may be increased by interventions which enhance individuals' perceptions of their continued necessity for HAART in the context of persistent HAART-side effects. Finally, the relationships identified in this study emphasise the need to continually develop new and better drugs, which have fewer side effects and thereby facilitate adherence.

References

Aikens, J.E., Nease, D.E., Jr., Nau, D.P., Klinkman, M.S., & Schwenk, T.L. (2005). Adherence to maintenance-phase antidepressant medication as a function of patient beliefs about medication. *Annals of Family Medicine*, *3*, 23–30.

Ammassari, A., Antinori, A., Aloisi, M.S., Trotta, M.P., Murri, R., Bartoli, L., et al. (2004). Depressive symptoms, neurocognitive impairment, and adherence to highly active antiretroviral therapy among HIV-infected persons. *Psychosomatics*, *45*(5), 394–402.

Ammassari, A., Murri, R., Pezzotti, P., Trotta, M.P., Ravasio, L., De Longis, P., et al. (2001). Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection. *Journal of Acquired Immune Deficiency Syndromes*, *28*(5), 445–449.

Bangsberg, D.R. (2006). Less than 95% adherence to nonnucleoside reverse-transcriptase inhibitor therapy can lead to viral suppression. *Clinical Infectious Diseases*, *43*(7), 939–941.

Bonfanti, P., Valsecchi, L., Parazzini, F., Carradori, S., Pusterla, L., Fortuna, P., et al. (2000). Incidence of adverse reactions in HIV patients treated with protease inhibitors: A cohort study. Coordinamento Italiano Studio Allergia e Infezione da HIV (CISAI) Group. *Journal of Acquired Immune Deficiency Syndromes*, *23*(3), 236–245.

British HIV Association (BHIVA). (1997). Guidelines Co-ordinating Committee. British HIV association guidelines for antiretroviral treatment of HIV seropositive individuals. *Lancet*, *349*(9058), 1086–1092.

British HIV Association (BHIVA). (2001). Guidelines for the treatment of HIV-infected adults with antiretroviral therapy. *HIV Medicine*, *2*(4), 276–313.

British HIV Association (BHIVA). (2003). Guidelines for the treatment of HIV-infected adults with antiretroviral therapy. *HIV Medicine*, *4*(Suppl. 1), 1–14.

Brown, C., Battista, D.R., Bruehlman, R., Sereika, S.S., Thase, M.E., & Dunbar-Jacob, J. (2005). Beliefs about antidepressant medications in primary care patients: Relationship to self-reported adherence. *Medical Care*, *43*, 1203–1207.

Carrieri, P., Cailleton, V., Le Moing, V., Spire, B., Dellamonica, P., Bouvet, E., et al. (2001). The dynamic of adherence to HAART: Results from the French

National APROCO cohort. *Journal of Acquired Immune Deficiency Syndromes*, 28(3), 232–239.

Chesney, M.A., Ickovics, J.R., Chambers, D.B., Gifford, A.L., Neidig, J., Zwickl, B., et al. (2000). Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: The AACTG adherence instruments. Patient Care Committee & Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG). *AIDS Care*, 12(3), 255–266.

Ciesla, J.A., & Roberts, J.E. (2001). Meta-analysis of the relationship between HIV infection and risk for depressive disorders. *American Journal of Psychiatry*, 158(5), 725–730.

Cohen, J., & Cohen, P. (1983). *Applied multiple regression.* Hillsdale, NJ: Erlbaum.

Cooper, V., Buick, D., Horne, R., Lambert, N., Gellaitry, G., Leake, H., et al. (2002). Perceptions of HAART among gay men who have declined a treatment offer: Preliminary results from an interview-based study. *AIDS Care*, 14(3), 319–328.

Duran, S., Spire, B., Raffi, F., Walter, V., Bouhour, D., Journot, V., et al. (2001). Self-reported symptoms after initiation of a protease inhibitor in HIV-infected patients and their impact on adherence to HAART. *HIV Clinical Trials*, 2(1), 38–45.

Gifford, A.L., Bormann, J.E., Shively, M.J., Wright, B.C., Richman, D.D., & Bozzette, S.A. (2000). Predictors of self-reported adherence and plasma HIV concentrations in patients on multidrug antiretroviral regimens. *Journal of Acquired Immune Deficiency Syndromes*, 23(5), 386–395.

Golin, C., Liu, H., Hays, R.D., Miller, L.G., Beck, C.K., Ickovics, J., et al. (2002). Prospective study of predictors of adherence to combination antiretroviral medication. *Journal of General Internal Medicine*, 17, 756–765.

Gross, R., Bilker, W.B., Friedman, H.M., & Strom, B.L. (2001). Effect of adherence to newly initiated antiretroviral therapy on plasma viral load. *AIDS*, 15, 2109–2117.

Gross, R., Yip, B., Wood, E., Bangsberg, D., Montaner, J., & Hogg, R. (2006, February 5–8). *Boosted PI are more forgiving of suboptimal adherence than non-boosted PI or NNRTI.* 13th Conference on Retroviruses and Opportunistic Infections, Denver, Colorado.

Horne, R. (1997). Representations of medication and treatment: Advances in theory and measurement. In K.J. Petrie & J.A. Weinman (Eds.), *Perceptions of health and illness: Current research and applications* (pp. 155–188). London: Harwood Academic Press.

Horne, R. (2003). Treatment perceptions and self regulation. In L.D. Cameron & H. Leventhal (Eds.), *The self-regulation of health and illness behaviour* (pp. 138–153). London: Routledge.

Horne, R., Buick, D., Fisher, M., Leake, H., Cooper, V., & Weinman, J. (2004). Doubts about necessity and concerns about adverse effects: Identifying the types of beliefs that are associated with non-adherence to

HAART. *International Journal of STD and AIDS*, 15, 38–44.

Horne, R., Cooper, V., Gellaitry, G., Leake Date, H., & Fisher, M. (2007) Patients' perceptions of HAART in relation to treatment uptake and adherence: The utility of the necessity-concerns framework. *Journal of Acquired Immune Deficiency Syndromes*, 45(3), 334–41.

Horne, R., & Weinman, J. (2002). Self regulation and self management in asthma: Exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. *Psychology and Health*, 17, 17–32.

Horne, R., Weinman, J., & Hankins, M. (1999). The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health*, 14, 1–24.

Justice, A.C., Rabeneck, L., Hays, R.D., Wu, A.W., & Bozzette, S.A. (1999). Sensitivity, specificity, reliability, and clinical validity of provider-reported symptoms: A comparison with self-reported symptoms. Outcomes Committee of the AIDS Clinical Trials Group. *Journal of Acquired Immune Deficiency Syndromes*, 21(2), 126–133.

Leventhal, H., & Cameron, L. (1987). Behavioural theories and the problem of compliance. *Patient Education and Counselling*, 10, 117–138.

Leventhal, H., Diefenbach, M., & Leventhal, E.A. (1992). Illness cognition: Using common sense to understand treatment adherence and affect cognition interactions. *Cognitive Therapy and Research, 16*, 143–163.

Leventhal, H., Nerenz, D.R., & Sraus, A. (1982). Self regulation and the mechanisms for symptom appraisal. In D. Michanic (Ed.), *Symptoms, illness behavior and help seeking* (pp. 55–86). New York: Watson Academic.

Llewellyn, C., Miners, A., Lee, C., Harrington, C., & Weinman, J. (2003). The illness perceptions and treatment beliefs of individuals with severe haemophilia and their role in adherence to home treatment. *Health Psychology*, 18, 185–200.

Lucas, G.M., Chaisson, R.E., & Moore, R.D. (1999). Highly active antiretroviral therapy in a large urban clinic: Risk factors for virologic failure and adverse drug reactions. *Annals of Internal Medicine*, 131(2), 81–87.

Mannheimer, S., Friedland, G., Matts, J., Child, C., & Chesney, M. (2002). The consistency of adherence to antiretroviral therapy predicts biologic outcomes for human immunodeficiency virus-infected persons in clinical trials. *Clinical Infectious Diseases*, 34(8), 1115–1121.

Moatti, J.P., Carrieri, M.P., Spire, B., Gastaut, J.A., Cassuto, J.P., & Moreau, J. (2000). Adherence to HAART in French HIV-infected injecting drug users: The contribution of buprenorphine drug maintenance treatment. The Manif 2000 study group. *AIDS*, 14(2), 151–155.

Mocroft, A., Ledergerber, B., Katlama, C., Kirk, O., Reiss, P., d'Arminio Monforte, A., EuroSIDA study group.

(2003). Decline in the AIDS and death rates in the EuroSIDA study: An observational study. *Lancet, 362*, 22–29.

Mocroft, A., Youle, M., Moore, A., Sabin, C., Madge, S., Lepri, A., et al. (2001). Reasons for modification and discontinuation of antiretrovirals: Results from a single treatment centre. *AIDS, 15*(2), 185–194.

Moss-Morris, R., Weinman, J., Petrie, K.J., Horne, R., Cameron, L., & Buick, D. (2002). The revised illness perception questionnaire (IPQ-R). *Psychology and Health, 17*(1), 1–16.

Neame, R., & Hammond, A. (2005). Beliefs about medications: A questionnaire survey of people with rheumatoid arthritis. *Rheumatology, 44*, 762–767.

O'Brien, M.E., Clark, R.A., Besch, C., Myers, L., & Kissinger, P. (2003). Patterns and correlates of discontinuation of the initial HAART regimen in an urban outpatient cohort. *Journal of Acquired Immune Deficiency Syndromes, 34*(4), 407–414.

Paterson, D.L., Swindells, S., Mohr, J., Brester, M., Vergis, E.N., Squier, C., et al. (2000). Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine, 133*(1), 21–30.

Siegel, K., Schrimshaw, E.W., & Dean, L. (1999). Symptom interpretation: Implications for delay in HIV testing and care among HIV-infected late middle-aged and older adults. *AIDS Care, 11*(5), 525–535.

Walsh, J.C., Mandalia, S., & Gazzard, B.G. (2002). Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. *AIDS, 16*(2), 269–277.

Watson, D., & Pennebaker, J.W. (1989). Health complaints, stress, and distress: Exploring the central role of negative affectivity. *Psychological Review, 96*(2), 234–254.

Weinman, J., Petrie, K., Moss-Morris, R., & Horne, R. (1996). The illness perception questionniare: A new method for assessing the cognitive representation of illness. *Psychology and Health, 11*, 431–445.

Wood, E., Hogg, R.S., Yip, B., Harrigan, P.R., O'Shaughnessy, M.V., & Montaner, J.S. (2003). Effect of medication adherence on survival of HIV-infected adults who start highly active antiretroviral therapy when CD4 count is 0.200–0.350 × 10 (9) cells/L. *Annals of Internal Medicine, 39*(10), 810–816.

Zigmond, A.S., & Snaith, R.P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandanavica, 67*(6), 361–370.