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Discrepancies between physician's perception of depression in HIV patients and self-reported CES-D-20 assessment: the DHIVA study

F. Marando[a], G. Gualberti[a], A.M. Costanzo[a], U. di Luzio Paparatti[a], M. Franzetti[b], A. Ammassari[c], A. Antinori[c] and M. Galli[b]

[a]Abbvie s.r.l., Campoverde, LT, Italy; [b]Infectious Diseases Unit, University of Milan, L. Sacco Hospital, Milan, Italy; [c]Istituto Nazionale Malattie Infettive L. Spallanzani, Rome, Italy

ABSTRACT

Depression in HIV/AIDS patients affects adherence and disease progression and often goes unnoticed. DHIVA is a cross-sectional epidemiologic survey, investigating the prevalence of depression in people living with HIV through use of a validated self-administered scale (CES-D-20), as well and the degree of concordance between the physician's perception and patients' reports. A total of 690 HIV-infected patients attending 24 centers across Italy were enrolled. Concordance was calculated by K statistics. Association between depression and subject characteristics were evaluated through univariate and multivariate logistic models (OR and 95% CI). The prevalence of depressive symptoms was 48.8% from patient's questionnaires and 49.5% from physicians' reports, with a low/fair concordance ($K = .38$, $p < .001$). CES-D-20 found severe depression in 22.5% of the patients vs 4% identified by physicians. 135/155 (87%) of the severely depressed patients (according to CES-D-20) were considered as non or mildly/moderately depressed by physicians. Risk of severe depression was associated with unemployment ($p < .001$), previous depression ($p < .001$), treatment failure ($p = .001$), and former smoking status ($p = .018$). Depression is frequent in HIV-infected patients in the HAART era, with significant discrepancy between physician perception and the self-reported CES-D-20 results. Screening should be mandatory in all HIV patients.

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Introduction

With the advent of highly active antiretroviral therapy (HAART), the disease pattern of HIV/AIDS has gradually evolved (Scandlyn, 2000) and the clinical approach to patients has changed, extending beyond pharmacological treatment and posing increasing attention towards the patient's overall well-being and quality of life. In particular, focus is being set on psychological distress and depression which are common to chronic conditions and which have been demonstrated to strongly influence clinical outcomes (Alciati et al., 2001; Hartzell, Janke, & Weintrob, 2008).

Several studies have confirmed a high but variable prevalence of depression among HIV/AIDS patients ranging from 22% to 45% (Benton, 2008; Ciesla & Roberts, 2001; Penzak, Reddy, & Grimsley, 2000). Despite these high-prevalence estimates there is evidence of an appreciable under-diagnosis of depressive symptoms, especially for severe depression (Asch et al., 2003; Rodkjaer et al., 2010; Rabkin, 2008).

As in other chronic settings as in cancer or chronic heart diseases, recognizing depression in HIV/AIDS patients (especially severe depression) and discriminating it from other physiological and emotional states may be difficult for the lack of specific skills to diagnose mental disorders, lack of time in busy hospital settings, and reluctance of the patient to discuss emotional well-being (Krebber et al., 2014; Thombs et al., 2008).

Consequently, appropriate depression individuation would generally require specific evaluation by a psychiatrist or psychologist (Gelenberg, 2009; Rabkin, 2008). However, this type of support is not always available or included in the routine clinical protocols, being left to the single hospitals/centers' initiative which can introduce a significant risk of underestimation (Asch et al., 2003; Israelski et al., 2007).

The aim of this study is to evaluate the extent of missed diagnoses of depression among HIV-infected subjects.

Patients and methods

The DHIVA study is a multicenter cross-sectional study involving 24 clinical HIV Centers across Italy. The

CONTACT F. Marando francesca.marando@abbvie.com

primary objective of the study was to compare the degree of concordance between assessments of depression as evaluated by a validated screening tool, the Center of Epidemiologic Studies Depression (CES-D-20) scale (Radloff, 1977) and the perception of the attending physician. Secondary objectives were to assess the prevalence and the severity of depressive symptoms and to describe the correlates of depression.

The study was performed within a fixed 10-day timeframe, enrolling for each site a maximum of 30 consecutive outpatients among those regularly attending the center. Inclusion criteria were age >18, a diagnosis of HIV >6 months, and consent to inclusion in the study; the sole exclusion criterion was the patient's inability to fill out the questionnaire. The attending physicians were asked to evaluate their patients' depression status according to their clinical experience and classify it as absent, mild, moderate, or severe. Each patient enrolled was asked to fill out the self-assessment CES-D-20 questionnaire, that classified the subject into one of four categories: absence of depression, mild, moderate, and severe depression (CES-D-20 score categories: <16, 16–20; 21–25; 26–60, respectively)

Patients were also given a second ad hoc questionnaire (the DHIVA questionnaire, Appendix – Figure A1) investigating subjective parameters and patients' behavioral and social indicators.

The study obtained approval/authorization by ethics committees as requested by local regulations. Prior to the inclusion in the study, all patients provided a signed informed consent form.

Statistical methods

All characteristics were described using frequency distributions for categorical variables and mean, median, standard deviation, interquartile range, and range for quantitative variables.

Agreement between physician's judgment and CES-D-20 results was assessed by means of Cohen's weighted kappa coefficient (Cohen, 1968). The weight matrix allows the specification of the degree of the disagreement. K statistics were calculated using two differently weighted systems (W1 and W2), both based on the "proximity/closeness" of the judgments or the "seriousness" of the disagreement. In the first system, the decrease is constant (1–.66–.33–0), while the second assigns weights so as not to penalize trial contiguous classes (1–.89–.56–0).

Data were analyzed through descriptive statistics and stratified according to the CES-D-20. Association between depression and subject characteristics were evaluated separately through univariate and multivariate logistic models (OR and 95% CI).

To perform univariate and multivariate logistic models, both diagnosis of depression (mild, moderate, and severe) and just severe depression were used as response variables and demographic/clinical conditions as regressors: multivariate logistic regression was performed with variables which were previously found with $p < .20$ in univariate logistic regression. From the regression model thus obtained the variables that had p-value >.10 were gradually excluded, one at a time. At each single step of the exclusion procedure the variable with the higher p-value was deleted, based on the value of the rank test.

Continuous variables were reported as mean +/− SD; comparisons were performed by a two-tailed independent samples t-test; discrete variables were reported as category counts; the comparisons were performed by a Pearson chi-square test.

Results

The study enrolled 709 patients: of these, 18 were excluded from the analysis due to inclusion criteria violation or incomplete questionnaires, resulting in 690 evaluable patients. The majority of patients were male (72.5%), Caucasian (96.5%), and between 45 and 54 years of age; a large proportion had primary/middle school education (47%), smoked (51%), and was not stably employed (38%) (Table 1). According to results attained by CES-D-20, 48.8% of respondents had some degree of depression: 14.3% of subjects had mild symptoms, 12.0% had moderate symptoms, and 22.5% had severe symptoms. According to the infectious disease physicians, 49.4% of patients suffered from depression: of these, 27% were classified as mild, 18.4% as moderate, and 4% as severe depression (Figure 1).

The degree of discrepancy/concordance between CES-D-20 results and clinical evaluation is reported in Table 2. Concordance was full in 296 cases (42.9%), whereas in the remaining 57.1% the two judgments disagreed about the presence or degree of depression.

Specifically, in some cases clinicians considered as "not depressed" patients who were depressed according to CES-D-20 criteria ($n = 116/690$ [16.8%], including 32 [4.6%] who were severely depressed). Conversely, some patients who were classified as not depressed by CES-D-20, were identified as depressed by physicians ($n = 120$; 17.4%).

Among patients classified as depressed by CES-D-20 ($n = 337$, Table 3), there was full concordance on the degree of depression in only 18.7% of cases ($n = 63/337$, dark grey boxes), while the depressive status was overestimated by physicians in 7.1% of cases (24/337) and underestimated in the remaining 74.2% (250/337;

Table 1. Demographic and clinical data: overall and by gender stratification.

Factors	Overall	Male ($n = 501$)	Female ($n = 189$)	p
Age (median, min–max years)	45 (18–77)	46 (19–77)	44 (18–76)	.014
Ethnic group, % (*N*)				.247
White	96.52 (666)	96.41 (483)	96.83 (183)	
Hispanic	1.88 (13)	2.20 (11)	1.06 (2)	
Black	1.16 (8)	.80 (4)	2.12 (4)	
Asian	.43	.60 (3)	.00 (0)	
Education, % (*N*)				
Primary school	7.39 (51)	5.99 (30)	11.11 (21)	.001
Middle school	39.57 (273)	37.72 (189)	44.44 (84)	
High school	35.80 (247)	35.93 (180)	35.45 (67)	
University	14.06 (97)	17.17 (86)	5.82 (11)	
Unknown	2.46 (17)	2.20 (11)	3.17 (6)	
Employment, % (*N*)				< .001
Unemployed	17.54 (121)	14.37 (72)	25.93 (49)	
Employed	62.03 (299)	69.06 (346)	43.39 (82)	
Self-employed	18.70 (129)	16.67 (115)	7.41 (14)	
Occasionally employed	3.91 (27)	2.79 (14)	6.88 (13)	
Housewife	4.64 (32)	0 (0)	16.93 (32)	
Other	11.88 (82)	13.77 (69)	6.88 (13)	
Number of cohabitants (mean +/− SD)	2.23+/−1.87	1.94 +/− 2.32	2.32 +/− 1.16	.001
Smoking				
Smoker	50.87 (351)	49.90 (250)	53.44 (101)	.791
Non smoker	30.43 (210)	30.94 (155)	29.10 (55)	
Ex-smoker	13.77 (95)	14.37 (72)	12.17 (23)	
Mode of HIV transmission, % (*N*)				
Sexual	70.43 (486)	71.46 (358)	67.72 (128)	.135
Vertical	.87 (6)	.80 (4)	1.06 (2)	
Drug addition	25.36 (175)	23.55 (118)	30.16 (57)	
Transfusion/blood products	.72 (5)	1.00 (5)	.00 (0)	
Infection duration (years from HIV diagnosis; mean +/− SD)	11.7 +/− 7.9	10.74 +/− 7.98	14.32 +/− 7.12	< .001
CD4 (cell/cmm; mean +/− SD)	580 +/−300	566 +/− 290	607 +/− 328	.109
Patients with undetectable viral load, % (*N*)	72.5	372	128	.182
Neoplasias. % (*N*)	5.36 (37)	4.59 (23)	7.41 (14)	.202
HBV co-infection, % (*N*)				.582
Yes	8.70 (63)	9.18 (46)	7.41 (17)	
No	83.04 (573)	82.83 (415)	83.60 (158)	
Unknown	8.26 (57)	7.98 (40)	8.99 (17)	
HCV co-infection, % (*N*)				.551
Yes	29.42 (203)	28.74 (144)	31.22 (59)	
No	64.64 (446)	65.47 (328)	62.43 (118)	
Unknown	5.94 (41)	5.79 (29)	6.35 (12)	
Cirrhosis, % (*N*)	3.04 (21)	2.79 (14)	3.70 (7)	.710

light grey boxes). Considering the CES-D-20 categories as a reference, physicians' underestimation was particularly high with regards to moderate (75.9%, $n = 63/83$) and severe depression (87.1%, $n = 135/155$).

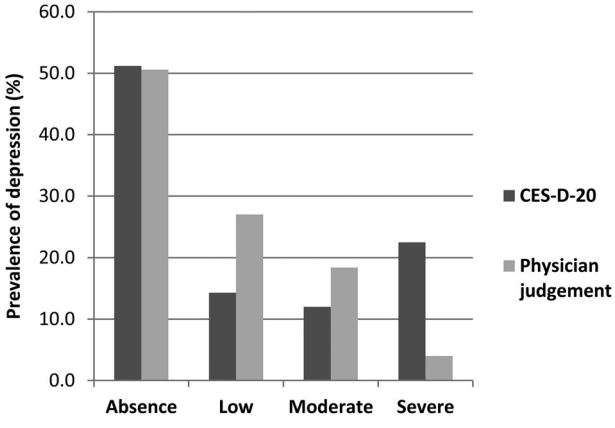

Figure 1. Prevalence of depression. Comparison between assessment by CES-D-20 (dark grey) and by the physician (light grey).

The comparison of the concordance between the two assessments as measured by K statistics evidenced an overall fair (K = .31 according to W1) or moderate (K = .43 according to W2) concordance between the CES-D-20 and physicians' evaluation.

A high variability of concordance among participating centers (Figure 2) was also observed.

Factors associated with depression at the univariate level are reported in Appendix (Tables A1 and A2).

Application of the multivariate model on clinical/demographic data showed that the independent factors significantly associated with depression were: un- or under-employment, liver cirrhosis, previous diagnosis of depression, living in smaller households, unknown HBV status, and current use of illicit drugs (Table 4). Multivariate analysis, with data derived from the DHIVA questionnaire, confirmed as independent correlates of depression the unsatisfactory perception of quality of life, sexual dysfunction (other than loss of libido),

Table 2. Concordance table between degrees of depression according to CES-D questionnaire and as perceived by the physician: results go from perfect concordance (dark grey boxes) to absolute discordance (white boxes).

	CES-D				
Physician assessment	Absence of depression	Mild depression	Moderate depression	Severe depression	Total
Absence of depression	*233*[a]	52[b]	32[c]	32[d]	349
	33.8[a]	7.5[b]	4.6[c]	4.6[d]	50.6%
Mild depression	95[b]	*26*[a]	31[b]	34[c]	186
	13.8[b]	*3.8*[a]	4.5[b]	4.9[c]	26.9%
Moderate depression	22[c]	19[b]	*17*[a]	69[b]	127
	3.2[c]	2.8[b]	*2.5*[a]	10.0[b]	18.4%
Severe depression	3[d]	2[c]	3[b]	*20*[a]	28
	0.44[d]	0.3[c]	0.4[b]	*2.9*[a]	4.1%
Total	353	99	83	155	690
	51.2%	14.4%	12.0%	22.5%	100.0%

a Total concordance
b Mild discordance
c Severe discordance
d Total discordance
Note: Top line: number of patients; bottom line: percentage.

use of sleeping pills /sedatives, and non-adherence to antiretrovirals in the last week (Table 5).

The number of patients classified by CES-D-20 as having severe depression was 155 (22.46%). The variables found to be associated with severe grade of depression in the univariate model, are listed in the Appendix (Table A3) while the multivariate model is showed in Table 6.

The parameters associated with concordance/discordance between the physician's judgment and the CES-D-20 assessment were analyzed at a univariate level. The previous diagnosis of depression and previous alcohol abuse are the factors that correlate with concordance between physicians' diagnosis of depression and CES-D-20 depression categories; the chance of being correctly recognized as depressed by the physician was 88% higher in patients with a previous diagnosis of depression ($p < .001$) and 76% higher in those using alcohol ($p = .04$). Conversely, depressed patients taking interferon for HCV co-infection had a 10-fold higher risk of not being recognized as depressed by the physician, compared to those not on interferon therapy (Appendix, Table A4).

Finally, the factors significantly involved in attributing depression by physicians to patients who were not depressed per CES-D-20 were: HBV or HCV co-infections ($p = .0189$ and $p = .011$), cirrhosis ($p = .033$), unknown education level ($p = .018$), employment status ($p = .012$), previous depression ($p = .002$), or treatment failure ($p = .006$) (Appendix, Table A5).

Table 3. Patients classified as "depressed" (different degrees) by CES-D-20: results go from perfect concordance (dark grey boxes) to discordance (light grey boxes).

	CES-D			
Physician assessment	Mild depression	Moderate depression	Severe depression	Total
Absence of depression	52[b]	32[c]	32[d]	116
	15.4[b]	9.5[c]	9.5[d]	34.4%
Mild depression	26[a]	31[b]	34[c]	91
	7.7[a]	8.2[b]	10.1[c]	27.1%
Moderate depression	19[b]	17[a]	69[b]	105
	5.6[b]	5.0[a]	20.5[b]	31.2%
Severe depression	2[c]	3[b]	20[a]	25
	0.6[c]	0.9[b]	5.9[a]	7.4%
Total	99	83	155	337
	29.4%	24.6%	45.9%	100.0%

a Total concordance
b Mild discordance
c Severe discordance
d Total discordance
Note: Top line: number of patients; bottom line: percentage.

Discussion

In patients living with HIV/AIDS, depression has been reported to be associated with non-adherence to therapy (Horberg et al., 2008; Nel & Kagee, 2011), faster progression of the disease (Kacanek et al., 2010; Pence et al., 2007) and diminished active and problem-focused coping strategy. Depression was considered as a main comorbidity (contributing, incidental, or confounder) for clinical assessment of HIV-associated neurocognitive disorder (HAND, Antinori et al., 2007) and a recent analysis of the CHARTER Research Cohort pointed out that major depressive disorder (MDD) is also linked to viral escape in CSF (Hammond, Crum, & Treisman, 2013).

Despite the burden of depression in HIV/AIDS patients the diagnosis can be frequently missed in this population and it may be difficult to discriminate depressive symptoms from normal fluctuations in mood state. Although questionnaires cannot replace the doctor–patient relationship, self-administered depression scales are generally considered a valid screening tool. The CES-D-20 self-administered depression scale (Radloff, 1977) is widely used to screen for depression status among people with HIV and has proved to be a tool with high sensitivity and somewhat

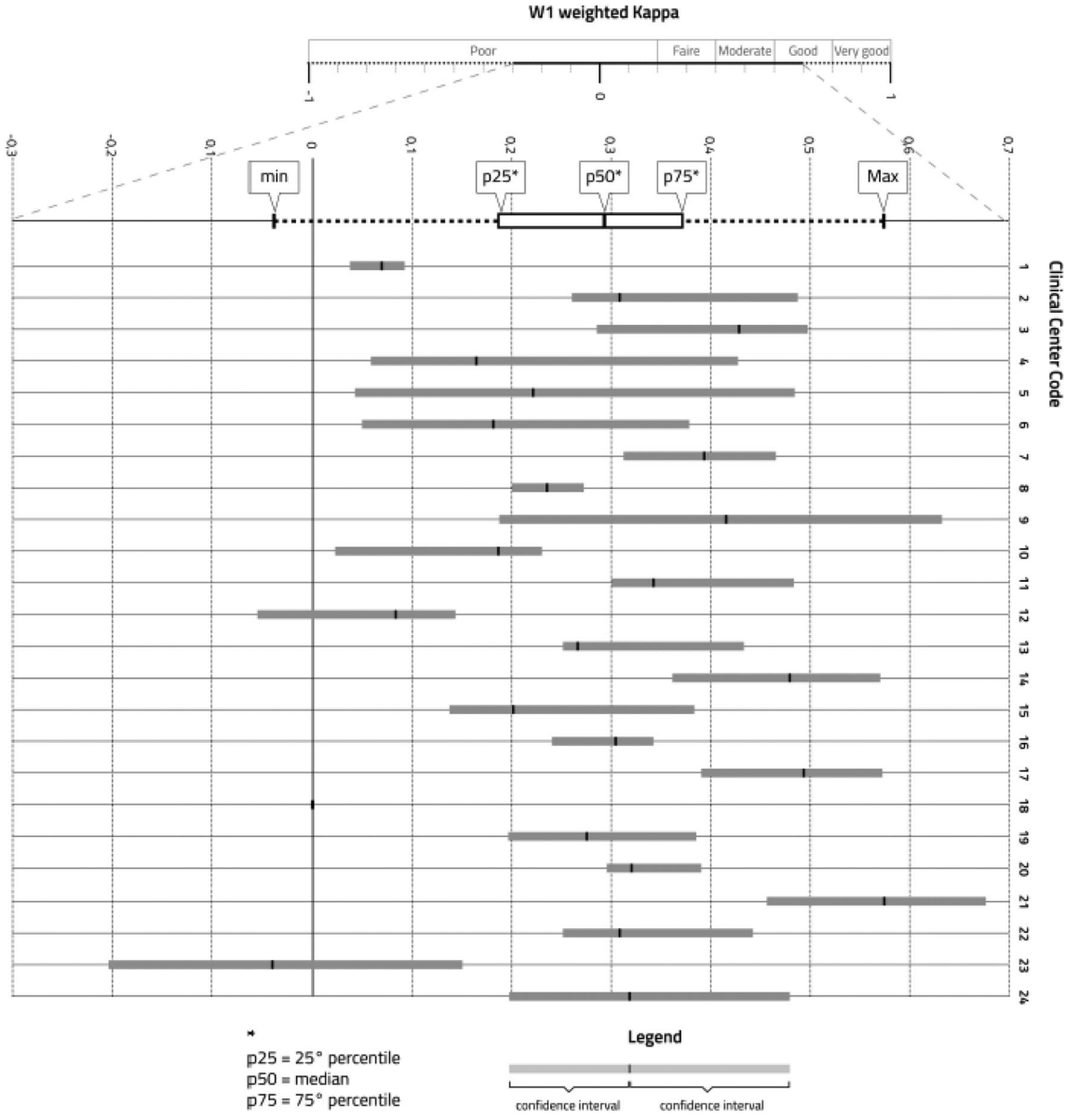

Figure 2. Agreement between physician's assessment and CES-D-20 scores. The weighted K (Cohen's kappa) coefficient measures the agreement between physician's assessment and CES-D-20 scores. Confidence intervals indicate the variability of kappa within each center (among physicians). The weighting system was defined according to the proxmity /closeness of the judgments within contiguous classes (W1, 1-.66-.33-0). Box plots (grey boxes) of weighted Cohen's K coefficients refer to hospitals. The figure shows that K values are scattered over a wide range; increasing distance from the 0 axis indicates a higher degree of concordance.

lower specificity (Balsamo & Saggino, 2007). Prevalence of depression in our cohort was high (approximately half of the population, considering all grades of depression and for both the physician and CES-D-20 evaluation).

The two evaluations gave us different prevalence distribution when considering the different categories of depression, thus suggesting that even when a depressive status has been correctly identified it may be difficult to discriminate the depression severity.

Full concordance between CES-D-20 assessment and physicians' judgment on the presence and severity of depression was achieved only in less than one-fifth of cases.

Discrepancy between the physician's perception and the CES-D-20 assessment was found especially in relation to the degree of depression. Considering the CES-D-20 categories as a reference, overestimation occurred in a minority of cases, while underestimation was more common than expected. In particular, 87.1% of subjects with CES-D-20 scores placing them in the severely depressed category were not perceived to be severely depressed by their physicians, with potential

Table 4. Socio-demographic factors associated with depression: data from multivariate logistic regression from CRF.

	Multivariate logistic model			
Factors	OR	95% CI	OR	*p*
Work status vs employed/self-employed				
Unemployed/occasionally employed	2.77	1.45	5.28	.002
Other status	1.62	.91	2.91	.103
HBV infection vs no				
Yes	.88	.39	2.01	.765
Unknown	3.87	1.43	10.45	.008
Hepatic cirrhosis: yes vs no	9.24	2.35	36.30	.001
Previous diagnosis of depression: yes vs no	4.48	2.09	9.61	<.001
Household size: >=1 vs 0	.43	.19	.96	.038
Use of drugs: yes vs no	6.32	1.79	22.34	.004

Note: Please refer to Appendix Table A1 for univariate data.

consequences for the patients' health and clinical management. The underestimation of depression among patients taking interferon-alpha is especially noteworthy, as its neuropsychiatric side effects are widely described (Mello, Segurado, & Malbergier, 2010).

It is conceivable that a certain degree of depression is considered by physicians so common in patients living with HIV/AIDS, as to be deemed the patient's baseline mood. Some HIV-related symptoms (e.g., fatigue) might further interfere with recognizing depression, and physicians might need specialized training to correctly diagnose depression in this setting.

It is important to note that the main concern of HIV physicians is to maintain an adequate suppression of HIV and an acceptable immunological function in patients, and this can lead them to overlook other clinically relevant aspects such as depression. Furthermore, attending physicians in Infectious Diseases units may not receive any specific training for depression diagnosis and care. We can speculate that the discrepancy of diagnostic accuracy across the participating centers could be explained also by the presence/absence of multidisciplinary teams that include mental health specialists, where it is possible that the multifaceted approach to global patients' health may lead them to monitor also non-strictly virological aspects.

Table 5. Socio-demographic factors associated with depression: data from multivariate logistic regression from DHIVA questionnaire.

	Multivariate logistic model			
Factors	OR	95% CI	OR	*p*
Frequency of other sexual disfunctions[a] *vs never*				
Often	4.72	2.58	8.64	<.001
Rarely	1.60	.81	3.14	.173
Not answered	1.97	.93	4.19	.077
Presence of other family members with depression				
No	.59	.34	1.03	.063
Not answered	.83	.23	3.03	.778
Missing antiretrovirals in the last week				
No	.26	.13	.53	<.001
Not answered	.33	.13	.84	.020
Frequency of use of sleeping pills/sedatives vs never				
Often	4.30	1.85	10.00	.001
Rarely	1.67	.81	3.44	.162
Not answered	2.55	.63	10.38	.189
Quality of life vs satisfactory				
Acceptable	6.23	3.67	10.56	<.001
Unsatisfactory	27.05	8.69	84.22	<.001
Not answered	1.11	.22	5.53	.901

Note: Please refer to Appendix Table A2 for univariate data.
[a]Other than loss of libido.

Table 6. Factors significantly associated to severe depression in multivariate logistic model.

Factors	OR	95% CI	OR	*P*
Gender (male vs female)	.592	.341	1.027	.062
Not/occasionally employed vs employed /self-employed	2.147	1.153	3.997	.016
Previous diagnosis of depression: yes vs no	3.815	1.889	7.704	<.001
Treatment failure: >1 vs 0	2.618	1.348	5.086	.004
Treatment failure: unknown vs 0	.326	.108	.985	.047
Smoke: ex-smoker vs smoker	.452	.208	.981	.045

Note: Please refer to Appendix Table A3 for univariate data.

On the other hand, in the presence of HBV and/or HCV co-infection or cirrhotic liver disease, physicians tend to overestimate depression. In these cases, the peculiar Italian epidemiological picture of viral liver diseases (Sagnelli, et al., 2005; Sagnelli et al., 2008) and the high prevalence of drug abuse among HIV patients (Istituto Superiore di Sanità, 2013) may have a confounding effect on clinical judgment. Drug abuse has already been associated with an increased risk of psychological alterations (Psaros et al., 2013) and co-infections with hepatitis B and C viruses represented an additional risk factor for depression (Raison et al., 2006; Weiss & Morgello, 2009). The association between unknown HBV status and depression found in our analysis does not have an obvious explanation: however, the number of patients with unknown HBV status was small (56 subjects), and this association is probably irrelevant. In our study hepatic cirrhosis was strongly associated with depressive symptoms, confirming previous reports (Mells et al., 2013).

Lower educational level and unemployment status were among the most powerful factors associated with depression, with unemployment being a strong predictor for the highest degree of depressive status. Although depression can arise as consequence of patients not being involved in a working activity, depression itself might also be the cause for becoming less efficient in the workplace and eventually lead to losing the job or not maintaining it (Bravo et al., 2010; Raison et al., 2006).

A very strong association has been detected between low perception of quality of life and depressive symptoms thus confirming existing data that suggest that psychological well-being and psychiatric comorbidities are important predictors of quality of life in this population (Briongos-figuero et al., 2011; Degroote et al., 2013; Douaihy & Singh, 2001). Nevertheless we have to

take into account that many determinants of quality of life and of depression overlap, therefore the strength of the association may be due to confounders. As shown for other chronic disorders (Grenard et al., 2011) and also HIV infection (Gonzalez et al., 2011), a strong association between depression and medication non-adherence has been found. Since it has been shown that antidepressant treatment improves antiretroviral adherence (Sin & DiMatteo, 2014), clinicians should be aware of these two frequently coexisting conditions and always investigate patients diagnosed with depressive symptomatology for correct pill intake and vice versa.

The number of previous treatment failures and female gender are specifically related to severe depression and did not emerge as correlate of risk for minor degrees of depression. In this respect, our data can be considered in agreement with the previously published literature (Ickovics et al., 2001); it is well established that women generally bear a greater combination of stress factors in relation to family planning, motherhood, lower income, and lack of emotional support compared to men (Mello et al., 2010; Rabkin, 2008) . Severe depression in women is also a predictor of disease progression and higher morbidity: depressed women with HIV/AIDS, however, are at increased risk for non-AIDS related deaths (Cook et al., 2004).

In our study population living alone, sexual dysfunctions, use of sleeping pills were significantly associated with current depression, confirming that people living with HIV may require further clinical, social, and emotional support.

The main limitation of the study is that possible differences among clinicians about specific training and experience on neuropsychiatric aspects have not been collected. Additionally, it has to be taken into account that CES-D-20 is an epidemiological screening tool designed and validated to identify individuals at risk for clinical depression and not to provide a clinical diagnosis. Furthermore, we acknowledge that some symptoms (such as fatigue possibly associated with treatment or disease itself) may cause the CES-D to overestimate the depression thus it is possible that part of discrepancy might have been driven by CES-D-20 false positive or negative.

Finally, the cross-sectional design was suitable to demonstrate association between investigated factors and depressive symptoms, but not causality.

Conclusions

Our study confirms that depression is a very frequent condition among the HIV-positive population also in the HAART era. Factors associated with severe depressive symptomatology were principally socio-demographic characteristics, previous diagnosis of depression, and treatment failure. The most relevant finding of this study, however, was an alarming discrepancy between psychological evaluation obtained by means of a standardized screening tool and by the clinician's assessment. Although clinicians may benefit from more education and training on depression diagnosis, and recognizing the presence of depression correlates may lead to fewer missed diagnoses, the use of a self-reported scale, such as CES-D-20, could represent an immediate and cost-effective screening tool for identifying patients with depressive symptomatology.

Nonetheless HIV has become a chronic infection that extends over several decades. Patients living with HIV/AIDS may often have a low quality of life especially driven by psychological aspects rather than physical symptoms. Greater attention of clinician's towards the quality of life in persons living with HIV/AIDS is mandatory and needs a multidisciplinary approach.

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DHIVA Study Group

Figoni M., Divisione Malattie Infettive ad Alta Complessità 2, Azienda Ospedaliera D. Cotugno, Napoli;

Andreoni M., Maffongelli G., UOC di Malattie Infettive e Day Hospital Fondazione Policlinico Tor Vergata, Roma;

Mercuri A., Clinica Malattie Infettive Ospedale S. Maria della Misericordia, Perugia;

Carosi G., Motta D., Istituto Malattie Infettive e Tropicali Azienda Ospedaliera Spedali Civili di Brescia;

Cattelan A.M., Sasset L., SOC di Malattie Infettive Ospedale "Santa Maria della Misericordia", Rovigo;

Cauda R., Ciccarelli N., Istituto di Clinica Malattie Infettive Università Cattolica, Roma;

Chirianni A., Sangiovanni V., III Divisione Malattie Infettive Azienda Ospedaliera D. Cotugno Napoli;

Colangeli V., Magistrelli E., U.O. di Malattie Infettive Azienda Ospedaliera Universitaria Policlinico S. Orsola Malpighi, Bologna;

Di Perri G., Trentini, L., Clinica Universitaria di Malattie Infettive Ospedale Amedeo di Savoia, Torino;

D'Arminio Monforte A., Comi L., Clinica Malattie Infettive Azienda Ospedaliera San Paolo, Milano;

Manzillo E., VIII Malattie Infettive Azienda Ospedaliera D. Cotugno, Napoli;

Lazzarin A., Fondazione San Raffaele del Monte Tabor di Milano;

Leoncini F., Martinelli C.V., SOD Malattie Infettive Azienda Ospedaliera Careggi, Firenze;

Blè C., Ospedale S. Maria Annunziata, Firenze;

Uglietti A., Clinica Malattie Infettive IRCCS Policlinico San Matteo, Pavia;

Montella F., Di Sora F., Dip.to delle Scienze Mediche U.O.C. Medicina 5 ad Indirizzo Immunologico, Roma;

Mughini M.T., Istituto Malattie Infettive ARNAS, A. O. Garibaldi di Nesima, Catania

Clinica Malattie Infettive Azienda Ospedaliera Universitaria di Sassari;

Narciso P., Bellagamba, IV Divisione Malattie Infettive IRCCS, Roma;

Parruti G., Vadini F., U.O Malattie Infettive e Tropicali, Pescara;

Rizzardini G., Capetti A., I°Divisione Malattie Infettive Ospedale L. Sacco di Milano;

Sighinolfi L., Segala D., U.O. Malattie Infettive Azienda Ospedaliero Universitaria di Ferrara

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Appendix

1. In the last 4 weeks have you had one or more of the following disorders?

	Never	Rarely	Often	Very often
Tiredness				
Mental confusion or memory problems				
Sleep disorders				
Anxiety				
Impaired concentration				

2. Over the past three months have you noticed one or more of the following changes?

	Never	Rarely	Often	Very often
Accumulation of fat in the body (stomach, back ...)				
Fat loss in the arms and / or legs				
Fat loss in face				
Decreased sexual desire				
Other sexual dysfunctions (eg. Vaginal dryness, erectile dysfunction etc.)				

3. Please rate your economic conditions
□ Very satisfactory □ Fairly Satisfactory □ Acceptable □ Not satisfactory
4. Please rate how satisfactory is your work
□ Very satisfactory □ Fairly Satisfactory □ Acceptable □ Unsatisfactory
5.Did you happen to make use of drugs and / or abuse alcohol?
□ Never □ Rarely □ Often □ Very often
6. Do you have first-degree relatives or partners who suffer from depression? □ Yes - □ No
7. Is your HIV status unknown to your family or to your partner? □ Yes - □ No
8. Indicate how many times you have taken antiretroviral therapy last month, placing a cross on the graphic below: Never _____ Always
(□ not on antiretroviral therapy)
9. In the last week did you forget to take your antiretroviral therapy? □ no, never
□ yes how many doses did you miss? □ 1 □ 2 □ 3 □ 4 or more
10. In the last three months did you stop by your initiative the antiretroviral therapy for two or more days? □ No, never □ Yes
11. How often do you use sleeping pills / painkillers? □ Never □ Rarely □ Often □ Very often
12. How would you rate your quality of life?
□ Very satisfactory □ Fairly satisfactory □ Acceptable □ Unsatisfactory

Figure A1. Dhiva questionnaire

Table A1. Factors associated with the presence of depressive symptoms in univariate logistic models (CRF).

	Univariate logistic model			
	Odds Ratio	[95% Conf.	Interval]	*p>t*
Educational degree: high school vs middle school/elementary	.57	.37	.87	.010
Education degree: university vs middle school/elementary	.37	.20	.70	.002
Educational degree: unknown vs middle school/elementary	.59	.19	.83	.365
Male vs female	.58	.38	.89	.014
Unemployed/occasionally employed vs employed/self-employed	3.93	2.22	6.96	.000
Other status vs employed/self-employed	1.56	.92	2.64	.098
Duration of infection: 12–59 months vs <12 months	2.56	.71	9.27	.152
Duration of infection: 60–119 months vs <12 months	3.07	.84	11.20	.089
Duration of infection: >120 months vs <12 months	3.48	1.00	12.16	.050
CD4: 200–350 cell/mm^3 vs <200 cell/mm^3	1.02	.40	2.56	.973
CD4: 351–500 cell/mm^3 vs <200 cell/mm^3	.93	.40	2.16	.862
CD4: >500 cell/mm^3 vs <200 cell/mm^3	.79	.36	1.73	.554
RNA: 50–1000 copies/ml vs <50 copies/ml	1.15	.68	1.97	.597
RNA: >1000 copies/ml vs <50 copies/ml	1.13	.62	2.05	.692
HBV: yes vs no	1.38	.67	2.84	.379
HBV: unknown vs no	3.09	1.29	7.41	.012
HCV: yes vs no	2.31	1.46	3.64	.000
HCV: unknown vs no	2.71	1.20	6.12	.017

(*Continued*)

Table A1. Continued.

	Univariate logistic model			
	Odds Ratio	[95% Conf.	Interval]	*p>t*
Hepatic cirrhosis: yes vs no	13.96	3.75	51.89	.000
Neoplasia: yes vs no	1.24	.54	2.86	.605
Previous diagnosis of depression: yes vs no	3.80	1.92	7.51	.000
AIDS events: yes vs no	1.05	.67	1.65	.832
Interferon therapy: yes vs no	1.48	.37	5.85	.580
Previous use of drugs: yes vs no	2.50	1.60	3.91	.000
Previous use of alcohol: yes vs no	4.27	1.84	9.90	.001
Adherence to ARV therapy	.98	0.91	1.05	.499
Mode of transmission: other vs sexual transmission	1.20	.52	2.76	.665
Mode of transmission: drug use vs sexual transmission	2.57	1.61	4.11	.000
Family size : >=1 vs 0	.49	.24	1.00	.051
Therapy failures: 1 vs 0	1.74	.93	3.26	.084
Therapy failures: >1 vs 0	1.61	1.00	2.58	.050
Therapy failures: unknown vs 0	.70	.32	1.52	.369
Use of drugs: yes vs no	6.78	2.34	19.64	<.001
Use of alcohol: yes vs no	2.88	.83	10.03	.097
Smoking: never smoked vs smoker	.55	.35	.87	.010
Smoking: ex-smoker vs smoker	.82	.47	1.43	.479

Table A2. Factors associated with the presence of depressive symptoms in univariate logistic models (DHIVA questionnaire).

	Univariate logistic model			
	Odds Ratio	[95% Conf.	Interval]	*p>t*
Tiredness: rarely vs never	1.96	.98	3.93	.057
Tiredness: often vs never	8.16	3.91	17.02	.000
Tiredness: very often vs never	9.32	3.48	24.98	.000
Tiredness: not answered vs never	2.95	1.07	8.20	.037
Mental confusion: rarely vs never	3.50	2.17	5.66	.000
Mental confusion: often vs never	7.81	3.81	15.99	.000
Mental confusion: very often vs never	10.20	2.67	38.99	.001
Mental confusion: not answered vs never	2.72	1.28	5.78	.009
Sleep disorders: rarely vs never	2.47	1.45	4.21	.001
Sleep disorders: often vs never	7.26	3.93	13.42	.000
Sleep disorders: very often vs never	21.30	7.88	57.61	.000
Sleep disorders: not answered vs never	4.83	2.08	11.23	.000
Anxiety: rarely vs never	2.51	1.46	4.30	.001
Anxiety: often vs never	13.96	7.14	27.29	.000
Anxiety: very often vs never	144.24	29.22	712.09	.000
Anxiety: not answered vs never	5.82	2.73	12.42	.000
Decreased concentration: rarely vs never	2.85	1.77	4.58	.000
Decreased concentration: often vs never	14.34	6.81	30.21	.000
Decreased concentration: very often vs never	77.82	9.68	625.77	.000
Decreased concentration: not answered vs never	2.55	1.09	5.98	.031
Trunk fat: rarely vs never	1.30	.75	2.24	.344
Trunk fat: often vs never	2.57	1.40	4.75	.003
Trunk fat: very often vs never	5.59	1.90	16.47	.002
Trunk fat: not answered vs never	1.90	1.01	3.56	.045
Loss of fat in limbs: rarely vs never	1.19	.70	2.04	.513
Loss of fat in limbs: often vs never	2.13	1.08	4.20	.030
Loss of fat in limbs: very often vs never	1.44	.55	3.81	.458
Loss of fat in limbs: not answered vs never	1.83	.96	3.48	.066
Loss of fat in face: rarely vs never	.95	.55	1.66	.858
Loss of fat in face: often vs never	2.39	1.20	4.76	.014
Loss of fat in face: very often vs never	2.08	.75	5.77	.159
Loss of fat in face: not answered vs never	1.47	.80	2.70	.219
Loss of libido: rarely vs never	2.17	1.31	3.61	.003
Loss of libido: often vs never	4.05	2.20	7.46	.000
Loss of libido: very often vs never	7.48	2.77	20.19	.000
Loss of libido: not answered vs never	1.71	0.91	3.21	.095
Other sexual disorders: rarely vs never	1.82	1.04	3.18	.035
Other sexual dysfunctions: often vs never	5.96	3.11	11.44	.000
Other sexual dysfunctions: very often vs never	10.56	2.81	39.77	.001
Other sexual dysfunctions: not answered vs never	2.30	1.30	4.09	.004
Financial status: fairly satisfactory vs very satisfactory	1.84	.59	5.75	.295
Financial status: acceptable vs very satisfactory	4.15	1.36	12.67	.013
Financial status: unsatisfactory vs very satisfactory	12.67	3.96	40.58	.000
Financial status: not answered vs very satisfactory	7.90	1.75	35.79	.007

(*Continued*)

Table A2. Continued.

	Univariate logistic model			
	Odds Ratio	[95% Conf.	Interval]	*p>t*
Work: fairly satisfactory vs very satisfactory	.92	.48	1.75	.797
Work: acceptable vs very satisfactory	2.00	1.04	3.82	.037
Work: unsatisfactory vs very satisfactory	6.38	3.05	13.35	.000
Work: not answered vs very satisfactory	2.04	.95	4.37	.068
Use of drugs and/or alcohol: rarely vs never	1.39	.86	2.27	.178
Use of drugs and/or alcohol: often vs never	3.77	1.69	8.40	.001
Use of drugs and/or alcohol: very often vs never	2.36	.87	6.41	.090
Use of drugs and/or alcohol: not answered vs never	3.00	1.16	7.75	.023
Family members suffering from depression: no vs yes	.51	.32	.80	.004
Family members suffering from depression: not answered vs yes	1.27	.41	3.94	.676
Seropositivity known to family and/or partner: no vs yes	.84	.52	1.37	.494
Seropositivity known to family and/or partner: not answered vs yes	1.62	.51	5.10	.410
Number of times ARV therapy was taken in past month	.85	.68	1.06	.161
Forgot to take therapy in past week: no vs yes	.30	.16	.56	.000
Forgot to take therapy in past week: not answered vs no	.33	.16	.68	.003
Therapy discontinuation in past 3 months: no vs yes	.63	.31	1.27	.197
Therapy discontinuation in past 3 months: not answered vs yes	.56	.26	1.23	.151
Use of sleeping pills/sedatives: rarely vs never	1.97	1.05	3.71	.036
Use of sleeping pills /sedatives: often vs never	5.93	2.49	14.13	.000
Use of sleeping pills /sedatives: very often vs never	10.39	2.69	40.14	.001
Use of sleeping pills /sedatives: not answered vs never	1.57	.89	2.79	.122
Quality of life: fairly satisfactory vs very satisfactory	15.66	4.91	49.98	.000
Quality of life: acceptable vs very satisfactory	78.10	24.22	251.87	.000
Quality of life: unsatisfactory vs very satisfactory	416.57	84.81	2046.18	.000
Quality of life: not answered vs very satisfactory	31.85	9.28	109.23	.000

Table A3. Univariate analysis of the factors associated with severe depression.

	Univariate logistic model			
	Odds Ratio	[95% Conf.	Interval]	*P>t*
Educational degree: high school vs middle school/elementary	.53	.32	.88	0.01
Educational degree: university vs middle school/elementary	.12	.04	.30	<.001
Male vs female	.42	.26	.68	<.001
Unemployed/occasionally employed vs employed /self-employed	4.08	2.29	7.26	<.001
Duration of infection: 12–59 months vs <12 monthss	9.60	1.14	76.78	.04
Duration of infection: 60–119 months vs <12 months	11.78	1.43	96.63	.02
Duration of infection: >120 months vs <12 months	15.75	2.00	124.05	.01
CD4: 351–500 cell/mm^3 vs <200 cell/mm^3	.34	.13	.85	.02
HCV: yes vs no	2.66	1.61	4.41	<.001
Cirrhosis: yes vs no	4.82	1.41	16.51	.01
Previous diagnosis of depression: yes vs no	4.33	2.30	8.15	<.001
Previous use of drugs: yes vs no	3.20	1.96	5.22	<.001
Previous use of alcohol yes vs no	5.63	2.65	10.84	<.001
Mode of transmission: drug use vs sexual	3.21	1.93	5.34	<.001
Family size: >=1 vs 0	.45	.22	.93	.03
Therapy failure: 1 vs 0	2.28	1.33	3.89	.00
Use of drugs: yes vs no	6.46	2.57	16.24	<.001
Use of alcohol: yes vs no	6.27	2.00	19.65	.00
Smoking: never smoked vs smoker	.44	.25	.76	.00
Smoking: ex-smoker vs smoker	.44	.21	.92	.03

Table A4. Univariate analysis of factors associated with physician's discordance in assessing depression – depressed patients according to CES-D.

	Univariate logistic model			
	Odds Ratio	[95% Conf.	Interval]	*p>t*
Educational degree: high school vs middle school/elementary	1.39	.73	2.66	.311
Educational degree: university vs middle school/elementary	2.18	.78	6.08	.134
Educational degree: unknown vs middle school/elementary	1.49	.33	6.79	.606
Male vs female	1.57	.83	2.98	.163
Not/occasionally employed vs employed/self-employed	.89	.44	1.81	.746
Other employed condition vs employed/self-employed	.61	.26	1.44	.258
Duration of infection: 12–59 months vs <12 months	.40	.05	3.06	.374
Duration of infection: 60–119 months vs <12 months	.31	.04	2.38	.258
Duration of infection: >120 months vs <12 months	.44	.06	3.19	.417
CD4: 200–350 cell/mm^3 vs <200 cell/mm^3	.58	.14	2.31	.436
CD4: 351–500 cell/mm^3 vs <200 cell/mm^3	.88	.25	3.05	.838

(*Continued*)

Table A4. Continued.

	Univariate logistic model			
	Odds Ratio	[95% Conf.	Interval]	*p>t*
CD4: >500 cell/mm^3 vs <200 cell/mm^3	.79	.24	2.53	.687
RNA: 50–1000 copies/ml vs <50 copies/ml	2.02	.94	4.35	.070
RNA: >1000 copies/ml vs <50 copies/ml	1.48	.60	3.63	.388
HBV: yes vs no	.82	.24	2.75	.742
HBV: unknown vs no	1.14	.45	2.88	.776
HCV: yes vs no	.59	.31	1.15	.124
HCV: unknown vs no	1.12	.41	3.07	.822
Cirrhosis: yes vs no	.35	.08	1.59	.173
Neoplasia: yes vs no	.64	.19	2.26	.495
Previous diagnosis of depression: yes vs no	.12	.03	.41	.001
AIDS events: yes vs no	1.02	.50	2.07	.963
Interpheron therapy: yes vs no	10.11	2.12	48.00	.004
Previous use of drugs: yes vs no	.84	.45	1.58	.588
Previous use of alcohol: yes vs no	.24	.06	.94	.040
Adherence to ARV therapy	.99	.88	1.11	.832
Mode of acquisition: other vs sexual	1.70	.49	5.85	.398
Mode of acquisition: drug use vs sexual	.80	.41	1.54	.503
Family size: >=1 vs 0	1.33	.50	3.56	.572
Therapy failure: 1 vs 0	1.54	.62	3.81	.352
Therapy failure: >1 vs 0	.87	.42	1.80	.704
Therapy failure: unknown vs 0	2.43	.82	8.23	.152
Use of drugs: yes vs no	1.06	.35	3.20	.919
Use of alcohol: yes vs no	1.51	.37	6.08	.564
Smoke: never smoker vs smoker	.65	.32	1.31	.228
Smoke: ex-smoker vs smoker	1.12	.48	2.60	.792

Table A5. Univariate analysis of factors associated with physician's discordance in assessing depression – Not-depressed patients according to CES-D.

	Modello logistico univariato			
	Odds Ratio	[95% Conf.	Interval]	*p>t*
Educational degree: high school vs middle school/elementary	1.55	.80	3.00	.194
Educational degree: university vs middle school/elementary	1.28	.55	2.94	.566
Educational degree: unknown vs middle school/elementary	7.04	1.40	35.47	.018
Male vs female	1.27	.64	2.50	.498
Not/occasionally employed vs employed/self-employed	1.70	.70	4.13	.241
Other employed condition vs employed/self-employed	2.65	1.24	5.68	.012
Duration of infection: 12–59 months vs <12 months	.30	.07	1.20	.088
Duration of infection: 60–119 months vs <12 months	.25	.06	1.09	.065
Duration of infection: >120 months vs <12 months	.40	.11	1.48	.167
CD4: 200–350 cell/mm^3 vs <200 cell/mm^3	.26	.07	.97	.046
CD4: 351–500 cell/mm^3 vs <200 cell/mm^3	.38	.11	1.29	.120
CD4: >500 cell/mm^3 vs <200 cell/mm^3	.36	.11	1.11	.075
RNA: 50–1000 copies/ml vs <50 copies/ml	.53	.21	1.31	.169
RNA: >1000 copies/ml vs <50 copies/ml	1.67	.71	3.95	.239
HBV: yes vs no	3.31	1.23	8.93	.018
HBV: unknown vs no	.27	.05	1.48	.130
HCV: yes vs no	2.49	1.23	5.04	.011
HCV: unknown vs no	.26	.05	1.37	.112
Cirrhosis: yes vs no	13.33	1.24	143.66	.033
Neoplasia: yes vs no	.30	.07	1.36	.119
Previous diagnosis of depression: yes vs no	7.97	2.16	29.18	.002
AIDS events: yes vs no	1.07	.54	2.12	.838
Interpheron therapy: yes vs no	2.09	.22	19.57	.517
Previous use of drugs: yes vs no	1.49	.72	3.05	.280
Previous use of alcohol: yes vs no	2.26	.50	10.26	.289
Adherence to ARV therapy	.93	.84	1.03	.156
Mode of acquisition: other vs sexual	.83	.24	2.87	.770
Mode of acquisition: drug use vs sexual	1.65	.77	3.53	.197
Family size: >=1 vs 0	.83	.24	2.87	.768
Therapy failure: 1 vs 0	3.59	1.45	8.87	.006
Therapy failure: >1 vs 0	1.16	.56	2.40	.693
Therapy failure: unknown vs 0	1.89	.71	5.04	.203
Use of drugs: yes vs no	4.53	.62	33.23	.136
Use of alcohol: yes vs no	5.85	.72	47.35	.098
Smoke: never smoker vs smoker	.92	.48	1.76	.807
Smoke: ex-smoker vs smoker	.77	.34	1.77	.537