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Depressive symptoms over the course of HIV infection before AIDS

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Abstract The objective of this study was to describe the prevalence and course of depressive symptoms before AIDS in HIV-infected homosexual men. A descriptive and comparative analysis of data from HIV-infected and -uninfected homosexual men in the Multicenter AIDS Cohort Study was performed. The Center for Epidemiologic Studies Depression Scale (CES-D) was the primary measure of depressive symptoms. The prevalence of depressive symptoms and CES-D caseness estimates in the AIDS-free HIV-infected homosexual men were stable over time. Small differences between HIV seropositive and seronegative men were detected on the CES-D and on three of its subscales. These were mostly accounted for by less hope, and by more fearfulness, insomnia, and anorexia in the seropositive cohort. We concluded that there does not appear to be an overall increase in depressive symptoms in HIV-infected homosexual men from the time of infection until prior to AIDS. However, this group of men consistently report specific depressive symptoms more often. Implications of these findings for the clinical care of HIV-infected patients is discussed.

Depressive symptomatology has widely been reported as frequently afflicting persons infected with the human immunodeficiency virus (HIV) [1]. More recently, it has been documented that major depressive disorder is less common in HIV-infected homosexual men than previously thought, with a 1-month prevalence between 4 and 14% [2–4]. The prevalence of depressive disorders in homosexual men may further increase at later stages of HIV infection before and after AIDS develops [5–7].

Risk factors for depression in this setting can be grouped into three types [8]. First is prior psychiatric

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morbidity – as evidenced by high lifetime rates of major depression [2–4] and concurrent personality disorder [9]. Second are psychological risk factors such as perceptions of limited social support [8], bereavement [8], and stressors that patients experience [10], although the latter finding is controversial [11]. A third group are medical risk factors, especially the presence of AIDS-related signs and symptoms [12–14]. Knowledge of HIV serostatus and CD4 cell counts has not been found to cause clinical depression [8].

It has long been postulated that an "organic" mood disorder occurs in association with HIV infection [15] and that this might be due to direct brain infection by the HIV itself [16]. This is particularly true since the virus has a predilection for the subcortex and the temporal/parietal lobes, areas associated with increased rates of depression in other diseases [17–20]. Since the virus appears in the central nervous system in the early stages of infection [16] an increased rate of depression might be expected around the same time.

Also supporting the "organic" hypothesis is the increased prevalence of manic syndromes in patients with AIDS associated with dementia [21, 22]. One study has observed an association between cerebrospinal fluid parameters and depressive symptoms [23]. Other studies of patients with HIV dementia have not seen an increase in the rates of associated depression [24, 25]. However, a lack of association of HIV-related dementia and depressive symptomatology does not disprove the possibility that HIV-specific biologic factors might be the cause of depressive symptomatology.

Sorting out questions relating to the etiology of depression in HIV infection will depend, in part, on careful epidemiologic study of depression and depressive symptoms over the entire course of HIV infection. Published studies on this topic have been retrospective or cross-sectional [8]. No published study has investigated prospectively the prevalence of depressive symptoms in early HIV infection. Additionally, it is important to consider appropriate comparison groups in interpreting such estimates given the high lifetime risk for depression in populations at risk for HIV infection, such as homosexual men.

A demonstration that soon after seroconversion there is a sustained, time-dependent increase in the prevalence of depressive symptoms would support the view that HIV-related biologic factors play a role in the genesis of depressive symptomatology. In contrast, if after seroconversion there is a period of relative quiescence when depressive symptomatology is not increased then these factors might not play a major role in depression. In view of the finding that depressive symptomatology rises rapidly within 6–12 months before clinical AIDS [6], an earlier period of quiescence would suggest that HIV-related biologic factors become important late in the course of HIV infection. This would pinpoint a time period just prior to the development of AIDS when an HIV-specific "organic" mood disorder might be developing that could be studied prospectively.

This paper uses data collected in a large, community-based, prospective study of homosexual men to address the following questions on the longitudinal course of depression in HIV-infected persons:

1. What is the time dependent prevalence of depressive symptomatology and of CES-D (Center for Epidemiologic Studies Depression Scale) caseness estimates in HIV-infected homosexual men before the development of AIDS?
2. What is the course of specific types of depressive symptomatology in the same context?
3. How do 1 and 2 above compare to the course of depressive symptomatology and CES-D caseness estimates in uninfected homosexual men?

Analyses were performed using data collected over 5 years in a continuing study of homosexual men at risk for and infected with the HIV. The CES-D [26], a well-standardized measure of caseness and depressive symptoms, was completed at 6-month intervals by these men.

Method

The Multicenter AIDS Cohort Study (MACS)

The MACS [27], which was designed to study the natural history of AIDS, enrolled homosexual and bisexual men without AIDS as participants in 1984–1985. Approximately 5000 community volunteers recruited from bars, doctors' offices, gay organizations, and newspaper advertisements were enrolled at centers in Baltimore/Washington, Chicago, Los Angeles, and Pittsburgh. Data from 8 years of follow-up were available for this analysis. Excluding deaths, total loss to follow-up in the entire cohort was approximately 25%. Baseline and semi-annual follow-up measures included a broad array of interview questions, physical examination, laboratory studies, as well as completion of the CES-D.

On later serologic testing of blood from stored samples, 1809 were found to be infected with the HIV at enrollment (the seroprevalent cohort). As well, over the course of the study, HIV seroconversion occurred with decreasing annual rates ranging from 5% to 1% per year [28], with over 400 individuals becoming infected after the study's start (seroincident cohort). We define AIDS here, by the 1987 Centers for Disease Control (CDC) criteria, as being present if one or more opportunistic infections occur in persons infected with the HIV and who are not otherwise immunocompromised [29]. A CD4 count below 200, used in the 1992 definition, was not a criterion for AIDS in this study. Onset of AIDS illnesses in individuals was obtained continuously using active and passive surveillance. More than 900 MACS participants have developed AIDS. Infected individuals are estimated to develop AIDS after a median incubation period of 10 years [30].

Subjects

For this analysis, HIV-infected persons were included from the MACS seroprevalent cohort. Many persons in this group progressed to develop AIDS a few years after the study started. A substantial rise in CES-D scores occurs within 1-2 years prior to a diagnosis of AIDS [6]. This effect would alter the group description of

depression rates and symptoms in early HIV infection. Thus, the study sample excluded from the seroprevalent cohort those who developed AIDS within 8 years of the study's start. This exclusion reduced the analytic sample from 1809 to 1041.

Initially seronegative MACS participants who did not subsequently HIV seroconvert during the initial 8-year period of follow-up were included for comparison. Data from seroincident men were excluded as others have shown that HIV is associated with "seroconverter's depression" that occurs after infection but before the body produces antibodies [31]. This narrowed the sample from 3361 to 2944.

Time Period of Interest

The analyses were focused on the 5-year period between the second and the sixth year of the MACS study. Data from study visit 1 to study visit 15 were available for analysis. Information from visits 1, 2, and 3 was excluded to negate transient effects of learning one's HIV status on CES-D scores as described by Huggins et al. [31]. Most MACS participants learned of their HIV status during the first 2 years of the study, immediately after a HIV test became available for general use. After that time, knowledge of HIV status did not change substantially [i.e. very few ($< 5\%$) of those who did not know their status by this visit were told of it later on]. Many respondents first learned of their serostatus during the early years of the MACS when the HIV test became available.

Comparison of baseline demographic characteristics and CES-D score at visit 1 between the final study sample and the excluded subjects from the entire MACS cohorts showed no significant differences ($P > 0.10$ in all cases, using t-tests or chi square tests).

Response measures and group comparisons over time

The primary measure of depression in both groups was the CES-D developed by Radloff [26] for the study of depressive symptomatology in general populations. This self-report scale has high test retest reliability [26, 32]. The CES-D is composed of 20 questions, each inquiring about a sign or symptom associated with depression. Total scores can range from 0 to 60.

The original author [26] also described a factor analysis based on population data in which four CES-D principal components were produced. These factors are: depressed mood, positive affects, somatic symptoms, and interpersonal relations. This analysis has subsequently been replicated in another community study [33] and in a large study of medically ill persons [32]. Thus, these factors are stable enough so that they can be used to construct subscales in order to distinguish the components of depressive symptoms ascertained by the scale [33]. These subscales, and even the individual items, are broad enough to give a good sense of subjectively experienced depressive symptoms.

The CES-D, with carefully determined cutoff levels, has been shown to be a sensitive, but not a very specific, screen for major depressive disorder [34–38]. The best CES-D score cutoff to use to predict a diagnosis of major depression is controversial and varies depending on the age, gender, and health status of the population under study. The appropriate cutoff may be lower in men and adolescents [38, 39]. Populations with general medical conditions are likely to have elevated items on the CES-D regardless of psychological status [40]. The "best" cutoff according to most authors is somewhere between 16 and 22 [26, 34, 36]. Some have expressed concerns and have recommended higher cutoffs in using the CES-D as a marker for major depressive disorder given a high rate of false-positives at the lower cutoffs [35, 37, 41].

Three categories of CES-D-based response measures were analyzed here, each for a different purpose: (1) total CES-D score and cutoff threshholds, (2) CES-D subscales, and (3) individual items.

Total CES-D score and cutoff thresholds

The mean total CES-D score was calculated for each consecutive visit and for each of the seronegative and seropositive cohorts separately. Cutoffs of greater than or equal to 16 or 22 on the CES-D were used to estimate prevalence rates of major depression in the two groups over time. The values of 16 and 22 were chosen because they represent the highest and lowest reasonable estimates of caseness using the CES-D based on the literature reviewed and discussed previously. Additionally, general population norms using the cutoff of 16 are available [26].

To compare the two cohorts on these measures, three statistical models were fitted to the pooled data from all visits. In order to adjust for the effect of repeated measures over time from the same individuals, all the variance in all models was corrected using General Estimation Equations (GEE) [42–43]. Adjustment for age, race, education, and occupation, variables on which seropositives differed somewhat from seronegatives, did not change the finding, so results of univariate CES-D comparisons are presented.

Two *logistic regression* models were fitted: the first estimated the probability of having a CES-D score of 16 or greater (response variable) as a function of serostatus (covariate); the second similar model used the probability of having a CES-D score of 22 or greater as its response variable. The third analysis of variance (ANOVA) model estimated whether the total CES-D mean (response variable) was significantly different in the two serostatus groups. Since the CES-D scores' distribution was highly skewed, the logarithmic transformation of log [CES-D + 0.5] was used as the best measure for statistical testing. P values for all three models are reported with the null hypothesis being that the serostatus groups did not differ significantly on each of the response variables.

Subscale means

Four CES-D subscales were constructed based on the factor analytic studies mentioned earlier [26, 32, 33]. Items 3 and 9 were excluded from all subscales because they partially loaded on several components, and did not load on any one with a loading of 0.5 or greater. For the remaining items, they were included on a subscale if their loading factor in the literature was 0.5 or greater in at least two of the published reports. Further confirmation using factor analysis with the MACS data showed that all included items consistently loaded on the appropriate subscale with a factor greater than 0.5 for both seropositive and seronegative men.

The Somatic Subscale included the following seven items 1, 2, 5, 7, 11, 13, and 20, all of which refer to typical neurovegetative signs and symptoms of major depression. This had a potential score range of 0 to 21 using the Likert scale for each item, with a higher score meaning more symptoms. The Positive Affects Subscale consisted of items 4, 8, 12, and 16, giving it a range of 0 to 12 with a higher score referring to *fewer* positive emotions. The Negative Affects Subscale was composed of items 6, 10, 14, 17, and 18. It had a range of 0 to 15 with a higher score meaning more negative emotions.

Means on these three subscales in the two serostatus cohorts over time are reported. In order to compare the cohorts for differences on subscale means over time, three GEE [43] corrected ANOVA models were fitted using each subscale score as the outcome and serostatus as the predictor variables (see discussion above for comparison of total CES-D scores). The null hypothesis was that the two groups did not differ in their mean subscale scores. P values testing this hypothesis were generated from these models and are reported in the Results. Since the distribution of scores on all subscales was skewed to the left, each participants' subscale score was log-transformed after adding 0.5 for these comparisons. The means of these logarithmic distributions were exponentiated, and 0.5 was subtracted, to generate geometric means for each group, on each subscale, at each visit.

Finally, items 15 and 19 composed the Interpersonal Subscale. Since approximately 75% of participants in both study groups

scored "0" on *both* these items the subscale was scored categorically rather than dimensionally. Thus, a participant was said to load positive on the scale if he scored a "1" or more on *either* of the scale's items, otherwise the scale score was zero.

The prevalence of any reported interpersonal problems over time in each of the serostatus cohorts was plotted graphically. The two cohorts were compared on this subscale using a GEE-adjusted logistic regression model–similar to the one used to test the hypothesis about the probability of scoring a total CES-D score of 16 or greater–testing the hypothesis that the probability of "loading" on this subscale was not significantly different in the two groups. The *P* value obtained from this model is reported.

Individual items

A participant's mean study score across all (at least five) visits was calculated for each item after adding 0.5 and taking the logarithmic transformation. This mean represents the central tendency of the participant's response to the item. This "individual item mean" was then averaged within each cohort to generate a cohort central tendency score for the item. The geometric means of these cohort scores, estimated by exponentiating the means of the logarithmic distributions and subtracting 0.5, are reported and compared between the seronegative and seropositive groups using *t*-tests, with the *P* values of these tests being reported as well. Geometric means were chosen because the distribution of arithmetic means was skewed to the left. The purpose was to assess how many specific CES-D items accounted for differences between the two cohorts.

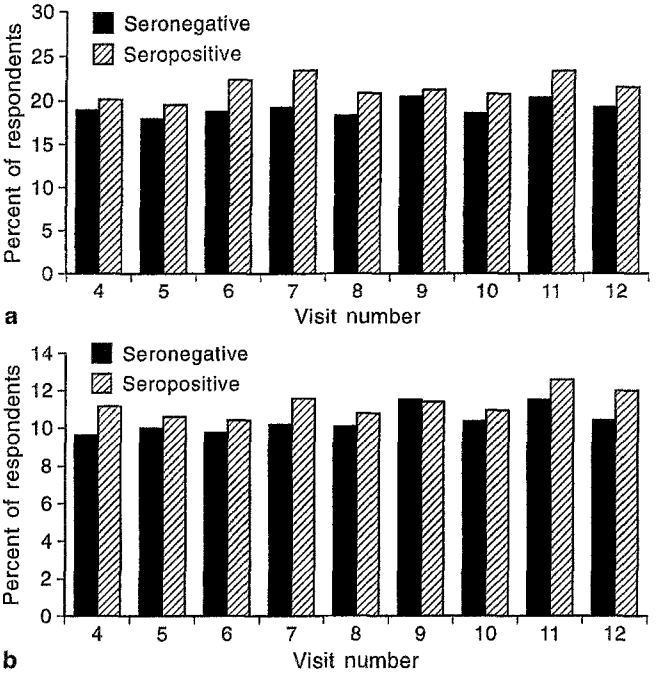

Fig. 1a, b Percentage of respondents in each cohort scoring equal to or above the Center for Epidemiologic Studies Depression Scale (CES-D) cutoff at each visit. **a** Percentage scoring equal to or above CES-D of 16. **b** Percentage scoring equal to or above CES-D of 22

Results

Table 1 contains a comparison of the seropositive and seronegative cohorts on certain demographic variables at visit 4. This Table illustrates the relatively select nature of the study participants: mostly of white, middle-class, well-educated homosexual men living in four major United States cities. Comparison of the two cohorts selected for these analyses to the original MACS cohort [27] suggested that both groups here were quite similar to the original group on these variables. However, seropositives were older, less likely to be white or Hispanic, less well educated, and less likely to hold better paying jobs, when compared to seronegatives.

Loss to follow-up occurred over the time in both groups: at visit 4 there were 750 seropositives and 2412 seronegatives; these numbers declined to 622 and 1968, respectively. However, loss was similar in the two cohorts: retention was 82.9% in the seropositives, and 81.6% in the seronegatives (chi square = 0.068, $P > 0.5$).

Figures 1a, b graphically show estimated CES-D caseness rates for depression in both seronegatives and seropositives at each visit using the CES-D cutoffs of 16 and 22, respectively. With the cutoff of 16 the prevalence of caseness was 18–20% for most visits in both groups and was stable over time. Differences between the two groups were small and not statistically significant. The *P* value of the GEE-corrected logistic model comparing the probability of scoring 16 or greater on the CES-D across all visits in the two groups was 0.19 ($n = 22\,689$ observations). However, seropositives tended to have slightly higher caesness rates at all visits.

With the more conservative cutoff of 22 a similar pattern emerged. As expected, the CES-D caseness

Table 1 Comparison of the seropositive and seronegative cohorts at the fourth study visit on demographic variables

Comparison variable		Seropositives $n = 750$	Seronegatives $n = 2412$
Age**	Mean	32.6	34.2
	SD	6.5	8.3
Race**	White or hispanic (%)	91.9	95.5
Gender	Male (%)	100	100
Education*	High school or less (%)	15.9	13.1
Occupation**	Managerial/professional (%)	49.5	55.2

*P of comparison < 0.05

**P of comparison < 0.001

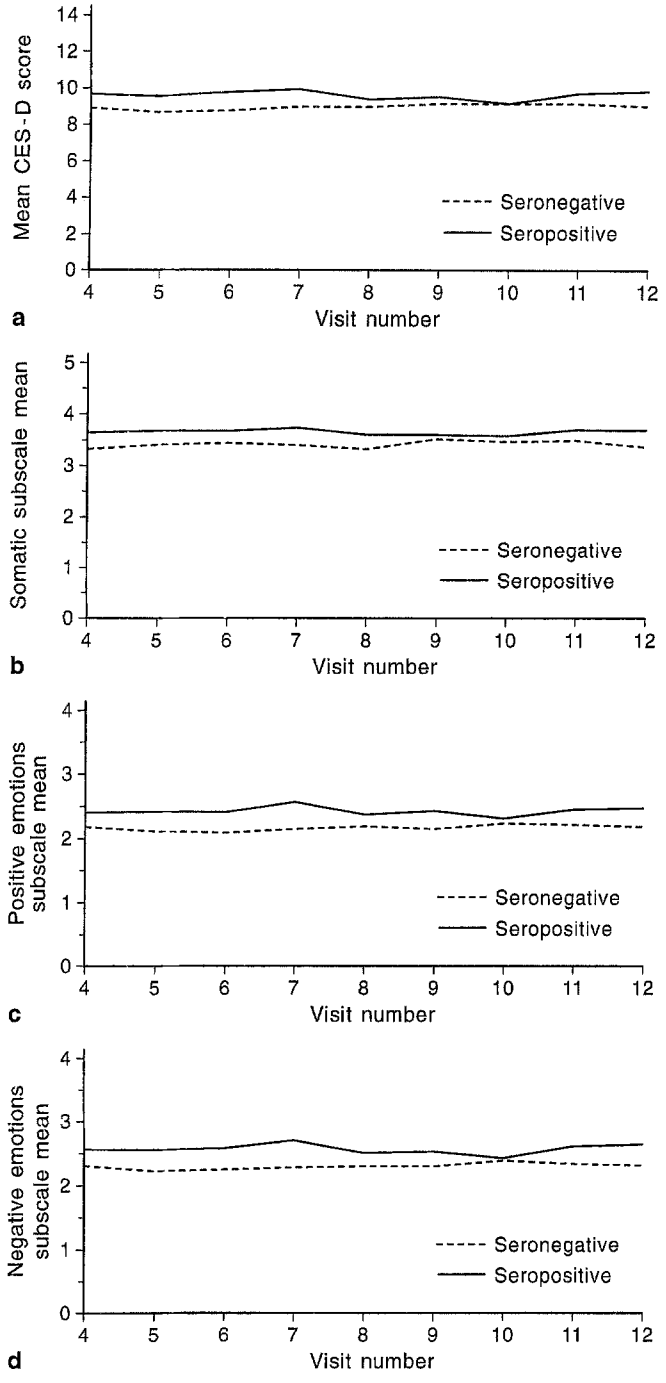

Fig. 2a–d Scale and subscale means for each cohort at each visit. **a** Total CES-D; **b** somatic subscale; **c** positive emotions subscale; **d** negative emotions subscale

rates for depression were lower at 9–12%. They were stable over time and similar in both groups. However, the trend for seropositives to have higher rates was less pronounced and was still not statistically significant ($P = 0.54$ across all visits for the GEE-corrected logistic model; $n = 22\,689$ observations).

Figures 2a–d and 3 depict the comparisons of the serostatus groups on the CES-D and its subscales over time. With regard to total scale (Fig. 2a) the means were

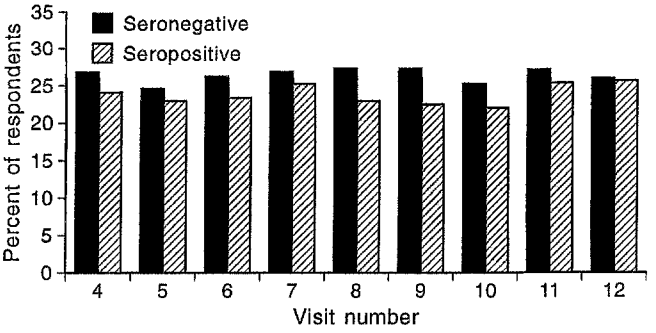

Fig. 3 Percentage of respondents in each cohort reporting an interpersonal problem at each visit

around 9.0–10.0 for both groups, but there was a sustained tendency for seropositives to score higher at all visits. However, absolute differences were quite small. These differences reached the level of statistical significance, with the P value of the GEE-adjusted ANOVA comparing the two groups across all visits being 0.0004 ($n = 22\,689$ observations).

Similar results were found for the somatic (Fig. 2b), positive emotions (Fig. 2c), and negative emotions (Fig. 2d) subscales where the seropositives consistently reported greater distress across all visits (GEE-corrected ANOVA: $P = 0.003$, $n = 23\,346$ observations; $P = 0.0008$, $n = 23\,345$ observations; $P = 0.003$, $n = 23\,341$ observations; respectively).

Finally, Fig. 3 shows the prevalence rate of reported interpersonal problems over time. In both cohorts approximately 25% of participants reported such problems at every visit. Although there was a very small tendency for the seronegatives to report more such problems, this did not reach statistical significance (GEE logistic regression across all visits: $P = 0.07$, $n = 23\,342$ observations).

Table 2 contains the cohort-specific geometric means for individual CES-D items averaged across all visits. It also shows the subscale on which each item was included, as well as the P value of the t-test comparison. Differences in subscale means were generally small. The results support the idea that differences between the groups were limited to a few CES-D questions. Using the 0.05 level to decide significance, only six items (numbers 2, 6, 8, 10, 11, and 19) were associated with P values below that level. All subscales were represented in these items. The largest differences were from seropositives being less "hopeful on the future" and more "fearful," and to a lesser extent for having "poor appetite," more "trouble sleeping," and being *less* likely to state "people disliked" them.

Discussion

This research presents a number of findings relating to depressive symptoms and their course before AIDS

Table 2 Comparison of geometric means on individual Center for Epidemiologic Studies Depression Scale (CES-D) items averaged across eight visits: each item's scale ranges from 0 to 3 (*SP* seropositive, *SN* seronegative)

Item	Content	Subscale	SP mean	SN mean	*P*
1	Bothered by things	Somatic	1.09	1.10	0.72
2	Poor apetite	Somatic	0.77	0.71	0.001
3	Could not shake blues	None	0.99	0.96	0.29
4	As good as other people	Positive	1.00	0.94	0.068
5	Trouble concentrating	Somatic	1.32	1.35	0.54
6	Depressed	Negative	1.43	1.34	0.033
7	Everything is an effort	Somatic	1.23	1.20	0.43
8	Hopeful on future	Positive	1.57	1.30	0.0001
9	Life is a failure	None	0.76	0.78	0.37
10	Fearful	Negative	1.22	1.04	0.0001
11	Trouble sleeping	Somatic	1.66	1.50	0.002
12	Happy	Postive	1.49	1.46	0.56
13	Like talking less	Somatic	1.03	0.99	0.14
14	Lonely	Negative	1.34	1.35	0.93
15	People are unfriendly	Interpersonal	0.75	0.78	0.082
16	That you enjoy life	Positive	1.31	1.29	0.72
17	Crying	Negative	0.66	0.64	0.12
18	Sad	Negative	1.29	1.22	0.084
19	People dislike you	Interpersonal	0.71	0.76	0.004
20	You could not get going	Somatic	1.32	1.26	0.15

P value of *t*-tests on log-transformed item scores

develops in the early and middle stages of HIV infection. These findings also provide a time-dependent quantification of subjective distress, and an indirect measure of quality of life [44]. What was shown in this study was that, until full-blown AIDS develops, HIV-infected patients experience a small, chronic elevation in depressive symptoms that is mostly composed of an increase in some negative emotions, a decrease in some positive emotions, and, to a lesser extent, an increase in the somatic symptoms of depression. In particular, they consistently reported feeling less hopeful and more fearful than their seronegative cohorts. They intermittently reported more trouble with sleep and appetite than seronegatives.

CES-D caseness prevalences in HIV-infected homosexual men were estimated at 10% using the more conservative CES-D cutoff of 22. This estimate is preferred because it improves the specificity of the case definition [35] and because it is closer to cross-sectional estimates of the disorder in HIV-infected men where major depression is defined using standardized psychiatric diagnosis [2–4].

The CES-D caseness prevalence in seropositives was not greatly elevated when compared to the uninfected homosexual men. Furthermore, these estimates were only slightly higher than the 1-year prevalence estimates for major depression among men (7.7%) reported in a national probability sample [45]. Also, the prevalence estimate of depressive disorder defined using a CES-D cutoff of 16 or greater in the populations in this study was similar to that reported in a United States normative community sample [26]. Thus, our findings suggested that major depression is not more prevalent in HIV-infected men early in the infection, and that this prevalence does not change over time.

These results led to two conclusions. First, there was no evidence for a substantial increase in depressive symtpomatology in HIV infection before AIDS. Therefore, an "organic mood disorder" caused by infection of the brain by the HIV is unlikely at early and middle infection stages. If such a disorder exists, as some evidence suggests [5–7], it probably manifests itself at the later stages of infection at or after the time that AIDS develops.

The second conclusion was that HIV-infected homosexual men before AIDS do not experience dramatic elevations in depressive symptoms as a psychological reaction to the knowledge of their HIV status. Furthermore, while these results did not prove that depression is not a risk factor for HIV infection in homosexual men, they did indicate that the overly depressed did not compose a large subset of those becoming infected with HIV.

HIV seropositive persons chronically report less hope, more fear about the future, loss of appetite, and more trouble sleeping, all of which likely impact on the quality of their lives. The elevated levels of poor appetite seen here amongst the seropositives before AIDS are noteworthy even though small in magnitude, as this may pose a threat to their nutritional status, and may contribute to the "HIV wasting syndrome" [29]. It is important to note that the chronic complaints of anorexia and insomnia could well be consequences of the viral infection and not indications of depressive disorders.

This is the first study to date to report on the CES-D taken longitudinally over 4 years in over 3000 persons. Consequently, the methods we used and the values we report regarding the percentage above the two thresholds, total CES-D over time, subscale scores, and

item scores for the seronegative cohort could be used by future investigators seeking approaches to using time-dependent CES-D data. Moreover, these results provide a baseline for comparison of changes in depression on entry into or soon after AIDS.

We temper our conclusions because of some methodological limitations. These findings apply to a convenience sample of homosexual men in four major United States metropolitan areas. They may not generalize to the general population of HIV-infected persons, particularly those who have other risk factors for infection such as injection drug use. Additionally, we have no information on treatments for depression that MACS participants may have received.

Second, persons who develop clinical AIDS within 5 years of initial HIV infection were excluded from consideration in this study because persons who seroconvert or who develop clinical AIDS within the first 5 years of the study were eliminated for other reasons. There is a minority of individuals who develop AIDS within the first 5 years of infection. They undoubtedly differ from those who develop AIDS later in variables that are unknown but might include more depression. Therefore, exclusion of these participants may have biased our findings toward the null hypothesis.

Next, it is possible that severely depressed persons were not motivated enough to participate in the MACS given the recruitment procedures and the demands placed on study participants in terms of time commitment. If severe depression is linked to becoming infected, either as a risk factor or as a protective variable, the differences shown here between seropositives and seronegatives may be artifactually small because the sample excluded severely depressed persons.

Finally, the use of the CES-D as the primary measure of depressive disorder and of depressive symptoms limits our ability to make conclusions about depressive disorders. CES-D is a self-report scale, and, thus, depressive symptoms ascertained in this way do not always correlate with those ascertained through clinical examination in a structured diagnostic interview. Also, the sensitivity and specificity of the CES-D in detecting clinical depression is well below 100%. Furthermore, the CES-D may be limited in its ability to distinguish between moderate and severe degrees of clinical depression.

However, the resources needed to diagnose depression clinically for each participant at each visit are impossible to obtain for a longitudinal study following 5000 men over 8 years. We believe the CES-D is a pragmatic substitute that enables us to obtain sufficient sample size and long-term follow-up. In particular, the use of a conservative cutoff to estimate the prevalence of depression partially overcomes this as it brings estimates of the depressive disorder closer to those made through cross-sectional psychiatric diagnosis. Also, using the CES-D to quantify and specify the amount and nature of depressive symptomatology has been shown repeatedly in other settings to yield results comparable to those with similar self-report measures of mood [for example 40, 46].

What do these findings imply for the preventive and clinical care of HIV-infected patients? First, as rates of major depressive disorder are not clearly increased compared to the general population in the early and middle phases of the infection, there is no need to anticipate a vast increase in patient care against depression for patients at these stages. This does not, however, mean that mood disorders should not be sought and treated aggressively as they are common and lead to substantial morbidity and mortality in patients who already experience the effects of several pressures. Indeed, the presence of a mood syndrome in early and middle stage HIV patients is likely to be treatable and, thus, should not always be construed as an understandable reaction to knowledge of having the HIV infection [8]. The CES-D itself might be used as a screening tool for this purpose given the extensive normative data reported here.

Since at early stages of HIV infection, patients are slightly less hopeful, more fearful, and might have more trouble with their sleep and appetite, special effort may be needed to seek and address these problems through psychotherapeutic or other interventions. The effect of such variables on medical outcomes should also be studied, particularly as they relate to compliance with treatment, substance use, time to AIDS, and general medical morbidity.

Finally, the effect of entry into AIDS on depression and depressive symptoms should be studied in more detail. Whether previous [5] findings can be replicated using CES-D subscale scores and higher CES-D cutoffs remains to be seen. Also, the risk factors and correlates for depression at the various stages of HIV infection should be more carefully assessed. If a significant change in the incidence of major depression can be shown at the later stages of the infection this might be good background for the definition and prospective study of an HIV-specific mood disorder.

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