Depression, Substance Use, and Sexual Orientation as Cofactors in HIV-1 Infected Men: Cross-Cultural Comparisons

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INTRODUCTION

The co-occurrence of major depression in medical populations has been the subject of much controversy in the past decade. Although some investigators have suggested that reports of an increased prevalence of depression may, in part, be due to misclassification based on physician reliance on self-report methods (Perez-Stable et al. 1990) or on failure to adjust for symptoms induced by physical illness (Plumb and Holland 1977), most studies have suggested that the prevalence of depression is high, although often undetected by the primary care physician (Perez-Stable et al. 1990; Schulberg et al. 1985). Schulberg and colleagues (1985) state that it is unclear whether this oversight reflects true limitations in the physician's diagnostic acumen, his/her lack of concern for social implications, or whether it is an artifact of existing classification procedures. Regardless of the reasons for its underreporting, the detection and treatment of depression is crucial, especially for medically ill patients, because depressive disorders may adversely affect survival, length of hospital stay, compliance with therapy, ability to care for oneself, and quality of life (Schulberg et al. 1985).

These concerns are particularly relevant to human immunodeficiency virus type 1 (HIV-1), where the co-occurrence of major depression has received only limited recent attention. Based on initial reports using chart reviews (Perry and Tross 1984), it has been suggested that over 83 percent of hospitalized acquired immunodeficiency syndrome (AIDS) patients have significant disturbances in mood. Unfortunately, anecdotal studies such as this fail to use structured diagnostic interviews to distinguish transitory dysphoria in response to the clinical condition and its treatment from syndromal depression. The latter disorder is more serious and merits direct clinical intervention because it may be predictive of more accelerated course and early mortality. In addition, such reporters do not investigate

other cofactors that could account for the co-occurrence of depression in HIV-1 disease.

The purpose of this chapter, therefore, is to examine the evidence of the co-occurrence of major depression in persons infected with HIV-1, with special attention to the potential role that cofactors such as substance use and sexual orientation (i.e., being gay or bisexual) might play in accounting for the association. The chapter is organized into two parts. Part I presents a brief summary of the literature on syndromal depression in HIV-1 that was part of a larger review on the assessment of mood disorder in medical populations (Satz et al., in press). Part II presents a reanalysis of data from two large recent cohort studies of HIV-1 in populations in the United States and abroad, the World Health Organization (WHO) Multicentre Study of HIV-1 (Maj et al. 1994*a,* 1994*b*). The latter provides a more direct test of the relationship of syndromal depression in HIV-1, with special focus on substance use and sexual orientation as important cofactors.

PART I

Syndromal Depression and HIV-1 (Summary Review)

There are eight studies in the literature that report the prevalence of current and/or lifetime major depression in HIV-infected adults. Each study used structured diagnostic interview instruments and *Diagnostic and Statistical Manual of Mental Disorders*, 3d ed. revised (DSM-III-R), or ICD-10 criteria to define syndromal disorder. The results from these studies, which are summarized in table 1, indicate two general findings. The first is that none of the studies found an association of HIV-1 with lifetime depression, and only one found an association with current (1 month) depression (Baldeweg et al. 1993). In addition, none of the studies reported an association between either lifetime or current depression and early (presymptomatic) HIV-1 infection.

The second finding is that, despite the general lack of association between major depressive disorders (MDD) and HIV-1, the rates for both current and lifetime depression in HIV-infected persons were significantly higher than the prevalence rates for depression in the general population reported in both the Epidemiologic Catchment Area (ECA) study (Regier et al. 1988) and in the more recent National Comorbidity Survey (NCS) (Kessler et al. 1994). The

average prevalence rates for lifetime MDD in HIV seropositive men (23.7 percent) was approximately fivefold higher than the average rate reported for men in the ECA (4.6 percent) and 1.8 times higher than reported for men in the NCS (13 percent). With respect to current depression, the observed rates were approximately 3.8 times higher than reported for 1-month ECA rates for men (2.3 percent). NCS rates for current major depression were available only for the past 12 months. Comparisons are presented for men only because the studies of HIV-1 included primarily well-educated, white, gay, male volunteers, which reflects the population most affected in the first wave of the disease. For example, in five of the studies the participants were described as gay or bisexual (Tross et al. 1987; Atkinson et al. 1988; Williams et al. 1991; Baldeweg et al. 1993; Perkins et al., in press). Given the population trends for this disease, it is very likely that the majority of the participants in these early studies were gay or bisexual.

Despite the generally null findings regarding the association between MDD and HIV-1, one must note that few studies contrasted the spectrum of HIV-1 infection (Tross et al. 1987; Atkinson et al. 1988; Baldeweg 1993), while other studies pooled cases of presymptomatic and sympto- matic HIV-1 infection (Perry 1990; Pace et al. 1990). The pooling of early stage and advanced stage patients could attenuate the HIV-MDD association if the latter is more likely to be present in advanced cases. Also, most studies had small sample sizes, which restricts power to detect an association between these putative comorbid outcomes.

The consistently high rates of MDD across studies, regardless of serostatus, raises the question of whether sexual orientation or other factors may be unexamined independent risk factors for major depression. Only one study (Atkinson et al. 1988) explored this hypothesis by including two small samples of noninfected gay (N = 11) and heterosexual (N = 22) controls. This study was the first to show an elevated rate of MDD in the gay and bisexual groups, independent of serostatus, suggesting that sexual orientation and lifestyle may be risk factors for major depression.

It is also noteworthy that despite evidence of significant substance abuse among those at highest risk for HIV-1 infection (Donahoe 1990; Parker and Carballo 1992), none of these studies investigated whether the increased prevalence of depression in their samples may have been attributable, either directly or indirectly, to the widespread abuse of alcohol and other substances.

TABLE 1. *Prevalence (%) major depressive disorder (MDD) for current (past month) and lifetime by studies versus ECA rates.*

Study	HIV-1 status	N	Sex. orient.	Percent Current	ECA	Percent Life	ECA	Comments
Tross et al. 1987	SN	149		4.7				No HIV effect
	ARC	40	G/B	15.0	2.2			High % MDD
	AIDS	90		13.0				
Atkinson et al. 1988	CONT	22	HET	0.0[1]		9.1		No HIV effect
	SN	11		9.1		36.4		High % MDD
	ASP	17	G/B	17.6		35.3		in G/B
	ARC	13		7.7		38.5		
	AIDS	15		6.7		13.3		
Perry1990	SN	103	Mixed	4.9		30.1		No HIV effect
	ASP	51		3.9	2.2	25.5	4.4	High % MDD Females higher % MDD
Pace et al. 1990	ASP	95	Mixed	5.8	2.8	5.3	7.0	No HIV test No increase MDD
Williams et al. 1991	SN	84		4.0		33.0		No HIV effect
	HIV+	124	G/B	4.0	2.2	32.0	3.0	High % MDD
Brown 1992	HIV+	442	Mixed	6.3	2.0	22.4	7.8	No HIV test High % MDD
Perkins et al., in press	SN	71		3.0		32.0		No HIV effect
	ASP	98	G/B	8.0	2.2	28.0	3.1	High % MDD
Baldeweg et al. 1993	SN	38		8.0[2]				HIV effect
	ASP	59		3.0				(current)
	SSP	48	G/B	31.0				High % MDD

KEY: 1 = Heterosexual control; 2 = currrent equals 6 months.

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In summary, these studies suggest that there does not appear to be a consistent association between HIV-1 serostatus and major depression, although groups at highest risk for this disease also appear to be at high concurrent risk for major depression. However, a more definitive test of the question of whether HIV-1 disease is associated with increased risk for depression will require larger study samples with adequate representation across the HIV-1 spectrum, including heterosexuals, gays, and bisexuals, to determine the independent and interactive effects of HIV disease and sexual orientation on major depression. Also, because most studies employed predominately well-educated, gay or bisexual, white male volunteers, results cannot be generalized to populations in developing countries, which now account for 85 percent of HIV-1 infection in the world and where primary transmission is through heterosexual intercourse (WHO 1992; Maj et al. 1994*a*). The results also cannot be generalized to ethnic minorities in the United States, especially to African Americans and Hispanic Americans, who constitute the groups at highest risk for infection in the second wave of the disease (Peterson and Marin 1988; Krueger at al. 1995). Finally, it is also possible that the widespread abuse of alcohol and other recreational drugs may enhance risk for both HIV-1 infection and major depression in high-risk groups (e.g., gays and bisexuals, intravenous (IV) drug users, and cocaine abusers).

The next section reviews and reanalyzes data from two large cohort studies of HIV-infected men that afford an opportunity to investigate the hypothesized role of sexual orientation and substance abuse as cofactors in the increased prevalence of MDD in HIV-infected men.

PART II

Cross-Cultural Comparisons: The WHO and AAHP Studies

The WHO Multicentre Study of HIV-1 Infection. The WHO project investigated the relationship of neuropsychological, neurological, and psychiatric correlates of HIV-1 infection in a large, representative sample of adults in the five geographic areas predominately affected by the HIV-1 epidemic: sub-Saharan Africa (Nairobi, Kinshasa), South America (Sao Paulo), Western Europe (Munich), and Southeast Asia (Bangkok). The two African sites were selected because they accounted for approximately 60 percent of the world's cases of HIV-1 during the late 1980s (WHO 1990). The additional sites were also selected to represent geographic areas disproportionately affected by the epidemic and that provided appropriate medical resources and

access to outpatient recruitment. A total of 955 subjects (203 in Nairobi, 205 in Kinshasa, 178 in Sao Paulo, 183 in Munich, and 186 in Bangkok) were recruited for the cross-sectional phase. Subjects were predominantly male (704/955 = 73.7 percent) and self-reported heterosexual (798/955 = 83.6 percent) across sites. Results of the pilot phase, including a description of the study, were reported by Maj and colleagues (1991). Results of the cross-sectional phase were reported separately for the psychiatric (Maj et al. 1994*a)* and for the neuropsychological and neurological findings (Maj et al. 1994*b*).

For purposes of this review, only the psychiatric results are presented and discussed. Psychiatric assessments in the WHO study were based on three measures: (1) the Composite International Diagnostic Interview (CIDI) (WHO 1987), which is a structured interview that yields ICD-10 (WHO 1992) and DSM-II-R diagnoses; (2) the 18-item version of the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham 1962); and (3) the Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg 1979). Because of possible linguistic and cultural differences between the samples, special care was taken to ensure the reliability and validity of these assessments.

Maj and colleagues (1994*a*) reported the results for each of the major psychiatric disorders for each study site. However, the present technical review discusses only results specific to syndromal major depression, both in terms of overall prevalence and of its association with HIV serostatus, sexual orientation, and substance use. Results for syndromal depression indicated that there was no association with HIV-1 and lifetime depression at any of the sites, and only one of the sites (Bangkok) showed an association between HIV seropositivity and current (past month) major depression. The results from the five study sites, when compared with the findings from the preceding eight studies, indicate no association between HIV-1 and lifetime occurrence in any of the studies, and only two studies reported association with current (past month) occurrence (Baldeweg et al. 1993; Maj et al. 1994*a*, Bangkok site). Comparisons of the prevalence rates for current and lifetime MDD in each WHO site and in other population surveys are in a later section of this chapter.

It is especially noteworthy that there is little support for the expected association of HIV-1 and major depressive disorder, even in individuals with great cultural, ethnic, and educational diversity. However, it is possible that the null findings may be attributable to small samples at each site (an average of 191 subjects/site) or to the

confounding of other risk or comorbid factors (i.e., sexual orientation, substance abuse). As noted previously, only one study (Atkinson et al. 1988) directly investigated the effects of sexual orientation on major depression and HIV-1, and no published study has investigated the effects of substance abuse on this association.

In testing the alternative hypotheses using the WHO data, subjects were pooled across sites (N = 955) to increase statistical power in testing the association between HIV-1 and current major depression (regardless of sexual orientation or substance abuse). In contrast to prior WHO findings (Maj et al. 1994a), the pooled results reveal a significantly greater preva- lence of current major depression as a function of HIV-1 disease stage (0_2 = 8.5, p < 0.01). In fact, there was almost a fivefold greater prevalence of current depression in the seronegative group (SN = 1.9 percent) when compared to the symptomatic seropositive group (SSP = 9.9 percent) (see figure 1).

There was also a significant association between HIV-1 status and lifetime major depression, indicating almost a threefold greater prevalence of major depression in the SSP group than in the SN group (23.5 percent versus 9.4 percent, 0_2 = 6.2, p < 0.01) (see figure 2). These pooled results differ from the original report (Maj et al. 1994b), which found no association when results were analyzed separately for each site. However, this difference may reflect, in part, the effects of increased sample size and power. For example, the difference between symptomatic seropositives and seronegatives for lifetime major depression was of the same magnitude in two of the WHO sites as in the pooled sample.

These results raise the additional question of whether the differences may be explained by the confounding of serostatus with other risk factors such as sexual orientation and comorbidity for substance abuse. The following analyses address this hypothesis, providing a reasonable but not ideal test because of the sample composition on the cofactors across four of the sites. For example, the two African samples (Nairobi and Kinshasa) included exclusively heterosexual and predominately non-intravenous drug users (non-IDU) (98 percent) participants. The Bangkok sample also included primarily heterosexuals (93 percent), but a significant majority were IDUs (74 percent). In contrast, the Sao Paulo sample included a majority of gays and bisexuals (51 percent) and non-IDUs (89 percent). The Munich sample was more heterogeneous with respect to these cofactors and was, therefore, dropped from the subsequent analyses.
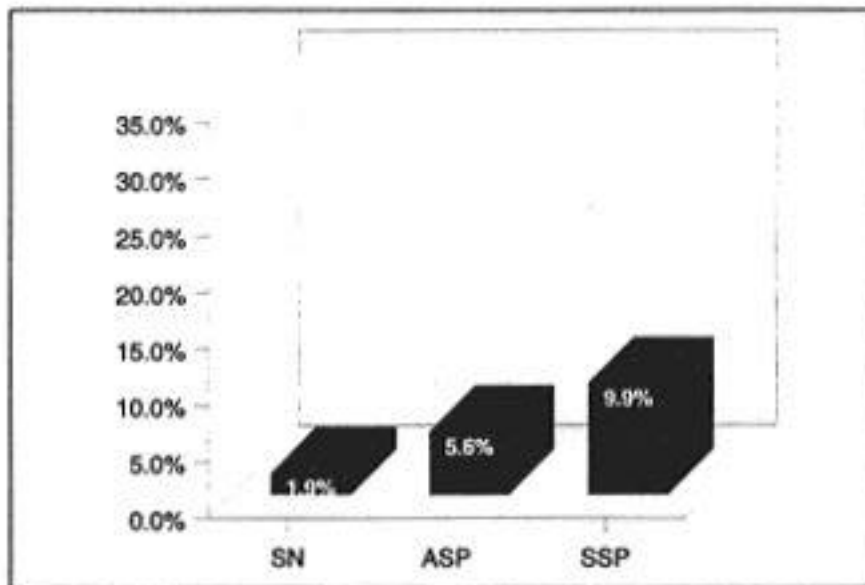
FIGURE 1. *Prevalence of major depressive episode (past 30 days) by serostatus among subjects in the WHO Multicentre Study (N = 955).*
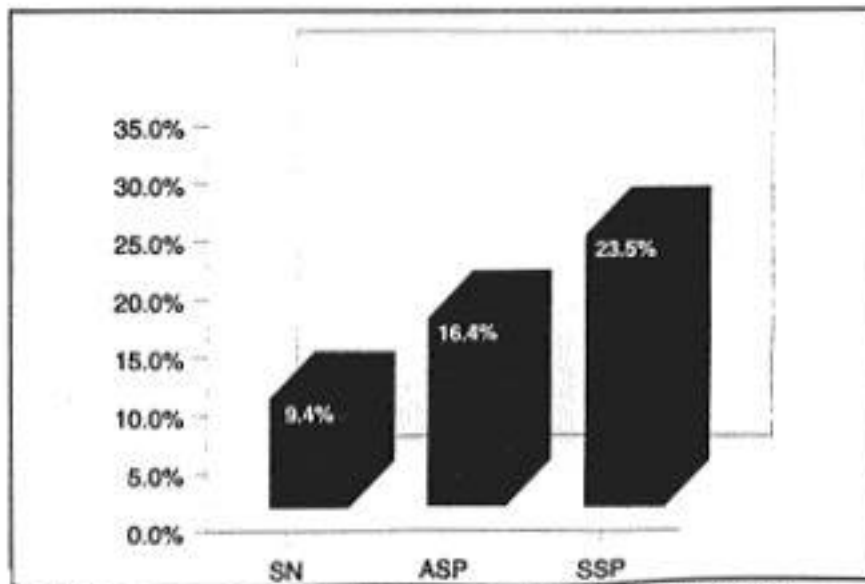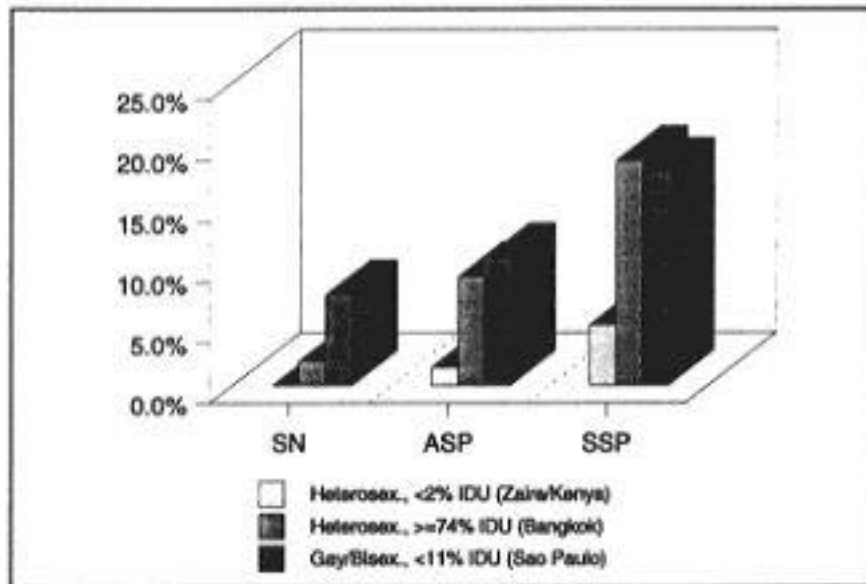

FIGURE 2. *Prevalence of major depression (lifetime) by serostatus among subjects in the WHO Multicentre Study (N = 955).*

The effects of the preliminary risk groupings and HIV status on current major depression are presented in figure 3. What is striking is the strong association of sexual orientation (being gay or bisexual) and IDU with current major depression. In fact, when these risk factors are excluded and one looks only at the non-IDU heterosexual group (Nairobi, Kinshasa), the association between HIV status and major depression disappears.

Similar and more robust effects of sexual orientation and IDU for lifetime major depression can be seen in figure 4. Again, excluding these risk groups eliminates the association between HIV status and major depression among the non-IDU heterosexuals. If replicable, these results are instructive with respect to the putative association between HIV status and major depression. If potential confounders, including comorbidity, are not controlled for, it is possible to reach quite different and misleading conclusions regarding a controversial hypothesis. However, caution should be used against overinterpreting even these findings because of the differences in sexual orientation and substance abuse across the WHO sites. The tests of sexual orientation and substance abuse noted above may be misleading due to the confounding of sexual orientation and ethnocultural origins. As noted in figure 3, the heterosexual/non-IDUs are all Africans, the heterosexual/IDUs are mainly Thais, and the gay/bisexual/IDUs are mainly Brazilians. It is possible that the observed effects could be attributed to unexamined sociocultural differences associated with sexual orientation, drug use, and major depression in these societies. Also, gay/bisexual/non-IDUs were not represented in these comparisons, which limits the test of sexual orientation independent of IDU status.

To partially control for some of these problems, a stepwise logistic regression analysis was conducted on the total sample pooled across the five study sites (N = 955) for current (1 month) and lifetime depression with drug use, sexual orientation, education, age, and serostatus entered as independent variables. Consistent with the first set of analyses of pooled data, the results showed that HIV status was the major predictor of both current ($0^2 = 8.2$, p < 0.01) and lifetime depression ($0^2 = 18.8$, p < 0.00001). However, drug abuse ($0^2 = 4.3.2$, p < 0.05) and gay or bisexual orientation ($0^2 = 4.1.2$, p < 0.05) were significant predictors of lifetime depression only in symptomatic seropositives compared to seronegatives. This suggests that serostatus is the best predictor of both current and lifetime major depression across the HIV spectrum, when

FIGURE 3. *Prevalence of current major depressive episode by serostatus and cofactors among subjects in the WHO Multicentre Study.*
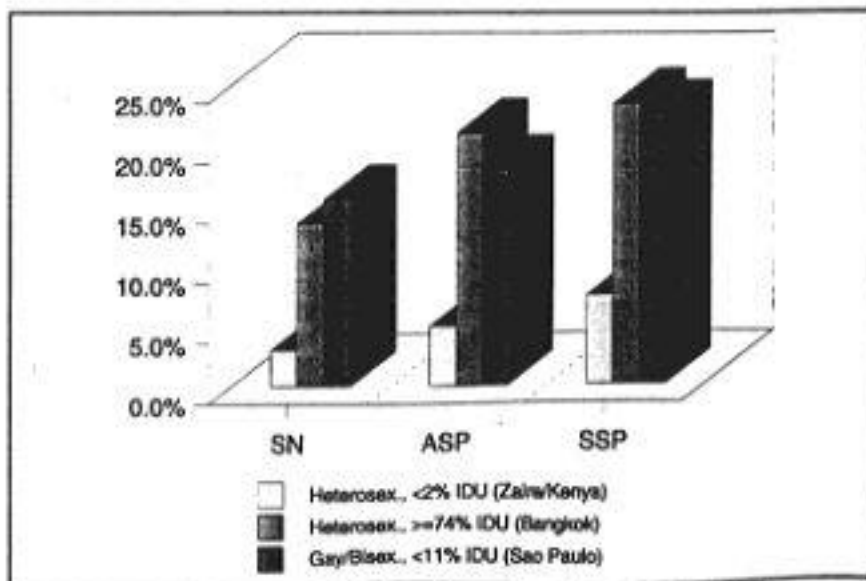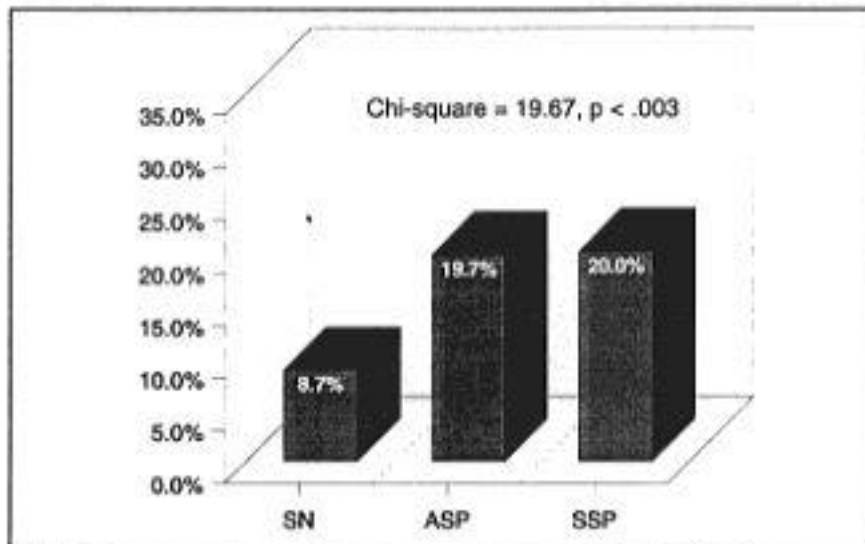

FIGURE 4. *Prevalence of lifetime depression by serostatus and cofactors among subjects in the WHO Multicentre Study.*

sexual orientation and substance abuse status are controlled for. The two latter cofactors, however, appear to be important in predicting enhanced risk for depression only in those with full-blown AIDS. Because of the noted caveats about the unbalanced representation of sexual orientation in the sample and the limited assessment of substance use, the findings need to be replicated before firm conclusions about the association among these predictors and major depression can be drawn.

The African-American Health Project (AAHP). The AAHP was designed to investigate the neurobehavioral sequelae of HIV infection and substance use in urban African-American men (Myers et al. 1994). The study used a cross-sectional design on a sample of 502 African-American men from Los Angeles who differed by serostatus, drug use status, and sexual orientation. Los Angeles was initially considered as a sixth study site of the WHO Multicentre Study and included the same psychiatric assessment protocol, along with several new assessment domains (psychosocial, neuroimaging, neurological, sexual orientation, and drug usage) and an expanded neuropsychological assessment battery. The AAHP study design and assessment features afford an opportunity to investigate more thoroughly the hypothesized relationship between HIV serostatus and major depression, while controlling for sexual orientation and substance abuse.

Sexual orientation and drug use were assessed by detailed interviews and questionnaires administered to all study participants. Approximately half of the cohort was heterosexual and half gay or bisexual. However, almost all of the heterosexuals (94 percent) were HIV seronegative (N = 233), whereas most of the gays and bisexuals (69 percent) were seropositive (N = 172). These demographics reflect, in part, the major risk for HIV-1 transmission in adult men, including African Americans, which is predominately male-male sexual contact. In fact, heterosexual transmission accounts for less than 2 percent of current AIDS cases (Los Angeles County Department of Health Services). A more detailed description of this study's design and overall preliminary results was reported recently by Myers and colleagues (1994).

The results of the analyses on the association between HIV status and current (past 12 months) major depression, unadjusted for sexual orientation or substance use, are presented in figure 5. A significantly greater prevalence of major depression was found in the two seropositive groups than in the seronegative group (20 versus 8.7 percent (0^2 = 19.7, p < 0.003).

FIGURE 5. *Prevalence of major depression (past 12 months) by serostatus among subjects in the AAHP (N = 502).*

The results for lifetime major depression are presented in figure 6. Again, there is a twofold greater prevalence of major lifetime depression in the two seropositive groups (27.6 percent and 29.1 percent) versus the seronegatives (14.1 percent ($\chi^2 = 21.1$, p < 0.002)).
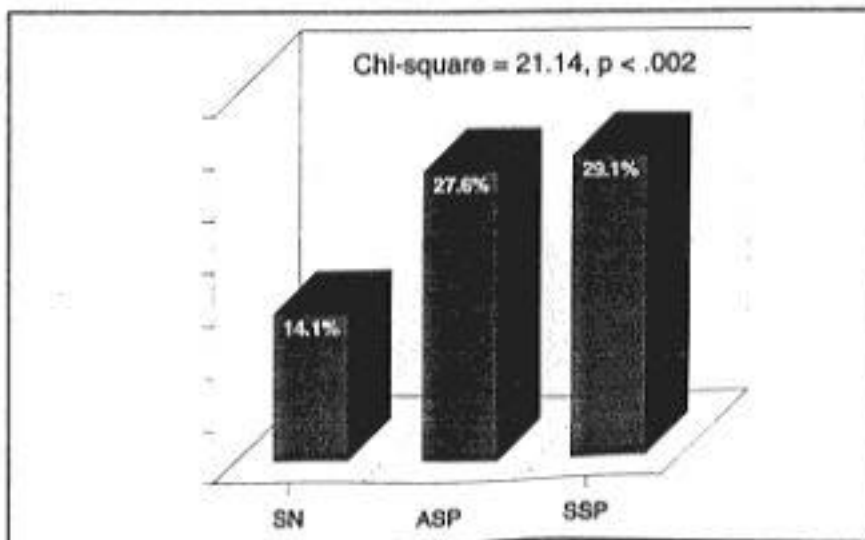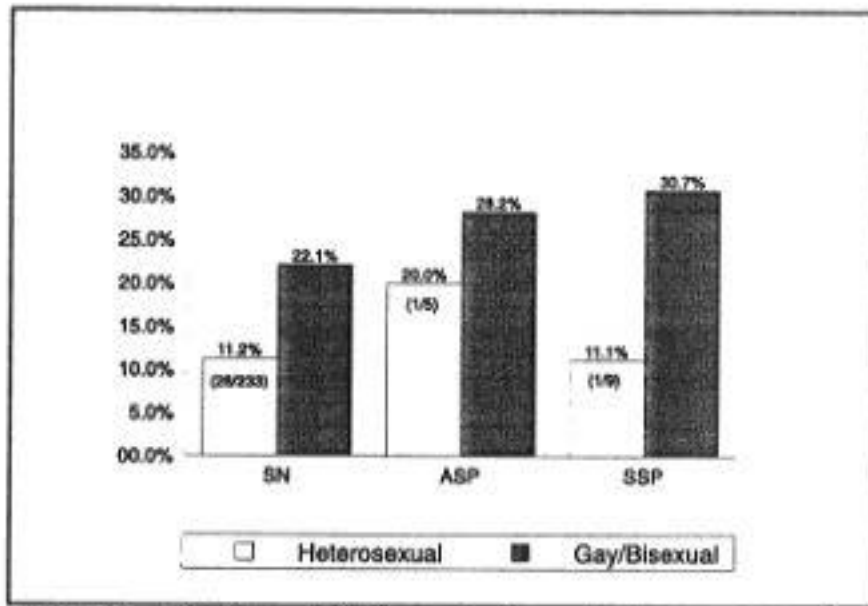

FIGURE 6. *Prevalence of major depression (lifetime) by serostatus among subjects in the AAHP (N = 502).*

To determine whether this association was partly accounted for by other risk factors, a stepwise logistic regression analysis was computed for both current and lifetime depression using a forward-stepping maximum-likelihood method. Demographic characteristics (i.e., age, education, and income), serostatus, sexual orientation, sexual orientation by serostatus interaction term, four indicators of drug use (i.e., years of drug use, past regular use, current drug use of six drugs by urine toxicology, and IDU status), and number of standard drinks of alcohol per week were entered in the analysis.

The results indicate that the best predictors of both recent (past 12 months) and lifetime depression in this sample were sexual orientation (OR = 3.36 and 2.25 for recent and lifetime, respectively) and years of cocaine use (OR 1.05 and 1.04, respectively). In other words, in both analyses, sexual orientation and duration of cocaine use accounted for most of the variance in the prevalence of recent and lifetime major depression, and were more important than serostatus.

It should be remembered, however, that sexual orientation and seropositivity were partially confounded in this sample due to the overrepresentation of gays and bisexuals among the seropositives. Therefore, this test of the relative contribution of serostatus is limited. However, as noted in figure 7, the effect of sexual orientation on major depression was quite robust, even when serostatus was controlled by comparing the prevalence of lifetime major depression among the seronegatives. The results indicate that there was a twofold greater prevalence of depression in the seronegative gays and bisexuals compared to the seronegative heterosexuals (22 percent versus 11 percent).

The results from the reanalyses of the WHO data and the AAHP data are contradictory: The WHO data indicate that serostatus is the best predictor of major depression, both current and lifetime, and the AAHP data indicate that sexual orientation and cocaine use are the better predictors. The questions of what accounts for these divergent findings are explored in the next section by considering differences between the two study samples.

35.0%
30.0%
25.0%
20.0%
15.0%
10.0%
5.0%
00.0%

11.2% (26/233)   22.1%   20.0% (1/5)   28.2%   11.1% (1/9)   30.7%

SN   ASP   SSP

☐ Heterosexual   ■ Gay/Bisexual

FIGURE 7. *Prevalence of lifetime major depression by serostatus and sexual orientation among subjects in the AAHP.*

Comparisons Between the WHO and AAHP Studies. There are striking differences in the rates of both current and lifetime major depression (both overall and as a function of HIV disease stage) in the WHO and AAHP samples, with the rates in the AAHP significantly higher (see figures 1 and 2 versus 5 and 6). Thus, for example, an average 5.8 percent (current) and 16.4 percent (lifetime) of the WHO sample met criteria for major depression, compared to 16 percent (current) and 23.6 percent (lifetime) of the AAHP participants. However, uncritical evaluation of these differences is misleading. For example, part of the threefold difference in the rate for current depression between the WHO and the AAHP is probably due to differences in the time referent (i.e., 30 days in the WHO and 12 months in the AAHP). A direct comparison of these rates is inappropriate. However, comparisons of lifetime rates are more appro-priate, and they indicate that the discrepancy between the WHO and AAHP is most striking among the asymptomatic seropositives (16.4 versus 27.6 per- cent, respectively) and smallest among the seronegatives (9.4 versus 14.1 percent, respectively). Possible factors that may account for this apparent differential vulnerability include the fact that the seropositives in the AAHP were primarily gays or bisexuals who, as noted previously, appear to be at greater risk for depression independent of HIV-1 serostatus. These results are also consistent

with the high rates of depression, regardless of HIV-1 status, noted in part I of this chapter (see table 1).

Factors in addition to sexual orientation that might be implicated include the psychological costs of racial conflict and relative socioeconomic deprivation in the context of a more affluent society, the stigma associated with HIV-1 as a disease transmitted primarily through homosexual contact, and possible differences in the degree of tolerance of homosexuality in African-American communities compared to other communities in the United States and abroad. In any event, these data suggest greater vulnerability to depression, at least lifetime, in the U.S. sample of African-American men than in the multiethnic/multinational samples studied in the WHO project.

Comparisons of the WHO and AAHP Studies Versus Community Surveys in the U.S. Some additional insights into the relationship between HIV-1 and major depression are afforded by comparing disorder rates in the two studies with those obtained in larger community epidemiologic surveys in which HIV-1 status was not a selection criterion. Such surveys provide a referent base rate for the prevalence of major depression in the population that is relatively independent of HIV-1. Two such surveys of the U.S. population are available for comparison, the ECA (Regier et al. 1988; Robins et al. 1984) and the more recent NCS (Kessler et al. 1994). Unfortunately, similar epidemiologic surveys in developing countries that would be a more appropriate reference for the WHO study are not available.

It was decided to use data from NCS rather than the ECA as the relevant sample for both cohorts for the following reasons: (1) In contrast to the ECA, the NCS was based on a stratified, multistage area probability sample of persons aged 15 to 54 years in the noninstitutionalized civilian population of the 48 contiguous States; (2) the NCS capture a lower and more representative age span than the ECA, which may contribute to higher rates of current and lifetime depression; (3) the NCS diagnoses using the structured CIDI are based on DSM-III-R rather than the DSM-III criteria used in the ECA; (4) the CIDI is also a more sensitive instrument and uses more detailed probes for depression than the ECA Diagnostic Interview Schedule (DIS) (Blazer et al. 1994), which tends to underdiagnose cases of major depression (Schulberg et al. 1985); and (5) the NCS interview contains a more comprehensive risk factor battery (including family psychiatric history using research diagnostic criteria) than the ECA interview.

The WHO Versus the NCS

Comparison rates for current and lifetime depression for the WHO and the NCS are presented in table 2. The table shows prevalence rates for the total WHO sample of seronegatives (pooled across sexual orientation and drug status) as well as for the seronegatives in the two African sites (Kinshasa and Nairobi), which were comprised almost exclusively of non-IDU heterosexuals (men and women). As noted earlier, the WHO rates of current depression (past 30 days) are likely to be lower than the NCS rates (12 months) due to the shorter time window. However, lifetime comparison rates are directly comparable.

The rates of current and lifetime depression in the WHO were lower in the African sites (0 and 3.45 percent, respectively), which may reflect the effects of gay or bisexual orientation and drug status.

However, the rate of lifetime depression in the NCS was almost twofold higher than for the seronegatives in the WHO (17.1 and 9.4 percent, respectively).

TABLE 2. *Prevalence of major depression (current and lifetime) in the NCS and AAHP studies.*

	NCS - Total sample (male)	AAHP - Heterosexual (SN) (male)	AAHP - Gay/bisexual (SN) (Male)
Current (past 12 months)	7.7%	5.6%	16.9%
Lifetime	12.7%	11.2%	22.1%

This finding was somewhat unexpected and is still difficult to explain. It is very likely that there may be important differences in the societies and cultures studied that confer greater risk for major depression to those in the United States compared to those in other less affluent societies. It is worth noting, however, that if the ECA rates had been used for comparison, using a similar time window, no differences would have been observed (ECA current = 2.2 percent, lifetime = 5.3 percent). Thus, some of the observed differences in the rates between the WHO and NCS samples may be due not only to differences in the time window in the societies studied, but also to possible cohort effects

within the United States that are reflected in increasing rates of depression, especially among the young (Kessler et al. 1994).

The AAHP Versus the NCS

The AAHP, as noted earlier, affords an opportunity to assess a wider range of potential risk factors for major depression in men at risk for HIV/AIDS; thus it allows researchers to better estimate the relationship between HIV serostatus and major depression, while controlling for other potential cofactors. Comparisons between the findings from the AAHP and from the nationally representative sample of men in the NCS (Kessler et al. 1994) allow one to assess whether the African-American men in the AAHP evidence comparable rates of depression to those in the national referent sample.

Comparisons for current and lifetime depression for the total NCS male sample and for the gay, bisexual, and heterosexual seronegative groups in AAHP are presented in table 3. What is striking in this table is the marked similarity in prevalence rates (current, lifetime) between the NCS

TABLE 3. *Prevalence of major depression (current and lifetime) in WHO and NCS studies.*

	WHO - Zaire/Kenya heterosexual (SN)	WHO - Total sample (SN)	NCS - Total sample
Current (past 30 days)	0%	1.9%	10.3%
Lifetime	3.45%	9.4%	17.1%

and the heterosexual seronegative sample from the AAHP (current = 7.7 versus 5.6 percent, and lifetime = 12.7 versus 11.2 percent, respectively).

However, there is almost a twofold difference in the rate of major depression in the AAHP gay and bisexual groups compared to the males in the NCS for current (16.9 versus 7.7 percent, respectively) and lifetime depression (22.1 versus 12.7 percent, respectively). Interestingly, these higher rates of depression in the seronegative gays and bisexuals closely match the higher rates of depression in the

female cohort of the NCS for current (16.9 versus 12.9 percent, respectively) and lifetime (22.1 versus 21.3 percent, respectively) depression.

Thus, the rates for depression among the heterosexual seronegative men in the AAHP are very similar to those obtained in the NCS, but the rates among the gays and bisexuals are strikingly higher. This provides further support for the hypothesis that being gay or bisexual appears to confer additional risk for major depression among males. A similar difference in major depression in gays and bisexuals was noted in the Atkinson and associates (1988) study, and was also suggested in the other studies in table 1 as well as in the WHO Bangkok site (Maj et al. 1994*a*). These results suggest that there may be common biological and/or psychosocial aspects of being gay or bisexual that are contributory to risk for major depression across ethnic groups. However, this conclusion is probably premature since there is suggestive evidence that being black and gay may be associated with greater risk for depression than being either black or gay. For example, results from both the ECA and the NCS indicate lower overall rates of depression in African-Americans than in white Americans (Robins et al. 1984; Blazer et al. 1994). In the NCS, the rates of major depression were significantly lower in black versus white males for current (1 month) (1.1 versus 4.0 percent) and lifetime depression (7.2 versus 13.5 percent). However, if one compares the rates for African-American males in the NCS with those for the gay and bisexual seronegatives in the AAHP, a more appropriate comparison than with the overall male sample in the NCS, one finds an even greater effect of sexual orientation than in table 3 for both current (1.1 versus 16.9 percent) and lifetime depression (7.2 versus 22.1 per-cent). Note that the Blazer and associates (1994) study used only a 30-day window for current depression in contrast to 12 months in the Kessler and colleagues (1994) study. Despite this difference in NCS case definition of current depression, the effect of sexual orientation is still provocative.

It is unfortunate that data on sexual orientation have not been reported in any of the structured diagnostic interview surveys to date, including the ECA and NCS, as well as smaller community surveys in this country (Myers et al. 1994) and in foreign countries, including Canada (Orn et al. 1988), Puerto Rico (Camino et al. 1987), Italy (Faravelli et al. 1990), New Zealand (Wells et al. 1989), and Taiwan (Hwu et al. 1986). Failure to probe for this information limits exploration of the range of key risk factors for major depression, and could artificially elevate the HIV-depression association. For

example, factors such as younger age and urbanicity are both associated with being gay or bisexual and HIV-1 prevalence, and there is growing evidence linking these factors with increased risk for depression. Thus, future studies should explore the independent and combined effect of each of these variables to vulnerability to major depression.

Although much has been written on psychosocial stresses and vulnerabilities that affect the gay and bisexual populations (e.g., McKirnan and Peterson 1993), very little of this information has been incorporated into the investigation of psychiatric morbidity and HIV-1. In addition, if the psychosocial stresses and stigmatization often associated with being gay or bisexual increase one's vulnerability, then what effects are likely among African-American and other ethnic minority gays who are stigmatized both on color and on sexual orientation? The comparisons reviewed here suggest that these groups are more vulnerable to depression than heterosexuals from their own cultures. Clearly, more research is needed to pursue these initial observations.

Another question that remains unanswered in this review concerns the probable etiology of major depression in each of the studies. While the increased prevalence of lifetime depression in most of these is compatible with a pre-HIV-1, or at least a pre-AIDS, diagnosis, no study has yet reported data on family history of depression to determine whether genetic or familial factors increase the risk for mood disorders, especially in individuals whose sexual orientation may confer additional biological or psychosocial burdens. Related to this question is the unexpected finding of similar high rates of major depression (current, lifetime) between the seronegative gay and bisexual males in the AAHP and the female sample of the NCS. It is possible that some of the factors currently believed to be associated with greater female vulnerability to depression may also be applicable to gay and bisexual men. A recent study by Kendler and colleagues (1993) used multidimensional latent construct modeling techniques to predict major depression in female twins, including biological (i.e., genetic), psychological (e.g., neuroticism), and psychosocial (history of trauma, stressful life events) predictors that may be heuristic in this regard. Some investigators have argued that some of the gender differences in vulnerability to depression may be attributed to differences in symptom reporting (i.e., women are more likely than men to report symptoms of distress that are criteria for depression), to greater dependence on social relationships and supports, to risk of trauma, and to power differences in relationships (Brown and Harris

1978; Roy 1978; Cutler and Nolen-Hoeksema 1991). Not all of these variables may be equally applicable to gays and bisexuals, but the approach could prove useful in formulating and testing explanatory and predictive models of depression in gay and bisexual males of different ethnic groups. Hopefully future studies will attempt to explain increased rates of major depression in terms of biological and/or psychosocial determinants.

There is also growing evidence of the possible priming role of abusable substances in both HIV-1 virus susceptibility (Friedman et al. 1988) and risk for major psychiatric disorders such as mood disorders (Regier et al. 1990). The results from the AAHP indicate that substance use, especially of cocaine, is a significant contributor to MDD independent of both sexual orientation and serostatus. Therefore, future studies of HIV-impacted populations should include careful assessments of patterns and severity of substance use and abuse to investigate whether the results reported here are replicated in other populations.

Finally, although the present technical review found inconsistent associations between major depression and HIV stage, the higher prevalence of major depression among gay and bisexual males, regardless of HIV stage, should be carefully investigated. It is possible that depression may confer additional risk for infection by encouraging more high-risk behaviors designed to cope with distress and dysphoria (e.g., substance use, unprotected sex with multiple partners). It may also hasten disease progression and mortality in those already infected, as suggested by studies that indicate greater resilience and longer survival in HIV-infected persons who are more hopeful and optimistic compared to the more pessimistic and dysphoric (Solomon et al. 1987; Rabkin et al. 1990). If these hypotheses are borne out, then greater attention should be given to the mental health needs of persons at highest risk for or living with HIV/AIDS, including psychiatric and substance abuse services. Hopefully, this chapter will stimulate more attention to the role of sexual orientation, substance use, and depression in HIV disease risk and progression.

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