Depression and clinical progression in HIV-infected drug users treated with highly active antiretroviral therapy

Anne-Déborah Bouhnik1, Marie Préau1,2, Emmanuelle Vincent1, Maria Patrizia Carrieri1, Hervé Gallais3, Gérard Lepeu4, Jean-Albert Gastaut5, Jean-Paul Moatti1, Bruno Spire1* and the MANIF 2000 Study Group

1INSERM U379/ORS-PACA, Marseilles, France
2University Aix-Marseille I, Aix en Provence, France
3Hôpital de la Conception, Marseilles, France
4Avignon Hospital, Avignon, France
5Department of Haematology, Institut Paoli-Calmettes and Day Care Unit, Hôpital Sainte Marguerite, Marseilles, France

*Corresponding author: Tel: +33 4 9610 2877; Fax: +33 4 9610 2899; E-mail: spire@marseille.inserm.fr

Objective: To disentangle the impact of adherence from that of injecting drug status and depressive syndrome on HIV clinical progression in a cohort of highly active antiretroviral therapy (HAART)-treated HIV patients infected through drug use.

Design: MANIF 2000 is a French cohort of HIV-infected drug users with scheduled medical visits every 6 months. Only patients enrolled in the MANIF 2000 cohort who had a CD4 cell count >200 cells/µl at HAART initiation were selected. The follow-up period included all post-HAART initiation visits.

Methods: HIV clinical progression was defined as either AIDS-related death or reaching a CD4 level <200 cells/µl. Adherence was assessed using a self-administered questionnaire and a structured face-to-face interview. Depressive symptoms were evaluated by a Center for Epidemiologic Studies Depression Scale (CES-D) score at each visit. Cox proportional hazards model was used to calculate crude and adjusted relative hazards and 95% confidence intervals and thus identify independent predictors of clinical progression.

Results: Of the 305 HAART-treated patients in the cohort, 243 had CD4 cell count >200 cells/µl at HAART initiation.

At the first visit after HAART initiation, median CD4 cell count was 466 cells/µl and 45% had undetectable viral load. Injecting drug users accounted for 17% of the study group. Over the follow-up period, 32 patients experienced HIV clinical progression. Probable depression was encountered in 46% of patients and non-adherence in 31% of the sample. After adjustment on baseline CD4 cell count, predictors of clinical progression were: having a higher level of cumulative non-adherence over the follow-up period [HR (95% CI)=1.2 (1.1–1.3) per 10% increase] and having a high score of depressive symptoms following HAART initiation [HR (95% CI)=5.3 (2.21–3.0)].

Conclusions: Although depressive syndrome is known to influence non-adherence behaviours that are amongst the major reasons for clinical progression, it is also a predictor of clinical progression in HIV-infected intravenous drug users on HAART, independently of non-adherence behaviours. HIV care providers should be more sensitive to depressive symptoms in order to detect them early and supply HIV patients with specific care. Further research is needed to determine whether treating depressive symptoms may improve adherence and thus delay disease progression and mortality.

Introduction

HIV patients infected through drug use represent a vulnerable population among HIV patients. They are thus less likely to be prescribed HAART, are presumed to be less adherent to antiretroviral therapy and are more subject to depressive syndrome [1–4] in comparison with other HIV patients.

Poor adherence has been shown to predict HIV disease progression [5] and has been associated with active drug use [6,7] and depressive syndrome [8,9]. These two factors may, however, have an effect on HIV clinical progression independently of non-adherence behaviours, in particular through their impact on the immune response of patients. Several studies have looked at the impact of injecting drug status on HIV disease progression and have resulted in discordant findings [1,2,10]. Conflicting results were also obtained when considering response to treatment adjusted on adherence to antiretroviral therapy.
Depressive syndrome, on the other hand, has been associated with disease progression and mortality [11,12], although other researchers have reported no association [15]. It is noteworthy that depression was not assessed simultaneously with adherence behaviours in these studies.

The present study was carried out to assess the role of psychological and socio-behavioural factors on clinical progression in individuals HIV-infected through injecting drug use (MANIF 2000 cohort study). More specifically, its main objective was to disentangle the effect of adherence from that of injecting drug status and depressive syndrome on HIV disease progression in the HAART era, while adjusting for relevant clinical and psychosocial factors.

Material and methods

MANIF 2000 is a cohort that enrolled 467 patients HIV-infected through injecting drug use. Its focus was the social and behavioural characteristics of HIV-positive patients who are intravenous drug users (IDUs). Medical visits were scheduled every 6 months [16,17].

At each visit, patients were asked to undergo a face-to-face interview detailing their experience with HIV infection. Patients were also asked to complete a standardized self-administered questionnaire that explored the use of illicit or psychotropic drugs and their psychosocial conditions.

The present study was conducted on patients initiating HAART with a CD4 cell count >200 cells/µl, who were on stage A or B of HIV disease and who had at least 1 year of follow-up data available while on HAART. All visits following HAART initiation were considered. Early virological response was defined as having undetectable viral load (<200 copies/ml) at the first visit after HAART initiation. HIV clinical progression was defined as either experiencing an AIDS-related event or reaching a CD4 level <200 cells/µl.

Material

At each visit, patients were classified according to their injecting drug status: patients who declared having injected at least once in the prior 6 months were defined as active drug users. The proportion of active drug users was calculated at each follow-up visit; the binomial distribution was used to compute the 95% confidence interval for this proportion at each visit.

Information about adherence to antiretroviral (ARV) therapy was collected in the self-administered questionnaire and the structured face-to-face interview. At a given visit, patients were considered ‘non-adherent’ if they reported in the face-to-face interview that they took less than 80% of the total dose of ARV drug prescribed during the week prior to the visit and/or if they reported in the self-administered questionnaire that they had not been ‘totally adherent’ to HAART during the same period [6]. A longitudinal measure of non-adherence was computed as the proportion of visits at which non-adherence was reported over the whole follow-up period.

Depression was measured using the French version of the Center for Epidemiologic Studies Depression Scale (CES-D) [18], which is a 20-item scale commonly used in population-based studies [19], particularly in studies involving HIV-infected patients [20,21]. Although not a diagnostic of clinical depression, a score of 16 or more is considered indicative of significant depressive symptoms [19]. In the present analysis, depression was assessed with three variables: i) a dichotomous variable using the complete CES-D score with 16 as a cutoff point, ii) a continuous variable using the complete CES-D score and iii) a continuous variable using the non-somatic CES-D score [22,23]. Similarly to adherence, a longitudinal measure of depression was calculated as the proportion of visits at which a CES-D score of 16 or more was obtained over the whole follow-up period.

Statistical methods

The association between adherence at first visit and early virological response was tested using a chi-squared test in order to validate the measure of adherence.

The impact of depression, adherence (longitudinal or at first visit), injecting status as well as other patient characteristics on HIV clinical progression was assessed using survival analysis. Patients who did not experience HIV clinical progression until the last visit in the cohort were right censored. The relationships between the cofactors listed above and HIV clinical progression were assessed using the Kaplan–Meier method and compared with log-rank tests. Graphs were displayed only when a comparison was found to be statistically significant.

Cox proportional hazards model was used to calculate crude and adjusted hazard ratios (HR) and their corresponding 95% confidence intervals (95% CI) so that independent predictors of HIV clinical progression could be identified. The proportional hazards assumption was checked by examination of the log-minus-log survival plot for each cofactor. Injecting drug status, which was updated at each visit, was tested twice: firstly, by introducing this factor as a fixed variable considering the first visit after HAART initiation and secondly, as a time-dependent variable considering all visits following HAART initiation. Variables with a P value <0.20 in the univariate analysis were considered eligible in the multivariate model except for the longitudinal depression.
This variable, although significant in univariate analysis was removed from the multivariate analysis as disease progression may itself cause depression [24].

Results

Among the 305 HAART-treated patients in the cohort, 243 were included in the present analysis. Women represented 28% of the study group. Only 14% of patients were naive of any ARV treatment at HAART initiation.

At the first visit after HAART initiation (V1), median age was 35 years, median CD4 cell count was 466 cells/µl and 45% had undetectable viral load. Active IDUs accounted for 17% of the study group and 53% of patients declared a main partner in the prior 6 months. The mean score of CES-D was 17.4 (SD=13.5), mean score of non-somatic CES-D was 12.6 (SD=10.4) and 46% of patients could be classified as having probable depression. The percentage of patients with a high score of CES-D did not vary among men and women: they were 45% and 48%, respectively (P=0.75). It was also not different among patients declaring a main partner and those who did not (42% vs 50%, respectively; P=0.20). Consumption of anxiolytics was reported in 25% of patients and consumption of antidepressants in 11%. Anxiolytics consumers were more likely to be depressed (78% vs 35%; P<10⁻³); similarly, patients reporting the use of antidepressants were also more likely to be depressed (89% vs 41%; P<10⁻³).

Non-adherence to HAART was encountered in 31% of patients. Among non-adherent patients, the proportion of patients with early virological response was significantly lower than among adherent patients (33% vs 51%; P=0.01).

These patients were followed for a total of 820 patient-years (median 3.4 years per patient). Over the follow-up period, the mean proportion of non-adherence was 27.5% (SD=31.1) – on average, the cohort experienced non-adherence in 221 out of the 820 patient-years of follow-up; mean proportion of probable depression (CES-D score ≥16) was 40.4% (SD=34.6). Twenty patients were hospitalized for depressive syndrome within the entire follow-up.

The proportion of active injectors slowly decreased over the follow-up: while they represented 17% at V1, they represented less than 10% at 42 months of follow-up (Figure 1).

Among these patients, 32 patients experienced a clinical progression: 12 reached stage C, 18 had CD4 <200 cells/µl and two patients died of AIDS.

Kaplan–Meier curves show that HIV clinical progression was faster for patients with initial non-adherence, that is, as reported at V1 (Figure 2A), with a significant log-rank test (P=0.02). When using the longitudinal measure of non-adherence over the whole follow-up period, the level of association of non-adherence with clinical progression was higher (P<10⁻³) using a univariate Cox model.

Figure 2B shows Kaplan–Meier survival curves for patients with high or low CES-D score at V1. The difference between these curves was highly significant using the log-rank test (P<10⁻³). The longitudinal measure of depression was also strongly associated with clinical progression (Table 1).

No significant association between injecting status and HIV clinical progression was found, either when considered at the visit following HAART initiation [HR (95% CI)=1.1 (0.5–2.7); P=0.81] or when introducing it as a time-dependent variable [HR (95% CI)=1.7 (0.7–4.0); P=0.21].

Gender, age and level of education did not predict clinical progression (Table 1); lack of a regular job and consumption of anxiolytics were weakly associated (P=0.06 and P=0.10, respectively), while the lack of a stable relationship (P=0.04) and consumption of antidepressants were significantly associated (P=0.04) with HIV disease progression.

Among clinical characteristics, the lack of early virological response predicted HIV clinical progression; having a CD4 cell count below 500 cells/µl at V1 and not being naive of any ARV treatment were only marginally associated (P=0.08 and P=0.10, respectively).

Using a multivariate Cox model, a higher level of cumulative non-adherence [HR (95% CI)=1.2 (1.1–1.3) per 10% increase; P=0.001] and a high score of depression following HAART initiation [HR (95% CI)=1.7 (0.7–4.0); P=0.21].
CI)=5.3 (2.2–13.0); \(P<10^{-3}\) were found to be independently associated with HIV clinical progression, after adjustment on CD4 cell count at V1 [HR (95% CI)=2.9 (1.2–7.0); \( P=0.021\)]. Substituting the dichotomous measure of depression by the continuous score of complete CES-D did not alter the results of the multivariate model [adjusted HR (95% CI) per 1 point of CES-D=1.05 (1.02–1.07); \(P<10^{-3}\)]. Finally, a similar multivariate model was found when substituting the dichotomous measure of depression by the continuous score of non-somatic CES-D [adjusted HR (95% CI) per 1 point of non-somatic CES-D=1.06 (1.03–1.09); \(P<10^{-3}\)].

**Discussion**

The aim of this study was to disentangle the impact of adherence from that of depressive symptoms on clinical progression in patients HIV-infected through injecting drug use. Our results state that depressive symptoms and non-adherence episodes, adjusted for baseline CD4 cell count, are independent predictors of HIV disease progression. Thus, depressive symptoms are a predictor of clinical progression in HIV-infected IDU patients on HAART independently of their influence on non-adherence behaviours [25–27]. Our results are of particular interest, considering that several studies have shown a higher proportion of depressive symptoms among IDUs [28,29]. In the pre-HAART era, 50% of IDUs experiencing depressive symptoms consulted a mental health specialist in the previous year and only a negligible proportion was treated with antidepressants [30]. Despite the decreasing occurrence of opportunistic infections in the HAART era, depressive syndrome still remains a major problem, especially among HIV-positive IDUs who are at higher risk of depressive symptoms than non-infected IDUs [31,32]. Fewer patients seem to experience depressive symptoms since the introduction of HAART. This benefit is seen in particular among HIV patients infected through sexual contacts [23]. In contrast, depressive syndrome is the second main cause of hospitalization for IDU patients, as shown previously in this cohort [33].

In the pre-HAART era, there was a considerable lack of consistency in findings concerning the role of depressive symptoms on HIV clinical progression [14,15] and mortality [14,20,21,34,35]. This may be due to the fact that depression assessment in the pre-HAART era included a physical deterioration induced by the disease. Only a few studies have been conducted so far on depressive syndrome and HIV progression in the HAART era. In this study, depressive symptoms, as assessed in the early phase of ARV treatment, have been found to play a major role in determining HIV clinical progression. Depressive symptoms at the first visit after HAART initiation were preferred as markers of depressive syndrome instead of depressive symptoms as assessed at visits during the follow-up period, to ensure that the cause (depression) could precede the effect (HIV clinical progression) and not the opposite.

**Figure 2.** Kaplan–Meier estimates of probability of HIV clinical progression, stratified by (A) adherence and (B) CES-D score at first visit after HAART initiation (n=243). MANIF 2000 Cohort Study

![Kaplan–Meier estimates of probability of HIV clinical progression](image-url)
The role of depressive symptoms in HIV clinical progression is consistent with research on biological mechanisms of depression among HIV-infected patients that shows that depression may have an impact on immune- and disease-related parameters in HIV disease [36,37]. These psychosocial immune relationships should be explained, notably by alterations in glucocorticoids and catecholamines [38,39].

**Table 1. Cox proportional hazards model for clinical progression [n=23]. MANIF2000 Cohort study**

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
<th>Crude HR (95% CI)</th>
<th>P value</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>176 (72.4)</td>
<td>1</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>67 (27.6)</td>
<td>1.4 (0.7–3.0)</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>Age (per 1 year increase)*</td>
<td></td>
<td>1.00 (0.93–1.07)</td>
<td>&lt;10-3†</td>
<td></td>
</tr>
<tr>
<td>Active drug use†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>201 (82.7)</td>
<td>1</td>
<td>0.81</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>42 (17.3)</td>
<td>1.1 (0.5–2.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has a regular job§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>154 (63.4)</td>
<td>1</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>89 (36.6)</td>
<td>0.4 (0.2–1.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level of education§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school certificate or higher</td>
<td>52 (21.4)</td>
<td>1</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>Less than high school certificate</td>
<td>191 (78.6)</td>
<td>1.9 (0.7–5.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main partner§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>115 (47.3)</td>
<td>1</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>128 (52.7)</td>
<td>0.47 (0.23–0.96)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CES-D score§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;16</td>
<td>131 (53.9)</td>
<td>1</td>
<td>&lt;10-3</td>
<td></td>
</tr>
<tr>
<td>≥16</td>
<td>112 (46.1)</td>
<td>5.7 (2.4–13.9)</td>
<td>5.3 (2.2–13.0)</td>
<td></td>
</tr>
<tr>
<td>Proportion of cumulative high score of CES-D over the whole follow-up (per 10% increase)$‡</td>
<td></td>
<td>1.4 (1.2–1.6)$†</td>
<td>&lt;10-3 §</td>
<td>1.2 (1.1–1.3)$†</td>
</tr>
<tr>
<td>Consumption of anxiolytics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>183 (75.3)</td>
<td>1</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>60 (24.7)</td>
<td>1.8 (0.9–3.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consumption of antidepressants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>216 (88.9)</td>
<td>1</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27 (11.1)</td>
<td>2.4 (1.1–5.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-adherence§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>168 (69.1)</td>
<td>1</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>75 (30.9)</td>
<td>2.2 (1.1–4.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of cumulative non-adherence over the whole follow-up (per 10% increase)$§</td>
<td></td>
<td>1.2 (1.1–1.3)$†</td>
<td>&lt;10-3 €</td>
<td>1.2 (1.1–1.3)$†</td>
</tr>
<tr>
<td>Clinical stage§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>108 (44.4)</td>
<td>1</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>135 (55.6)</td>
<td>0.8 (0.4–1.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 cell count &lt;500 cells/µl§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>79 (32.5)</td>
<td>1</td>
<td>0.08</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>164 (67.5)</td>
<td>2.2 (1.0–5.4)</td>
<td>2.9 (1.2–7.0)</td>
<td></td>
</tr>
<tr>
<td>Early virological response$§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>110 (45.3)</td>
<td>1</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>133 (54.7)</td>
<td>2.2 (1.0–4.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naive of ARV before HAART§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>208 (85.6)</td>
<td>1</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>35 (14.4)</td>
<td>0.2 (0.1–1.4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*At first visit after HAART initiation. †Calculated per unit increase of measurement used (age: 1 year; proportion of cumulative high score of CES-D and proportion of cumulative non-adherence: 10%). ‡In the 6 months prior to the visit. §Eligible for multiple Cox model. ¶This variable is significant in a multivariate model [adjusted HR (95% CI)=1.2 (1.1–1.4)] if CES-D score at V1 is removed from the model.
Independently of depressive symptoms, adherence to treatment during follow-up also appears as a significant predictor of disease progression. This result confirms previous results of the impact of adherence on survival and immunovirological outcomes of HIV-infected patients [5,25,40].

It is interesting to note that injecting drug status at the first visit following HAART initiation was not a determinant of clinical progression: active injecting drug users and former injecting drug users were not found to be different in terms of HIV clinical progression. Furthermore, the persistence of drug injection over time was not statistically associated with clinical progression. These results differ from those observed in a previous study where active drug users on HAART were more likely to have a virological failure [12]. A possible explanation for our results is the decrease in injection practices associated with HAART initiation, leading to a substantial reduction in the number of injecting patients [41], including patients on drug maintenance treatment [42].

In our study, gender was not associated with higher risk of depression, although several studies have shown that HIV-infected women reported significantly more depressive symptoms than men with HIV [43,44]. This may be due to the limited number of women in our sample (n=67) or because of the IDU specificity of the cohort. A difference of access to treatment is unlikely to explain the low proportion of women in the selected group since a previous study from the same cohort did not show any difference in access to care between men and women [17].

Some limitations of our study must be acknowledged. Firstly, our assessment of behaviours was based on self-reports, in which the occurrence of socially desirable responding cannot be excluded. More specifically, our study shares the limits of most socio-behavioural research using patients’ self-reports to measure adherence [45]. Various studies of HAART-treated patients have indeed shown that self-reports tend to overestimate adherence in comparison with alternative methods of measurement (such as electronic medication monitors and unannounced pill counts) [46,47], especially in a population such as drug users [48]. Nevertheless, several studies have confirmed that self-reports of non-adherence are reasonably reliable and correlate well with PI levels below detection levels [5,48], in particular among IDU patients [49]. Moreover, as in previous studies among other groups treated with HAART [6,47], a significant association between viral load and adherence assessment based on patients’ declarations was found in our study.

Concerning drug use, evidence supporting the accuracy of self-reports has been provided by various studies [50–52], including our own MANIF 2000 cohort study in which a substantial agreement between self-reported heroin use and morphine detection in urine was documented [53].

Secondly, it is important to underline that using the CES-D as our sole measure of depressive symptoms limits our ability to make conclusions about depressive disorders. Most commonly, only a proportion of patients who self-report depressive symptoms actually meet criteria for clinical depression. Thus, we may have overestimated the proportion of patients with depression [54,55]. However, the CES-D draws our attention to probable depression among HIV-infected patients and has been used routinely in several research studies [23,26,42]. We did not find any difference in the result when taking or not taking into account the somatic dimension of depression. One study suggested that including the somatic dimension could overestimate the number of individuals who actually have clinical depression because of an overlap between depressive and HIV symptoms [56]. Our results did not support these findings but are consistent with other studies reporting that the somatic symptom subscale does not drive the total depression score [22,23,30].

The fact that the association between consumption of antidepressants and clinical progression was found in the univariate analysis, but not in the multivariate model, suggests that the CES-D better captures patients with probable depression than the reporting of antidepressant consumption.

Another limitation of our study is that it included both naive and experienced individuals. Although the likelihood of achieving successful response to HAART is known to be higher among naive patients [57], we did not find this characteristic significant in our study, maybe due to the low proportion (14%) of naive patients in the selected group.

In conclusion, the major roles of adherence and depressive symptoms in HIV clinical progression appear indisputable among a population HIV-infected through drug use. Through the identification of these two independent predictors of clinical progression, our study shows the necessity of developing two distinct types of psychosocial supporting interventions: interventions aimed at optimizing adherence to ARV treatment and interventions addressing the management and care of depressive symptoms. On the one hand, the role of depressive symptoms at initiation of treatment in HIV clinical progression clearly indicates that HIV care providers should be particularly sensitive to the occurrence of these symptoms in patients starting HAART in order to identify these patients. They may then address the patient’s need for adequate psychiatric care and monitoring through scheduled psychiatric consultations. The treatment of depressive symptoms should thus be addressed...
separately from therapeutic education. On the other hand, repeated psychosocial interventions that have been shown to improve adherence [40, 58, 59] should also be planned and provided for patients prone to non-adherence behaviours, whether they are subject to depressive symptoms or not.

**Grants**

This research was supported by the French National Agency for AIDS Research (ANRS, France), the charity organization ECS-SIDACTION (France) and the Departmental Council (Bouches-du-Rhône, France).

**Acknowledgements**


Special thanks go to all the physicians and nurses who were involved with the cohort and to all patients living with HIV who took part in this study.

**References**


Cruess DG, Petitto JM, Leserman J, Douglas SD, Gettes DR, Ten Have TR & Evans DL. Failure to maintain adherence to HAART in HIV-infected patients: from a predictive to a longitudinal course over 3 years. AIDS 1997; 11:507–515.


Wagner GJ & Rabkin JG. Measuring medication adherence: are missed doses reported more accurately than perfect adherence? AIDS Care 2000; 12:405–408.


Received 22 June 2004, accepted 30 September 2004