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A RANDOMIZED TRIAL OF THE EFFICACY OF GROUP THERAPY IN CHANGING VIRAL LOAD AND CD4 COUNTS IN INDIVIDUALS LIVING WITH HIV INFECTION*

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ABSTRACT

Objective: This randomized pilot study evaluates whether seropositive patients who are randomly assigned to receive a supportive-expressive group therapy plus education intervention show greater improvements in increased immune function and decreased viral load compared to those randomly assigned to an education-only intervention. *Method:* Fifty-nine individuals

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who had been HIV-seropositive for at least 6 months prior to inclusion in the study and had been receiving standard pharmacologic treatment were entered in a prospective randomized trial of the effects of weekly supportive-expressive group therapy on changes in immune status. Participants were matched for AIDS status and sex and randomized to receive weekly sessions of group psychotherapy plus educational materials on HIV/AIDS, or to receive the educational materials alone. Participants were assessed before treatment and then 12 weeks later. *Results:* Individuals who were randomized to group therapy showed a statistically significant increase in CD4 count and decrease in HIV viral load. Among individuals randomized to the education only condition, no significant change occurred in CD4 count or viral load. *Conclusions:* These results provide preliminary data suggesting that HIV-seropositive individuals who receive supportive-expressive group psychotherapy may experience concomitant improvements in CD4 cell count and viral load. Further research with a larger sample should examine the possible underlying mechanisms of such benefits.

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Key Words: HIV/AIDS, group therapy, CD4 cell count, immunity, viral load, disease

INTRODUCTION

The increasing evidence of the efficacy of the pharmacologic treatment of HIV infection [1-5] and of its psychiatric comorbidities [6, 7] has sometimes led clinicians to minimize the importance of psychological interventions as an adjunctive treatment. These pharmacologic breakthroughs require patients to adhere to complicated treatment regimens that are not curative, nor are they fully suppressive of HIV replication in all instances [8-11]. In addition, some HIV-seropositive persons are less likely to receive state-of-the-art pharmacotherapy; they tend to be women, injection drug users, African Americans, and those with less education [12].

Psychosocial interventions can play a role in enhancing the quality of life for HIV-seropositive individuals [13-16]. Intensive psychotherapeutic treatments have been shown to be especially effective in reducing distress among those infected with HIV. Group-based interventions have been effective as well. Chesney and colleagues [16] reported that coping effectiveness training resulted in reduced stress and anxiety among men living with HIV. Kelly et al. [17] found that supportive-expressive group therapy was significantly more effective than a cognitive–behavioral comparison treatment in reducing psychological disturbances among HIV-seropositive men. Furthermore, there is evidence that such psychosocial support may contribute to an enhancement of physical health. A wide range of biological, psychological and social factors such as depression, social support, coping style, and life events are related to markers of HIV disease

progression such as CD4 count, natural killer cell activity and viral load [18, 19] as well as to disease progression itself [20-22]. Additional research on the effect of psychosocial interventions on markers of HIV-related disease seems warranted.

Currently, the results of randomized trials provide optimistic preliminary evidence regarding the biological benefits of psychosocial interventions for people with HIV/AIDS. Recently, Petrie [23] reported that patients randomly assigned to write about emotional compared to neutral topics had lower viral loads and increased CD4 counts. A cognitive-behavioral stress management intervention with asymptomatic gay and bisexual men found that those who enrolled in treatment after learning of their HIV-seropositive serostatus had significantly higher CD4 counts in comparison to their no-treatment counterparts [24]. Ironson et al. [25] found that HIV-seropositive men who participated in a cognitive-behavioral stress management intervention were more likely to be symptom-free two years later. Goodkin and colleagues [26] found that participants in a bereavement support group for HIV-seropositive individuals, that took place for 10-weeks, 90 minutes each week, had greater CD4 cell counts and fewer physician visits during the 6-month follow-up period compared to a control group. Lutgendorf et al. [27] found that HIV-seropositive gay men, randomly assigned to a 10-week, group cognitive behavioral stress management intervention, compared to those in a control group, showed more reduction in herpes simplex virus–type 2 immunoglobulin G antibody tests. However, Coates et al. [28] did not find any significant benefits in immune status associated with stress reduction training. Thus there is a need for further research on psychoneuroimmunologic effects of psychosocial intervention among those with HIV infection [29].

The current study was designed to explore the efficacy of supportive-expressive group therapy in improving the immunological status in both HIV-seropositive men and women, as measured by HIV (RNA) viral load level and CD4 cell count. Each is important, as change in their levels correlates with disease progression [30-34]. To our knowledge, this is the first randomized clinical trial testing the efficacy of supportive-expressive group therapy in improving health outcomes in HIV-seropositive individuals.

METHOD

Study Design

This study used a 2-group (experimental and control) randomized trial focusing on the changes occurring after 12 weeks of supportive-expressive group therapy. The primary dependent variables were changes in CD4 cell count and changes in HIV viral load.

Recruitment

Fifty-nine HIV-seropositive individuals (16 men, 43 women) who ranged in age from 20-51 years (M = 38.5, SD = 7.6) were recruited for the current pilot

study in years 1997-1999 from a larger parent study. Participants were recruited from the San Francisco Bay Area and Sacramento through newspaper advertisements and through two major county hospitals, a university hospital, and community medical clinics. Approximately three people were approached for every one who agreed to be screened. All subjects were documented HIV-seropositive, over age 21, and had sufficient proficiency in English to comprehend questionnaires and participate in group therapy if assigned.

Informed Consent

All subjects were willing and able to provide informed consent and to be able to attend psychotherapy group meetings on a weekly basis if randomized to the group therapy condition. Exclusion criteria included severe psychiatric disorders, particularly those that could be anticipated to require psychiatric hospitalization. Other exclusion criteria included: Acute tuberculosis, participating in an ongoing HIV/AIDS related support group or attending at least three months of an HIV/AIDS related support group within the previous year, mental retardation (IQ < 70) or deafness. Patients currently enrolled in any psychotherapeutic clinical trial were also excluded. Childcare was subsidized and transportation supplements were provided to lower the barrier to attend assessment and group therapy sessions. Participants were those recruited in the latter phase of the larger study. In comparing the 59 participants in this analysis to the other 127 participants in the larger study, several significant differences were found in demographic characteristics or medical status. Compared to other participants in the parent study, participants in this analysis were significantly more likely to be female (72.9% vs. 30.7%, χ^2 (1) = 4.14, $p < .05$), African American (44.4% vs. 28.8%, χ^2 (1) = 4.14, $p < .05$), less likely to be White/European American (46.3% vs. to 62.4%, χ^2 (1) = 4.00, $p < .05$), younger (M = 38.5 years vs. M = 41.3, t (176) = 2.21, $p < .05$), and had completed fewer years of education (M = 12.9 vs. M = 14.0, t (172) = 2.32, $p < .05$). This is largely due to our focus on recruiting women and ethnic minorities into the latter part of the parent study, to ensure that our overall sample would include sufficient women and minority representation.

Participants in this study ranged in age from 23 to 50 (M = 38.5, SD = 7.3), and had completed 3 to 20 years of education (M = 12.9, SD = 2.8). Eighty-nine percent of participants had annual family incomes below $20,000. Ethnicity was reported as 44.4% as African American, 46.3% White/European American, 9.3% Latino/Hispanic, 7.4% Native American, and 3.7% Pacific Islander (13.0% of respondents reported two or more ethnic backgrounds). Most participants were heterosexual (59.3%), 33.3% were lesbian/gay, and 7.4% bisexual. Most were either single (44.4%), separated (9.3%), divorced (9.3%), or widowed

(9.3%), with only 24.1% reporting being married or living as though married. Most participants did not meet T cell count criteria for AIDS at baseline (59.3%). Sixty-four percent (64%) of the subjects reported that they were taking antiviral medications.

Procedure

The current investigation explored whether biological measures of HIV changed in response to psychosocial intervention. Informed consent was obtained for each participant based on a protocol approved by the appropriate institutional review boards. Subjects completed baseline assessments and then were randomly assigned to an intervention or control condition. Randomization was made by a computerized random-number generator, stratifying by gender and by whether or not subjects' CD4 cell count was equal to or greater than 200 or lower than 200. Thirty-two were randomly assigned to the group therapy plus education condition, while 27 were randomly assigned to receive the education-only intervention. Current anti-retroviral medication status was the only statistically significant medical status or demographic that differed between the treatment group and the control group, with participants assigned to the treatment group less likely to be taking anti-retroviral medications than those assigned to the control group (53% vs 78%, χ^2 (5) = 3.8, p = .049). Participants were compensated $25 for their baseline assessment and $25 for the follow-up assessment.

Treatment Conditions

Educational Materials Only

All patients in both study conditions received pharmacologic treatment at the community's standard of care. Prescribing physicians were blinded as to the nature of treatment given to our subjects, who were told not to reveal to their physician if they were receiving group psychotherapy. If the patient was seeing a psychiatrist or psychologist for individual therapy, they were asked to not enter group psychotherapy with their current or any other practitioner. In addition to this usual care, patients received a packet of carefully selected educational materials about HIV/AIDS. The educational materials comprised a selection from scores of educational materials reviewed by researchers, HIV-positive persons, and physicians specializing in HIV/AIDS care. Educational materials also included a list of referral agencies/individuals. This condition was included so that the participants randomly assigned to the educational control condition would receive some personal benefit and would not be demoralized if they were not offered group therapy.

Supportive-Expressive Group Therapy Plus Education

Patients assigned to the experimental treatment received standard medical care and were enrolled in supportive-expressive group psychotherapy composed of weekly sessions of 90 minutes, each aimed at exploring seven main issues: social support, expression of emotion, detoxifying dying, reordering life priorities, family support, effective communication with physicians, and symptom management [35-38]. These components comprise an existentially based psychosocial model [39] and are guided by three theoretical rationales: social support, developing active coping responses and emotional expression [40]. Supportive-expressive therapy differs from conventional group psychotherapy in several important areas: 1) it is designed to create a new network of social support and encourages contact outside of the therapy setting; 2) it encourages expression of emotion related to the illnesses and other life stressors; 3) it focuses on existential issues, including working through fears of dying and death, grieving losses in the group and reordering priorities in life; and 4) it focuses away from examination of the effects of early life experiences and relationships in the genesis of current problems. The therapy was also designed and implemented to ensure sensitivity to ethnic issues and to address possible psychopathology or substance use among participants. Therapists guided active exploration of issues by group members but did not offer solutions to problems. Instead, therapists insisted on the group members exploring their feelings and developing solutions to their problems. The last ten minutes of the group was devoted to a self-hypnosis exercise using visual imagery to teach patients how to manage their pain, place problems in a new perspective, and cope with physical health symptoms. Groups typically were comprised of 7-10 group members and two group leaders. Participants assigned to receive this group therapy intervention also received a packet of educational materials that was identical to that received by the participants assigned to the education group.

Assessments

We obtained several important pieces of medical information from the patients' medical records, with their agreement and that of their physicians. This information included the HIV diagnosis and date of diagnosis and whether or not the patients had developed AIDS, which we were able to document for all patients. In addition, the baseline psychiatric status of the patient was determined by clinical interview using the Structured Clinical Interview for DSM-III (SCID) [41], the standard research tool used to establish reliable and valid DSM-IV diagnosis. No participants were excluded from this sample due to psychiatric reasons. Participants also completed a brief demographic survey that assessed age, marital status, religious affiliation, number of children, ethnicity, sexual orientation, education, employment, and family income. All subjects were assessed

before therapy/education began and 12 weeks later (after the last therapy session for those randomized to that modality). HIV viral load and CD4 count were measured by plasma assay. These methods have been extensively explained elsewhere [42]. All outcome variables were assessed by persons blinded to patients' treatment group assignment.

Analysis

Descriptive analyses indicated large variability in CD4 counts, HIV viral load, and their respective change scores across time. The data were not normally distributed and there was substantial heterogeneity of variance across treatment groups. Log transformations did not result in normality. These violations precluded the planned statistical strategy of a one-way repeated measures analysis of variance (ANOVA). Therefore, two non-parametric analyses were conducted. Wilcoxon rank tests were utilized to test for changes over time in CD4 count and HIV viral load within each treatment group. Additionally, Mann-Whitney tests compared CD4 and viral load change scores between the two treatment conditions (group therapy plus education versus education only). Alpha was set at .05, and one-tailed tests were used because the hypotheses for the effects of the intervention were directional. For nine subjects, data were missing either at baseline or outcome due to laboratory failure to obtain. No imputations of missing data were done; rather, the analyses were conducted only for the modified intent-to-treat sample.

RESULTS

Table 1 shows the demographic characteristics of the study participants.

CD4 Counts

CD4 counts were available at both baseline and follow-up from 24 patients (96%) in the education only control condition and 26 patients (90%) in the group psychotherapy condition. Subjects randomized to education only showed no statistically significant change in CD4 counts (median difference score = –24.5, range of difference scores: –231 to +407; $z = -.49$, $n = 24$, $p = .31$). A statistically significant increase in CD4 cell count was observed among those randomly assigned to receive group psychotherapy (median difference score: +22.00; range of difference scores: –106 to +307; $z = -1.8$, $n = 26$, $p = .033$). Comparison of change scores indicated a greater increase in median CD4 counts among those participants randomized to received group therapy plus education ($z = 1.63$, $n = 50$, $p = .051$); this difference was at the threshold for statistical significance (effect size: Area Under the Curve (AUC) = .64).

Table 1. Baseline and Outcome Characteristic of Study Participants

	Education Only	Intervention
Demographics		
Age (mean in years)	38.7 ± 7.7	38.4 ± 7.7
Years of education	13.5 ± 2.9	12.4 ± 2.7
Female gender	67%	78%
HIV positive	100%	100%
AIDS status from medical records	37%	44%
Currently taking anti-retroviral medication	78%	53%
Number of alcoholic drinks—past 3 months	6.4 ± 14.5	8.0 ± 18.3
Number of marijuana uses—past 3 months	6.4 ± 19.6	6.0 ± 14.3
CD-4		
Minimum change score	–231	–106
Maximum change score	+407	+307
Median change score	–24.5	+22.0
Viral load		
Minimum change score	–39,000	–734,000
Maximum change score	+240,000	+6900
Median change score	–15.00	–160.00

HIV Viral Load

HIV viral load data were available at baseline and outcome from 25 patients in the education only condition and 29 patients in the intervention condition. Patients who were randomly assigned to the education only condition showed no statistically significant change in viral load over the study period (median difference score = –15.0, range of difference scores: –39,000 to +240,000; $z = –.47$, $n = 25$, $p = .32$). In contrast, patients who were randomly assigned to receive group psychotherapy in addition to education showed a statistically significant decrease in viral load (median difference = -160.0, range of difference scores: –734,000 to + 6900; $z = –1.9$, $n = 29$, $p = .029$). However, a comparison of the two groups on viral load change scores was not statistically significant ($z = 1.11$, $n = 54$, $p = .13$; AUC = .41).

Adherence to Medication

Patients reported the number of days that they missed taking their medication. In the control group, 71.4% reported zero days of skipped medication (range 0-4 days). Similarly, 70.6% of patients in the intervention group reported zero days of skipped medication (range 0-2 days).

DISCUSSION

To our knowledge this is the first study that measured biological outcomes for HIV-seropositive patients randomized to supportive-expressive group psychotherapy as the experimental intervention. A number of studies have examined the efficacy of psychosocial interventions on biological outcomes for HIV-seropositive individuals, but despite its widespread use with breast cancer patients, little previous research, outside of that done by Kelly et al. [17], has been done using supportive-expressive group therapy for patients living with HIV. The overall results of this study provide preliminary data which suggest that supportive-expressive group therapy may be effective in modulating important biological markers of HIV disease progression, particularly that of CD4 count. For viral load, the within-group analysis showed statistically significant improvements in the group therapy condition over time. However, in the between groups comparison of the two treatment arms, the difference in viral load was not statistically significant. Therefore, further research with larger samples is warranted by these preliminary results.

Generalizability of the findings is enhanced by the fact that women as well as men living with HIV infection were included in this study, which is relatively rare in HIV psychosocial intervention research. The sample was ethnically diverse and predominantly low income, which is representative of the emerging epidemiological profile of HIV-seropositive patients in the United States. Another strength of this study is its prospective nature. The generalizability of this study's findings is enhanced by the variability that may have been introduced by having multiple therapists conducting the intervention. This suggests that a wider group of professionals could be trained to conduct effective group psychotherapy for persons living with HIV.

Supportive-expressive group psychotherapy may be useful as an adjunctive treatment with maintenance antiretroviral pharmacotherapy to improve health in HIV-seropositive patients. The results of this study suggest possible immunity benefits of incorporating psychotherapeutic intervention in the treatment of HIV infection.

Future research is needed to try to replicate and extend these preliminary results. A major direction requiring further investigation is to examine possible mechanisms that could account for the observed improvements among the participants who received the supportive-expressive group therapy intervention. It is possible that the observed effects were attributable to increased social support provided by the intervention rather than to particular aspects of supportive-expressive therapy. Recently, Burgoyne [43] has explored the directionality of the relationship between viral load and social support improvement, asserting that social support improvement is likely the predecessor. One possibility would be that the group therapy intervention bolsters immunity by improving adherence to medical treatment. In a previous research with the larger study sample, no

significant improvement in adherence was found among the patients who received group therapy compared to those who did not [44]. Therefore, the greater increase in CD4 cell count among patients who received group therapy compared to those who received education only may not be attributable to adherence to medication. Supportive-expressive group therapy may help to bolster immunity among HIV-seropositive patients in other ways, such as through its effects in reducing the stress response of the hypothalamus-pituitary-adrenal axis, a response that is known to down-regulate immunity [45].

A limitation of this and similar randomized psychotherapy pilot trials is that the design and sample size did not permit identification of the specific mechanisms underlying the effects of the psychosocial intervention on the biological outcomes. Therefore, this study raises questions for further research, such as whether group participation bolsters mental well-being and/or buffers stress, which in turn enhance immunity [46-49]. Further thought and study should determine effective intervention strategies for optimizing physical health among persons living with HIV.

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REFERENCES

1. Collier AC, Coombs RW, Schoenfeld DA , Bassett RL, Timpone J, Baruch A, Jones M, Facey K, Whitacre C, McAuliffe VJ, Friedman HM, Merigan TC, Reichman RC, Hooper C, Corey L. Treatment of human immunodeficiency virus infection with saquinavir, zidovudine, and zalcitabine. *New England Journal of Medicine* 1996; 334(16):1011-1018.
2. Danner SA, Carr A, Leonard JM, Lehman LM, Gudiol F, Gonzales J, Raventos A, Rubio R, Bouza E, Pintado V, et al. A short-term study of the safety, pharmacokinetics, and efficacy of ritonavir, an inhibitor of HIV-1 protease. European-Australian collaborative ritonavir study group. *New England Journal of Medicine* 1995;333(23): 1528-1533.
3. Gulick RM, Mellors JW, Havlir D, Eron JJ, Gonzalez C, McMahon D, Richaman DD, Valentine FT, Jonas L, Meibohm A, Emini EA, Chodakewitz JA. Treatment with indinavir, zidovudine, and lamivudine in adults with human immunodeficiency virus infection and prior antiretroviral therapy. *New England Journal of Medicine* 1997;337(11):734-739.

4. Markowitz M, Conant M, Hurley A, Schluger R, Duran M, Peterkin J, Chapman S, Patick A, Hendricks A, Yuen GJ, Hoskins W, Clendeninn N, Ho DD. A preliminary evaluation of nelfinavir mesylate, an inhibitor of human immunodeficiency virus (HI)-1 protease, to treat HIV infection. *Journal of Infectious Diseases* 1998;177(6): 1533-1540.
5. Moyle GJ, Youle M, Higgs C, Monaghan J, Prince W, Chapman S, Clendeninn N, Nelson MR. Safety, pharmacokinetics, and antiretroviral activity of the potent, specific human immunodeficiency virus protease inhibitor nelfinavir: Results of a phase I/II trial and extended follow-up in patients infected with human immunodeficiency virus. *Journal of Clinical Pharmacology* 1998;38(8):726-743.
6. Elliott AJ, Uldall KK, et al. Randomized, placebo-controlled trial of paroxetine versus imipramine in depressed HIV-positive outpatients. *American Journal of Psychiatry* 1998;155:367-372.
7. Vitiello B, Burnam MA, Bing EG, Beckman R, Shapiro MF. Use of psychotropic medications among HIV-infected patients in the United States. *American Journal of Psychiatry* 2003;160:547-554.
8. Deeks SG, Hecht FM, Swanson M, Elbeik T, Loftus R, Cohen PT, Grant RM. HIV RNA and CD4 cell count response to protease inhibitor therapy in an urban AIDS clinic: Response to both initial and salvage therapy. *AIDS* 1999;13(6):F35-F43.
9. Fatkenheuer G, Theisen A, Rockstroh J, Grabow T, Wicke C, Becker K, Wieland U, Pfister H, Reiser M, Hegener P, Franzen C, Schwenk A, Salzberger B. Virological treatment failure of protease inhibitor therapy in an unselected cohort of HIV-infected patients. *AIDS* 1997;11(14):F113-F116.
10. Ledergerber B, Egger M, Opravil M, Telenti A, Hirschel B, Battegay M, Vernazza P, Sudre P, Flepp M, Furrer H, Francioli P, Weber R. Clinical progression and virological failure on highly active antiretroviral therapy in HIV-1 patients: A prospective cohort study. *Lancet* 1999;353(9156):863-868.
11. Hecht FM, Grant RM, Petropoulos CJ, et al. Sexual transmission of an HIV-1 variant resistant to multiple reverse transcriptase and protease inhibitors. *New England Journal of Medicine* 1998;339:307-311.
12. Andersen R, Bozzette S, Shapiro M, St. Clair P, Morton S, Crystal S, Goldman D, Wenger N, Gifford A, Leibowitz A, Asch S, Berry S, Nakazono T, Heslin K, Cunningham W. Access of vulnerable groups to antiretroviral therapy among persons in care for HIV disease in the United States. HCSUS Consortium. HIV Cost and Services Utilization Study. *Health Services Research* 2000;35(2):389-416.
13. Beckett A, Rutan JS. Treating persons with ARC and AIDS in group psychotherapy. *International Journal of Group Psychotherapy* 1990;40(1):19-29.
14. Markowitz JC, Klerman GL, Perry SW. Interpersonal psychotherapy of depressed HIV-seropositive outpatients. *Hospital and Community Psychiatry* 1992;43(9): 885-890.
15. McCain NL, Zeller JM, Cella DF, Urbanski PA, Novak RM. The influence of stress management training in HIV disease. *Nursing Research* 1996;45(4):246-253.
16. Chesney MA, Chambers DB, Taylor JM, Johnson, LM, Folkman S. Coping effectiveness training for men living with HIV: Results from a randomized clinical trial testing a group-based intervention. *Psychosomatic Medicine* 2003; 65:1038-1046.
17. Kelly JA, Murphy DA, Bahr GR, Kalichman SC, Morgan MG, Stevenson LY, Koob JJ, Brasfield TL, Bernstein BM. Outcome of cognitive-behavioral and support group

brief therapies for depressed, HIV-infected persons. *American Journal of Psychiatry* 1993;150(11):1679-1686.
18. Evans DL, Leserman J, Perkins DO, Stern RA, et al. Severe life stress as a predictor of early disease progression in HIV infection. *American Journal of Psychiatry* 1997; 154(5):630-634.
19. Evans DL, Ten Have TR, Douglas SD, Gettes DR, Morrison M, Chappini MS, Brinker-Spence P, Job C, Mercer DE, Wang YL, Cruess D, Dube B, Dalen EA, Brown T, Bauer R, Petitto JM. Association of depression with viral load, CD8 lymphocytes, and natural killer cells in women with HIV infection. *American Journal of Psychiatry* 2002;159(10):1752-1759.
20. Goodkin K, Fuchs I, Feaster D, Leeka J, Rishel DD. Life stressors and coping style are associated with immune measures in HIV-1 infection—A preliminary report. *International Journal of Psychiatry in Medicine* 1992;22:155-172.
21. Ironson G, Solomon GF, Balbin EG, O'Cleirigh C, George A, Kumar M, Larson D, Woods TE. The Ironson-Woods Spirituality/Religiousness Index is associated with long survival, health behaviors, less distress, and low cortisol in people with HIV/AIDS. *Annals of Behavioral Medicine* 2002;24(1):34-48.
22. Leserman J, Petitto JM, Golden RN, Gaynes BN, Gu H, Perkins DO, Silva SG, Folds JD, Evans DL. Impact of stressful life events, depression, social support, coping, and cortisol on progression to AIDS. *American Journal of Psychiatry* 2000;157(8): 1221-1227.
23. Petrie KJ, Fontanilla I, Thomas MG, Booth RJ, Pennebaker JW. Effect of written emotional expression on immune function in patients with human immunodeficiency virus infection: A randomized trial. *Psychosomatic Medicine* 2004;66: 272-275.
24. Antoni MH, Baggett L, Ironson G, LaPerriere A, August S, Klimas N, Schneiderman N, Fletcher MA. Cognitive-behavioral stress management intervention buffers distress responses and immunologic changes following notification of HIV-1 seropositivity. *Journal of Consulting Clinical Psychology* 1991;59:906-915.
25. Ironson G, Friedman A, Klimas N, Antoni M, Fletcher MA, LaPerriere A, Simoneu J, Schneiderman N. Distress, denial, and low adherence to behavioral interventions predict faster disease progression in gay men infected with Human Immunodeficiency Virus. *International Journal of Behavioral Medicine* 1994;1:90-105.
26. Goodkin K, Feaster DJ, Asthana D, Blaney NT, Kumar M, Baldewicz T, Tuttle RS, Maher KJ, Baum MK, Shapshak P, Fletcher MA. A bereavement support group intervention is longitudinally associated with salutary effects on the CD4 cell count and number of physician visits. *Clinical & Diagnostic Laboratory Immunology* 1998; 5(3):382-391.
27. Lutgendorf SK, Antoni MH, Ironson G, Klimas, et al. Cognitive-behavioral stress management decreases dysphoric mood and herpes simplex virus-Type 2 antibody titers in symptomatic HIV-seropositive gay men. *Journal of Consulting & Clinical Psychology* 1997;65(1):31-43.
28. Coates TJ, McKusick L, Kuno R, et al. Stress reduction training changed number of sexual partners but not immune function in men with HIV. *American Journal of Public Health* 1989;79:885-887.
29. Solomon GF, Temoshok L. A psychoneuroimmunologic perspective on AIDS research: Questions, preliminary findings, and suggestions. In Temoshok L & Baum A

(eds.), *Psychosocial perspectives on AIDS: Etiology, prevention, and treatment,* 1990:239-258.

30. Hughes MD, Johnson VA, Hirsch MS, Bremer JW, Elbeik R, Erise A, Kuritzkes DR, Scott WA, Spector SA, Basgoz N, Fischl MA, D'Aquila RT. Monitoring plasma HIV-1 RNA levels in addition to CD4 lymphocyte count improves assessment of antiretroviral therapeutic response. *Annals of Internal Medicine* 1997;126(12):929-938.
31. Mellors JW, Rindaldo CR Jr., Gupta P, White RM, Todd JA, Kingsley LA. Prognosis in HIV-1 infection predicted by the quantity of virus. *Science* 1996;272:1167-1170.
32. Mellors JW, Munoz A, Giorgi JV, Margolick JB, Tassoni CJ, Gupta P, Kingsley LA, Todd JA, Saag AJ, Detels R, Phair JP, Rinaldo CR Jr. Plasma viral load and CD4 lymphocytes as prognostic markers of HIV-1 infection. *Annals of Internal Medicine* 1997;126(12):946-954.
33. O'Brien WA, Hartigan PM, Daar ES, Simberkoff MS, & Hamilton JD. Changes in plasma HIV RNA levels and CD4 lymphocyte counts predict both response to antiretroviral therapy and therapeutic failure. *Annals of Internal Medicine* 1997; 126(12):939-945.
34. Vlahov D, Graham N, Hoover D, Flynn C, Bartlett JG, Margolick JB, Lyles CM, Nelson KE. Smith D, Holmberg S, Farzadegan H. Prognostic indicators for AIDS and infectious disease death in HIV-infected injection drug users. *Journal of the American Medical Association* 1998;279:35-40.
35. Classen C, Butler LD, Koopman C, Miller E, DiMiceli S, Giese-Davis J, Fobair P, Carlson RW, Spiegel D. Supportive-expressive group therapy and distress in metastatic breast cancer patients. *Archives of General Psychiatry* 2001;58:494-500.
36. Spiegel D, Glafkides MC. Effects of group confrontation with death and dying. *International Journal of Group Psychotherapy* 1983;33(4):433-447.
37. Spiegel D, Yalom I. A support group for dying patients. *International Journal of Group Psychotherapy* 1978;28:233-245.
38. Spiegel D, Bloom JR, Yalom I. Group support for patients with metastatic cancer. A randomized outcome study. *Archives of General Psychiatry* 1981;38(5):527-533.
39. Yalom ID, Greaves C. Group therapy with the terminally ill. *American Journal of Psychiatry* 1977;134(4):396-400.
40. Gore-Felton C, Spiegel D. Enhancing women's lives: The role of support groups among breast cancer patients. *Journal of Specialists Group Work* 1999;24: 274-287.
41. Steinberg M, Rounsaville B, Cicchetti DV. The Structured Clinical Interview for DSM-III-R Dissociative Disorders: Preliminary report on a new diagnostic instrument. *American Journal of Psychiatry* 1990;147(1):76-82.
42. Mandy FF, Nicholson JKA, McDougal JS. Guidelines for performing single-platform absolute CD4 determinations with CD45 gating for persons infected human immunodeficiency virus. *MMWR* 2003;52:1-13.
43. Burgoyne RW. Exploring direction of causation between social support and clinical outcome for HIV-positive adults in the context of highly active antiretroviral therapy. *AIDS Car*e 2005;17(1):111-124.
44. Koopman C, Gore-Felton C, Gill M, Israelski D, Chesney M, Flamm J, Durán R, Classen C, Ney N, Spiegel D. An evaluation of the effects of group therapy on pain, mood, sexual risk behavior, and treatment adherence for women and men with HIV/AIDS. Unpublished manuscript, 2004.

45. Cole SW, Kemeny ME. Psychobiology of HIV infection. *Critical Reviews in Neurobiology* 1997;11:289-321.
46. Andersen BL, Farrar WB, Golden-Kreutz D, Kutz LA, MacCallum R, Courtney ME, Glaser R. Stress and immune responses after surgical treatment for regional breast cancer. *Journal of the National Cancer Institute* 1998;90(1):30-36.
47. Glaser R, Kiecolt-Glaser JK. Stress-associated immune modulation: relevance to viral infections and chronic fatigue syndrome. *American Journal of Medicine* 1998; 105(3A):35S-42S.
48. Glaser R, Kiecolt-Glaser JK, et al. The influence of psychological stress on the immune response to vaccines. *Annals of New York Academy of Science* 1998;840:649-655.
49. Kiecolt-Glaser JK, McGuire L, Robles TF, Glaser R. Psychoneuroimmunology: Psychological influences on immune function and health. *Journal of Consulting and Clinical Psychology* 2002;70(3):537-547.

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