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## The ABC's of Trait Anger, Psychological Distress, and Disease Severity in HIV

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### Abstract

**Background**—Trait anger consists of affective, behavioral, and cognitive (ABC) dimensions and may increase vulnerability for interpersonal conflict, diminished social support, and greater psychological distress. The concurrent influence anger and psychosocial dysfunction on HIV disease severity is unknown.

**Purpose**—Examine plausible psychosocial avenues (e.g. coping, social support, psychological distress) whereby trait anger may indirectly influence HIV disease status.

**Methods**—377 HIV seropositive adults, aged 18–55 years (58% AIDS-defined) completed a battery of psychosocial surveys and provided a fasting blood sample for HIV-1 viral load and T-lymphocyte count assay.

**Results**—A second-order factor model confirmed higher levels of the multidimensional anger trait was directly associated with elevated psychological distress and avoidant coping ( $p < .001$ ) and indirectly associated with greater HIV disease severity ( $p < .01$ ) (CFI=.90, RMSEA=.06, SRMR=.06).

**Conclusion**—The model supports ABC components of anger may negatively influence immune function through various psychosocial mechanisms; however longitudinal study is needed to elucidate these effects.

### Keywords

HIV/AIDS; anger; hostility; coping; social support; psychological distress; disease severity

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\*Authors' Statement of Conflict of Interest and Adherence to Ethical Standards:

Authors Roger C. McIntosh, Barry E. Hurwitz, Michael Antoni, Alex Gonzalez, Julia Seay and Neil Schneiderman declare that they have no conflict of interest. All procedures, including the informed consent process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.\*

## Introduction

In this era of combination antiretroviral therapy (cART), the morbidity and mortality of persons infected with Human Immunodeficiency Virus (HIV) has dramatically decreased (1, 2). Although HIV viremia can be reliably reduced to levels below the limit of detection, HIV cannot be eradicated with currently available cART medications and lifelong treatment is required (3). There remains large variability in the beneficial impact of cART treatment on disease severity and progression (4). Some have suggested psychological and behavioral factors may be mediating influences that contribute to HIV disease severity and progression over and above established risk factors, such as treatment adherence and illicit drug use and abuse (5–7). Numerous studies using animal models have shown that chronic stress may impact infectious disease progression through a host of immunomodulatory mechanisms (8, 9). We have previously shown that HIV viral load moderates the relationship between specific immunocellular subsets, including T-helper memory cells and B-cells, and a composite index of psychological distress, which included measures of life stress, HIV/AIDS-related anxiety and depressive symptoms (10). Subsequently, we examined this composite distress measure to evaluate its association with the cytotoxic T cell subset and with HIV disease severity, as indexed by T helper cell count and HIV-1 viral load (11). With HIV disease progression, the cytotoxic T-cell subset undergoes an expansion that is associated with an increase in cytotoxic T-cell activation, a signal that the adaptive immune system is marshaling defense mechanisms (12, 13). Our previous findings indicated that the association between greater distress and HIV disease severity was mediated by increased T cytotoxic cell subset activation (9). Thus, chronic stress and negative emotions, such as depression and anxiety, may exacerbate HIV disease severity, through inflammatory, neuroendocrine and other mediating processes (14). However, the impact of negative emotions, such as anger and hostility, on immunocellular function in the context of HIV spectrum disease is less explored.

Trait anger has been theorized to be a multidimensional construct consisting of the so-called “ABCs” of underlying psychological dimensions, affective, behavioral, and cognitive (15). The affective dimension of anger describes the tendency to experience this emotion anywhere on a continuum from mild irritation and annoyance to rage (16). The behavioral dimension of anger consists of aggressive behaviors, which may include verbal (e.g., insult, rudeness, sarcasm) or physical (e.g., badgering, harassment, assault) expressions of anger (17). Such behaviors are often displayed within the context of HIV disease as a protective measure to buffer the psychosocial effects of HIV-related stigma and discrimination (18–20). In contrast, the cognitive dimension of anger includes hostile cognitions, which may manifest in cynical worldviews and include thoughts of skepticism, alienation and mistrust (16, 21). In HIV-infected persons, skepticism and mistrust of the intentions of others has been shown to affect decisions regarding disclosure of HIV status to individuals in an extended social network, resulting in poorer social support (22).

Anger has been shown to negatively influence the quality and diminish the frequency of social interactions (23). Hostile individuals, in particular, display an increased psychosocial vulnerability and experience elevated distress due to more frequent interpersonal conflict, which results in social alienation and estrangement (23–26). The availability of social

support may mediate the effect of anger on health in many ways (27–29). For example, in HIV-infected persons, suspicions regarding the role of government officials in addressing the HIV/AIDS epidemic along with greater distrust for health professionals is associated with a reluctance to participate in medically-sanctioned prevention and treatment programs (30–33). Notably, diminished social support is also associated with greater HIV-disease severity and faster disease progression (34–36).

In persons with high trait anger, social interactions tend to have a more negative tone due to their tendencies for greater negative emotional reactivity and expression (27, 37, 38). Thus, heightened stress levels from such interactions place angry individuals at greater risk for developing depression, anxiety and negative mood (39–43). Greater levels of anger and hostility also relate to major depression, dysthymia and anxiety in HIV-infected persons (44, 45). In addition, several prospective observational studies have reported that more stressful life events are associated with depressive symptomatology and a faster rate of clinical progression of HIV disease (46, 47).

In both HIV seronegative and seropositive individuals, those who report coping with life stress through the use of avoidant (e.g., disengagement, self-blame, and denial) rather than problem-focused strategies also report greater levels of anger and hostility (44, 48, 49). Moreover, recent evidence shows that HIV-infected individuals employing avoidant coping were more likely to exhibit poorer psychological (e.g., depression and anxiety), behavioral (e.g., health behaviors and medication adherence) and health outcomes (T helper cell count and HIV-1 viral load) (50–52).

In sum, existing studies broadly support the notion that trait anger, indexed by affective, behavioral, and cognitive components, may result in a vulnerability to experience interpersonal conflict, diminished social support, and greater distress (i.e., depression, anxiety and perceived stress) in persons living with HIV/AIDS. However, understanding of the complexity of these relationships is limited because this literature has focused on only subsets of these psychosocial factors in the context of HIV spectrum disease. The present study will examine how these psychosocial factors might work together to contribute to or buffer against HIV disease severity, indexed by T helper cell count and HIV-1 viral load, in HIV-infected men and women by using a quantitative method to derive a comprehensive model based on this integrative conceptual framework.

## Methods

### Participants

Men and women who resided in Florida's Miami-Dade, Broward and Palm Beach counties were recruited by newspaper advertisement, flyer distribution at HIV/AIDS clinics, and support groups, as well as physician and chain referrals. Several HIV exposure categories, from asymptomatic pre-AIDS to symptomatic AIDS, were present within the sample. Study eligibility criteria required participants to: (1) provide written informed consent; (2) have documented diagnosis of HIV-1 infection; (3) provide proof of age 18–55 years; (4) be non-substance abusing as confirmed by the Structured Clinical Interview for the DSM-IV (SCID-1 Version 2.0); (5) have no indication of surgery 3 months prior to study entry; (6)

have no history of diabetes or cardiovascular condition, or other major systemic diagnosis unrelated to HIV; (7) be receiving no pharmacological treatment for cardiovascular (e.g., beta-blockers, calcium antagonists, ACE inhibitors), diabetic (e.g., hypoglycemics, insulin sensitizers), psychiatric (e.g., antipsychotics), or endocrine (e.g., estrogen hormonal replacement) conditions; (8) for Hepatitis C virus (HCV) seropositive persons, have not been treated previously for this infection or if treated, to have been treated more than 6 months prior to study entry; (9) for women, not be pregnant.

## Procedures

Following telephone screening, those meeting inclusion and exclusion criteria were invited for the laboratory assessments. Upon arrival to the laboratory, the HIV and HCV seropositive participants provided written confirmation from their physician verifying their infection(s). For these participants, blood was drawn for confirmation of their serostatus. HIV status was confirmed by Enzyme Immunoassay (EIA) and if a self-reported seronegative person tested positive, the EIA was confirmed by Western Blot. HCV status was determined using the anti HCV antibody EIA assay and, if positive, this status was confirmed by an RNA Quantitative PCR to obtain viral load. All current medical conditions and any preexisting medical history and physical exam information were considered through a comprehensive interview with the subject by the staff physician. The Center for Disease Control (CDC) HIV/AIDS symptom classification stage was determined using a combination of history, lab data (historical nadir and current T helper cell count), and a focused physical exam (focused on weight, fat redistribution, oral, chest, abdomen, skin, and neurological findings) (53). Adherence to prescribed cART medications was assessed with the Adult AIDS Clinical Trial Group (ACTG) structured interview (54). Sociodemographic information was obtained and then the subject underwent casual blood pressure, 12-lead ECG, height, weight, and waist and hip girth assessments. A urine sample was tested with a toxicology screen (i.e., alcohol, barbiturates, benzodiazepines, cannabinoids, LSD, PCP, THC, morphine, and amphetamines), and for women, a urine pregnancy screen. Substance use and dependence/abuse history was assessed by the SCID-1 using module E: Substance Use Disorders. Psychosocial surveys were administered to derive measures of anger, hostility, coping strategies, social support, perceived stress, HIV-related anxiety, and depression.

## Blood Assays

HIV-1 viral load was determined using an *in vitro* nucleic acid amplification test (AMPLICOR HIV-1 Monitor Test, Roche Diagnostics, Branchburg, NJ) with ultrasensitive methods (range 50–750,000 HIV-1 RNA copies/ml) and repeated with standard methods, if viral load met the upper detection limit (range 400–10 million copies/ml). Lymphocyte subset counts, including T-helper cells (CD3+CD4+), were derived using the mean of two serially collected peripheral blood samples analyzed with flow cytometry (Epics XL-MCL flow cytometer, Coulter, Hialeah, FL). HCV antibodies were assessed using EIA (Ortho-Diagnostics, Raritan, NJ; specificity 99.5%) and positive assays (i.e., signal to cutoff ratios < 8.0) were confirmed using immunoblot analysis (CHIRON RIBA HCV v3.0 SIA method, Ortho-Diagnostics, Raritan, NJ).

## Psychosocial Measures

**Trait Anger**—To reflect the affective, behavioral, and cognitive components of trait anger, six anger and hostility scales were chosen from an exploratory analysis described previously (15). The emotional dimension of anger, Angry Affect, was measured with Spielberger's Trait Anger Scale (TAS), a 10-item survey that includes the Angry Temperament subscale (TAS-T) and the Angry Reactivity subscale (TAS-R) (55). The TAS-T consists of four items that assess the tendency to experience anger without provocation (e.g., "I have a fiery temper"), whereas the TAS-R assesses the respondent's perceived frequency of angry emotions that results from provocation, e.g., "I get angry when slowed down by others' mistakes."

The behavioral dimension of anger, Aggressive Behavior, was measured with two scales: (1) the Anger-out subscale of the Anger Expression (AX) Scale, and (2) the antagonistic behavior subscale of the Cook Medley Hostility (CM) Scale (55, 56). The AX-Out subscale consists of 8 items related to outward acts of aggression (e.g., "I strike out at whatever infuriates me"), which participants rated from 1 (almost never) to 4 (almost always). The antagonistic behavior subscale (CM-A) is derived from 17-items that assess antagonistic behavioral expression (e.g., "I have at times had to be rough with people who were rude or annoying") (15).

The cognitive dimension of anger, Hostile Cognition, was measured using two previously described subscales from of the Cook Medley Scale (57). The Cynicism (CM-C) subscale contains 24 items that reflect negative beliefs of human nature (e.g., "I think most people would lie to get ahead"). The Cook-Medley Paranoid Alienation (CM-PA) subscale consists of 15 items that describe thoughts of persecution (e.g., "I feel like someone has it out for me"). These scales characterize the extent that weak interpersonal bonds are based on perceptions of mistrust in the intentions of others (57). The AX and the CM surveys have acceptable psychometric properties (15).

**HIV-specific Coping Strategies**—Three scales from the COPE were chosen to reflect approach coping, i.e., positive reappraisal and growth, acceptance, and active coping. Self-blame, denial and behavioral disengagement were selected to reflect avoidant coping. Participants were instructed to select answers that best reflected how they "dealt with HIV concerns or problems" during the last month. The items were rated on a 4-point Likert scale ranging from 1 (not at all) to 4 (a lot). These COPE subscales have demonstrated acceptable psychometric properties (58).

**Social Support**—Perceived social support was measured using the Social Provisions Scale (SPS) (59). The five measures of relational provisions used in this study included Attachment (emotional closeness and sense of security), Social Integration (sense of belonging to a group similar to oneself), Reassurance of Worth (recognition of one's value by others) and Guidance (advice or information) The SPS scale demonstrates acceptable psychometric properties (59).

**Distress**—Indicators were selected to reflect the affective, behavioral and cognitive components of psychological distress using three surveys, as previously described (10, 11).

The Impact of Events Scale (IES) is a 15-item measure of emotional disturbance and anxiety (60). Participants were asked to report on their thought intrusions and avoidances associated with life situations regarding their HIV infection. The Beck Depression Inventory (BDI) contains 21 items reflecting the affective/cognitive (13 items) and somatic (8 items) features of depression (61). The Perceived Stress Scale (PSS) is a 14-item survey that assesses the degree to which one appraises life as stressful due to unpredictable, uncontrollable and overwhelming experiences over the past month (62). The BDI, IES and PSS surveys have acceptable psychometric properties (60–62).

### Statistical Analysis

Standard preliminary data screening and variable transformations for variables violating normality were performed. Full information maximum likelihood estimates were used for data presumed to be missing at random (63). A variation of the traditional two-step approach to structural equation modeling (SEM) was followed that allowed for a measurement model, consisting of first and second order latent factors, to be tested while simultaneously examining the structure of paths within a recursive model (64). The statistical program, Mplus v.3.2 (65), was used to simultaneously run confirmatory factor analysis and produce unbiased parameter estimates of the direct and indirect relationships among the latent variables in the theorized model before and after accounting for demographic and treatment covariates. Factor loadings and residual error variance for the factors were tested for significance at the 0.05 level. Based on the extant literature summarized above, a model of the inter-relationships of anger with coping strategy, social support, distress, and HIV disease severity was hypothesized. As depicted in Figure 1, the hypothesized model included three pathways from: (1) Trait Anger to Approach Coping to Distress to HIV Disease Severity; (2) Trait Anger to Social Support to Distress to HIV Disease Severity; and (3) from Trait Anger to Avoidant Coping to Distress to HIV Disease Severity.

Before evaluating model fit indices, two considerations were used to meet the criteria for an indicator to be retained in the final model. First, each observed variable needed to load on one main latent factor that it was purported to measure. Second, the factor loading for each indicator had to be equal to or greater than 0.40 (66). A reference indicator was selected for each latent factor with the loading set at 1.00 for the purpose of scaling. Measures for model fit included Bentler's comparative fit index (CFI), root-mean-square error of approximation (RMSEA), and standardized root-mean-square residual (SRMR) (67–69). The criteria used to determine acceptable model fit included: (1) CFI  $\geq$  .90; (2) RMSEA  $<$  .07; and (3) SRMR  $<$  .08 (69, 70). Because the  $\chi^2$  fit statistic may be inflated with large sample sizes (e.g.,  $>200$ ), it was not included as an indicator of model fit (68, 71). Model modifications were performed based on the initial assessment of the hypothesized model. In addition, indices of the proportion of variability explained ( $R^2$ ) were derived for each latent and observed variable in the model. After a path model solution was derived from the data, secondary analyses regressed each latent construct on the following covariates before subsequent model trimming: age (years); sex (1 = female; 0 = male); education (years completed); ethnicity (1 = Black, 0 = other race), income, time since HIV diagnosis (months); cART (1 = on cART treatment, 0 = not ART treated), and Hepatitis C Virus (HCV) co-infection (1 = HCV<sup>+</sup>, 0 = HCV<sup>-</sup>).

## Results

### Participant Characteristics

Demographic information for the cohort is presented in Table 1. Approximately 69% of the cohort were men and over 90% identified themselves as racial/ethnic minorities. On average, participants were early middle-aged and reported an annual household income below the U.S. poverty line (U.S. Census, 2002). Nearly half the sample exhibited an undetectable HIV-1 viral load and approximately one-quarter were also HCV seropositive. Based on conventional criteria for HIV disease staging (Centers for Disease Control and Prevention, 1993), most study participants (65%) were classified as AIDS with the majority reporting current immunodeficiency symptoms. Over 80% of the cohort were currently taking a cART regimen that included a protease inhibitor. The self-reported antiretroviral therapy (ART) adherence among those who were treated with a cART regimen, as indexed by the ACTG measure, was relatively high.

### Step 1: Measurement Model Validation

The factor structure of eight first-order latent factors were operationalized as follows: (1) Angry Affect used TAS-T and TAS-R scores; (2) Aggressive Behavior used CM-A and AX-Out scores; (3) Hostile Cognitions used the CM-C and CM-PA scores; (4) Approach Coping used the COPE positive reappraisal, acceptance and active coping scores; (5) Social Support used the SPS attachment, social integration, reassurance of worth, guidance and nurturance scores; (6) Avoidant Coping used the COPE self-blame, behavioral disengagement and denial scores; (7) Distress was indicated by the IES, BDI and PSS total scores; and (8) HIV Disease Severity was indicated by HIV-1 viral load and T-helper cell count. Of additional interest was the structure of Trait Anger and whether it should be subsumed within a broader construct, “Negative Affect”, along with Distress or alternatively maintained as separate factors. These alternatives were tested using the Akaike Information Criteria (AIC) (72). The model wherein Trait Anger was subsumed with Distress within a Negative Affect factor yielded a larger AIC = 43,363 relative to the alternative model, AIC = 42,909. Thus, as hypothesized (see Figure 1), the analyses supported a hierarchical structure for Trait Anger that included the first-order latent factors, Angry Affect, Aggressive Behavior, and Hostile Cognitions independent of the Distress factor. In sum, the overall measurement model, including first- and second-order factors, demonstrated sufficient fit to proceed with path evaluation (CFI = .91, RMSEA = .07, SRMR = .07). As displayed in Table 2, adequate construct validity for the Trait Anger factor was demonstrated by a significant correlation greater than .40 between each measured indicator and the respective latent factor.

The intercorrelations among the observed variables used in the latent factors are displayed in Table 3. Among latent factors, Trait Anger factor was positively associated with Avoidance Coping ( $r = .47, p < .001$ ), Distress ( $r = .46, p < .001$ ), and HIV Disease Severity ( $r = .25, p < .001$ ). In addition, greater Distress was related to greater HIV Disease Severity ( $r = .25, p < .01$ ), less Approach Coping ( $r = -.17, p < .05$ ), less Social Support ( $r = -.21, p < .001$ ), and more Avoidant Coping ( $r = .73, p < .001$ ). Greater Social Support was associated with more Approach Coping ( $r = .34, p < .001$ ) and with less Avoidant Coping ( $r = -.26, p < .001$ ). In addition, greater HIV Disease Severity was related to more Avoidant Coping ( $r = .$

26,  $p < .01$ ). Of note, the second-order factor structure of Trait Anger explained 66% of the variance in Angry Affect, 97% of the variance in Behavioral Aggression and 97% of the variance in Hostile Cognitions.

## Step 2: Model Evaluation

The test of the structure of the hypothesized model (see Figure 1) did not exhibit adequate fit (CFI = .89, RMSEA = .07, SRMR = .09). Multiple paths from the theoretical model were significant, including Trait Anger to Avoidant Coping ( $\beta = .46$ ,  $z = 8.67$ ,  $p < .001$ ), Avoidant Coping to Distress ( $\beta = .76$ ,  $z = 14.60$ ,  $p < .001$ ), and Distress to HIV Disease Severity ( $\beta = -.14$ ,  $z = -2.15$ ,  $p < .05$ ). However, a number of paths were not significant, including Trait Anger to Social Support, ( $\beta = -.05$ ,  $z = -.81$ ), Trait Anger to Approach Coping, ( $\beta = -.01$ ,  $z = -0.02$ ), and Social Support to Distress ( $\beta = -.05$ ,  $z = -0.78$ ); these paths were removed from the model.

Modifications of the hypothesized model, based on the initial SEM analysis, included pathways from Avoidant Coping to Social Support, ( $\beta = -.23$ ,  $z = -3.71$ ,  $p < .001$ ), and Social Support to Approach Coping ( $\beta = .34$ ,  $z = 6.18$ ,  $p < .001$ ). The final model included a direct path from Trait Anger to Distress ( $\beta = .34$ ,  $z = 4.02$ ,  $p < .001$ ). The model also included two indirect paths from Trait Anger to Distress; these paths were: (1) from Trait Anger to Avoidant Coping ( $\beta = .48$ ,  $z = 7.30$ ,  $p < .001$ ) and from Avoidant Coping to Distress ( $\beta = .58$ ,  $z = 10.56$ ,  $p < .001$ ), and; (2) from Trait Anger via Avoidant Coping to Social Support ( $\beta = -.23$ ,  $z = -3.71$ ,  $p < .001$ ), and from Social Support to Approach Coping ( $\beta = .34$ ,  $z = 6.18$ ,  $p < .001$ ), and from Approach Coping to Distress ( $\beta = -.12$ ,  $z = -1.97$ ,  $p < .05$ ). In addition, the model indicated a direct path from Distress to HIV Disease Severity, ( $\beta = .27$ ,  $z = 4.23$ ,  $p < .001$ ). The cumulative association for the indirect paths linking Trait Anger to HIV Disease Severity was also significant ( $\beta = .14$ ,  $z = 3.04$ ,  $p < .01$ ). This model demonstrated adequate fit to the data (CFI = .93, RMSEA = .06, SRMR = .06).

Each latent construct in the trimmed model was regressed on the covariates; HCV serostatus and income were not associated with model factors ( $r$ s were  $-.08$  to  $.10$  for HCV serostatus and  $-.03$  to  $.03$  for income). Significant paths that were retained included: a path from age ( $\beta = -.16$ ,  $z = -2.94$ ,  $p < .01$ ) and ethnicity ( $\beta = .20$ ,  $z = 3.60$ ,  $p < .001$ ) to Trait Anger; a path from sex ( $\beta = .16$ ,  $z = 3.10$ ,  $p < .01$ ) and education ( $\beta = .13$ ,  $z = 2.27$ ,  $p < .05$ ) to Social Support; paths from time since HIV diagnosis ( $\beta = -.12$ ,  $z = -2.20$ ,  $p < .05$ ) and education ( $\beta = -.22$ ,  $z = -4.03$ ,  $p < .001$ ) to Avoidance Coping; and from cART use to Distress ( $\beta = -.13$ ,  $z = -2.56$ ,  $p < .05$ ) and Disease Severity ( $\beta = -.33$ ,  $z = -6.73$ ,  $p < .001$ ). These covariates contributed to explaining an additional 4.7% of the variance in Avoidance Coping, 3.1% in Social Support, 0.7% in Distress and 10.2% in Disease Severity.

Because 16% of the cohort were not prescribed or taking anti-HIV medications, and thus were not missing medication adherence data at random, the inclusion of this measure as a covariate was inappropriate. However, to determine whether controlling for medication adherence, as indexed by ACTG, changed the significance of any pathways in the model, the model was evaluated using only the 312 participants that reported taking anti-retroviral medications. This analysis indicated model goodness of fit (CFI = .90, RMSEA = 0.06,



SRMR = 0.06) and that all of the significant paths within the hypothesized model were retained.

Figure 2 shows the final trimmed model, indicating that when accounting for all significant associations among latent factors and covariates, the model demonstrated good fit to the data (CFI = .90, RMSEA = .06, SRMR = .06). Overall, this model accounted for 92.8% of the variance in Hostile Cognitions, 83.5% in Aggressive Behavior, 73.7% in Angry Affect, 11.6% in Approach Coping, 41.8% of Avoidance Coping, 9.5% in Social Support, 61.4% in Distress, and 17.2% in Disease Severity.

## Discussion

Being HIV seropositive creates social stigma and isolation, and numerous chronic stressors (e.g., interpersonal, financial and others) that are often unpredictable and uncontrollable (19, 73). Besides the threat of mortality, these stressors are associated with increased dysphoria, anxiety, anger, hostility, the feeling of being overwhelmed and may be associated with negative coping strategies including avoidant coping, denial and distancing (5, 74). The present study used a quantitative modeling methodology to examine putative inter-relationships among factors reflecting these influences in the context of HIV disease severity while controlling for demographic (age, sex, education, and ethnicity) and disease-related (time since HIV diagnosis, and cART treatment) measures. In addition, the study extends these findings by demonstrating that higher levels of trait anger, both directly and indirectly, were associated with greater psychological distress. Specifically, the model indicated one direct and two indirect pathways between trait anger and increased psychological distress accounting for 68% of the variance in distress and 18% of the variance in HIV disease severity. The indirect model pathways indicated that greater anger was associated in one path with elevated distress through increased avoidant coping, whereas in a second path greater anger was associated with increased avoidant coping, which was related to decreased social support and in turn associated with decreased approach coping.

This study has replicated previous lines of research pertaining to the structure of the Trait Anger factor and its relationship with distress and HIV disease severity. The literature suggests a considerable overlap among the constructs of anger, anxiety and depression in psychological regulation and in their association with chronic disease (42, 75). The present model, however, suggested that Trait Anger and Distress better fit the data when included as distinct factors, rather than as subsumed within an umbrella construct of negative affect. The final model (see Figure 2) shows the hierarchical factor structure for Trait Anger. Although this is the first study to demonstrate the multidimensionality of this trait in HIV-infected persons, others have demonstrated the affective, behavioral and cognitive dimensions of this trait in non-clinical samples (15, 76, 77). In addition, the observed association between Trait Anger and Distress derives support from a previous report citing positive associations between hostility, anxiety, life stress and major depression in HIV seropositive men (44). The final model also shows greater symptoms of depression, HIV-related anxiety and perceived stress, indexed by the Distress factor, were related to more severe HIV Disease Severity, indexed by greater HIV-1 viral load and lower T helper cell count. This finding replicates our research describing psychoimmune models in HIV-positive men and women

(11). Collectively, these findings coincide with an extensive body of research suggesting that depressive symptoms, anxiety and HIV-related stress lead to accelerated HIV disease progression in the post-cART era (50, 78, 79). However, it should be noted that worsening HIV disease severity may result in greater distress and consequently greater avoidant coping and anger. Thus, it is possible that some components of the model operate in an opposite direction from that tested in the model or may even be bi-directionally linked (80, 81).

The present study extends previous findings by providing specification for the linkage of Trait Anger with the Distress-Disease Severity pathway via a vis the specification of one direct pathway to Distress and two indirect pathways to Distress through coping and social support mechanisms. The linkage between Trait Anger and Distress that occurs indirectly via Avoidant Coping is plausible and well-supported by theoretical and empirical studies linking negative coping behaviors with anger as well as with depression, anxiety and perceived stress (82–86). Another study finding was the lack of replication of previous reports showing that approach coping mediates the direct association between greater anger with greater psychological distress. Instead, the present results suggest a more nuanced inter-relationship among these psychosocial variables, wherein trait anger was positively related to distress indirectly via greater use of avoidant coping which, in turn, was related to both lower social support and approach coping. Numerous studies have provided support for the association between maladaptive coping strategies and diminished social support in persons with HIV (36, 45, 87–89). Furthermore, the use of approach coping strategies, such as positive reappraisal, acceptance and direct action, have been associated with lower levels of psychological distress in HIV positive persons (45, 90–92). Thus, these findings suggest that anger influences distress more proximally via its effect on negative coping strategies, which then may influence distress either directly or indirectly via its effect on social support and positive coping strategies.

It is pertinent to note that our research in HIV-infected individuals has shown that group-based cognitive behavioral interventions, which taught coping skills, and relaxation and interpersonal skills, such as anger management (93), may modulate coping strategies (decrease avoidance coping and increase approach coping (94), increase social support (95), and reduce distress states (94, 96–99). Of note, such interventions have been shown to improve potential neuroendocrine biomediators (i.e., cortisol, norepinephrine) that may influence immune system function (97, 100). In addition, in other reports, we have shown that cognitive behavioral interventions in HIV-infected men and women can have a demonstrable impact on immune system reconstitution (101), and result in decreased HIV viral load (98) and reduced incidence of opportunistic neoplasias (99).

The present study controlled for the influence of several demographic in an effort to evaluate the unique effects of the latent constructs. In so doing, the model accounted for a greater percentage of explained variance in Trait Anger, Social Support and Avoidance Coping. Greater trait anger was associated with younger age, a finding that conflicts with previous studies of HIV negative cohorts (102, 103). However, study findings are supported by previous HIV studies, which have shown that seropositive individuals, with advancing age, report feeling less cheated by life, have more patience dealing with others, and experience less anger and frustration when confronting personal functional limitations (104,

105). The analyses also indicated that greater psychological distress was associated with self-identifying as Black or African American. Previous literature supports the notion that perceived stress, anxiety and depression has greater prevalence in low SES African American communities (79, 106, 107). Similarly, studies have shown that African Americans endorse higher rates of anger and hostility than their Caucasian counterparts (108, 109). Although these findings are likely related to factors such as education and access to resources, evidence continues to mount suggesting higher levels of anger and hostility may further increase risk for severe chronic disease in members of the African Americans community (21, 109, 110).

There is no question that anti-retroviral medication adherence plays an important role in influencing CD4 count, HIV viral load and ultimately HIV disease severity (111). Moreover psychosocial functioning may have a marked influence on adherence to HIV medication regimens (112, 113). Medication regimen adherence, as indexed by the ACTG measure, averaged about 91% among the cohort. This self-report retrospective measure is commonly used in the HIV literature (54). Notably, when the cohort was restricted to those taking anti-retroviral medications, the analysis showed that the model fit adequately, when the ACTG was controlled. Although HCV coinfection did not account for significant variance in the model factors, the analyses indicated significant relationships between other HIV-related covariates and the latent factors. Time since HIV diagnosis was inversely related to Avoidant Coping and Distress suggesting greater psychosocial adaptation to the disease over time (114–116). The use of cART was also associated with levels of Distress and HIV Disease Severity. Others have shown cART use to predict slower HIV disease progression and reductions in depression, anxiety and chronic stress over time (117–119). Overall, the present study findings replicated established associations of relevant HIV-related factors with key model constructs and controlled for these factors in the model derivation.

### Limitations

Although the inter-relationships among coping strategies, social support and distress measures used in this study have been previously evaluated to varying extents in studies of HIV/AIDS cohorts, this study provided evaluation of trait anger multidimensionality and its putative linkages with psychological distress and HIV disease severity. Any conclusions regarding the derived model reported in this study must be restricted to the operational definitions of the constructs employed. Notably, the study cohort demographics, in terms of age range, and sex and minority composition, were comparable to the general HIV/AIDS population in the U.S.(120). The model plausibility is supported by the use of key sociodemographic and disease-related variables including age, sex, education, ethnicity, time since HIV diagnosis and cART treatment. Notably, study entry criteria were stringent with regard to excluding those with comorbid systemic and psychiatric conditions; hence, potential confounding influences related to these factors were minimized. Nevertheless, the study findings may only generalize to those persons with comparable demographic, psychological and disease-related characteristics as present in the study cohort. Sample size considerations prohibited inclusion of other variables associated with HIV disease, such as illicit substance use, dependence and abuse, indices of immunocellular enumerative or functional relevance other than T helper cell count and HIV-1 viral load, or measures of

coinfection other than HCV. In addition, factors such as job status (121, 122) and sexual orientation (123, 124), which have been associated with poorer psychosocial functioning and HIV disease severity, were not controlled in the present assessments. Although the present study provided a meaningful conceptual model, the cross-sectional design does not permit conclusions regarding directionality. Hence, it is possible that model pathways may operate in the reverse direction or that the model pathways include bidirectionality. Longitudinal observations of disease progression would permit more definitive conclusions regarding directional influences of the examined psychosocial and disease-related factors in HIV spectrum disease.

## Conclusion

In sum, the present study describes a hierarchical structure of trait anger and suggests conceptually reasonable psychosocial avenues by which this trait may influence perceived distress and ultimately HIV disease severity. The derived model is consistent with the behavioral science literature pertaining to the inter-relationships among anger, coping strategies and social support and explains a substantial amount of variance in psychological distress and its covariance with HIV disease severity, independent of numerous demographic and HIV-related factors. Negative emotions, such as anger, in the context of HIV spectrum disease, may induce an environment where adequate social provisions are not received. The consequences of which, in addition to its deleterious impact on psychosocial factors, may extend to an acceleration of pathophysiological mechanisms that drive HIV disease progression. To this point, these mechanisms have not yet been elucidated. Some have suggested that the psychoneuroimmunological transaction associated with negative emotionality is mediated by inducing an exacerbation of inflammatory status directly or indirectly via a neuroendocrine axis dysregulation of cortisol (14, 125–127). Furthermore, heightened proinflammatory status has been associated with an imbalance of oxidative metabolism that results in the expression of reactive oxygen species, greater HIV replication, destruction of the T helper cell subset and further disease progression (128, 129). Some have suggested that a similar set of psychoneuroimmunological mechanisms play a role in facilitating comorbidities commonly found in persons with HIV such as the metabolic syndrome, diabetes and cardiovascular (CV) disease (130–133). Indeed, elevated CV risk has been associated with anger and hostility in HIV negative populations and may be an appropriate area for further research given the incidence of coronary artery disease in HIV positive persons. Although the present study underscores the potential avenues by which trait anger and its linkages with psychosocial factors influence HIV disease severity, further research will be needed to evaluate the extent to which these factors are central or more tangential in their influence on HIV pathophysiological mechanisms and disease progression.

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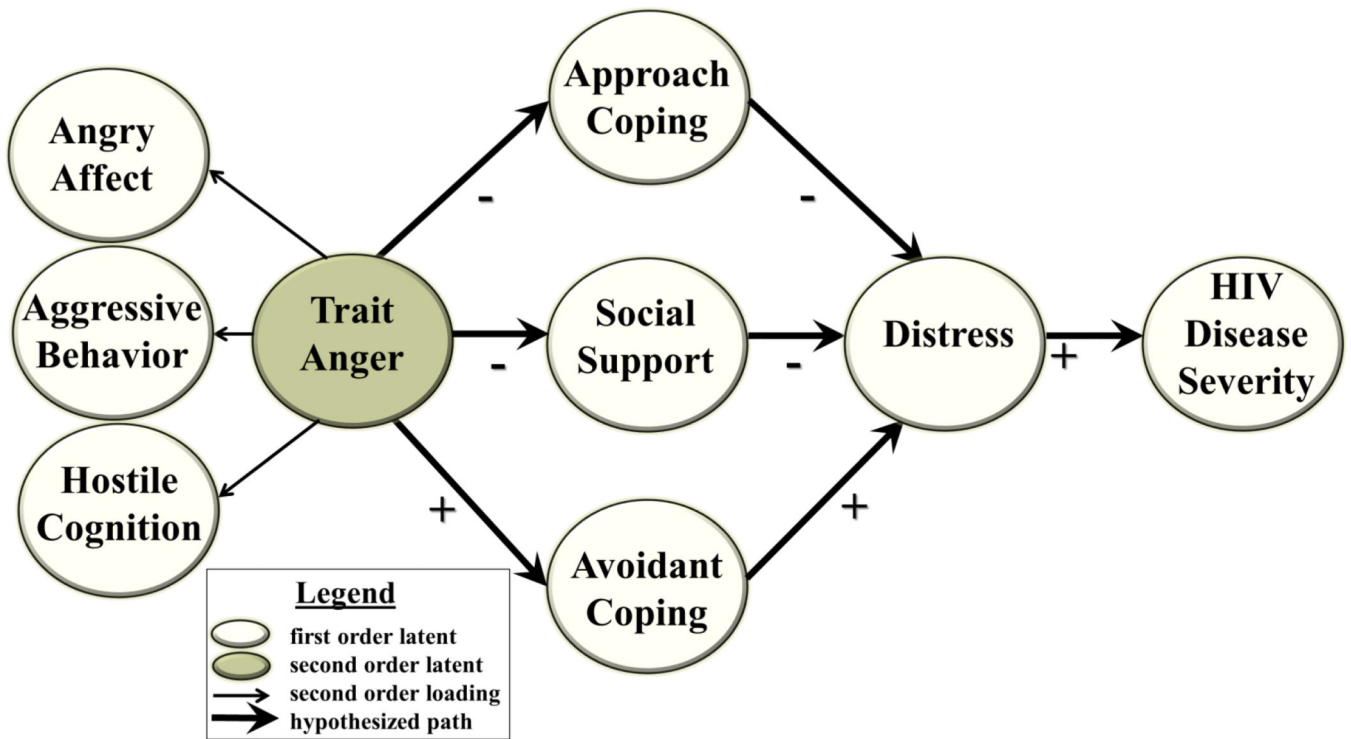
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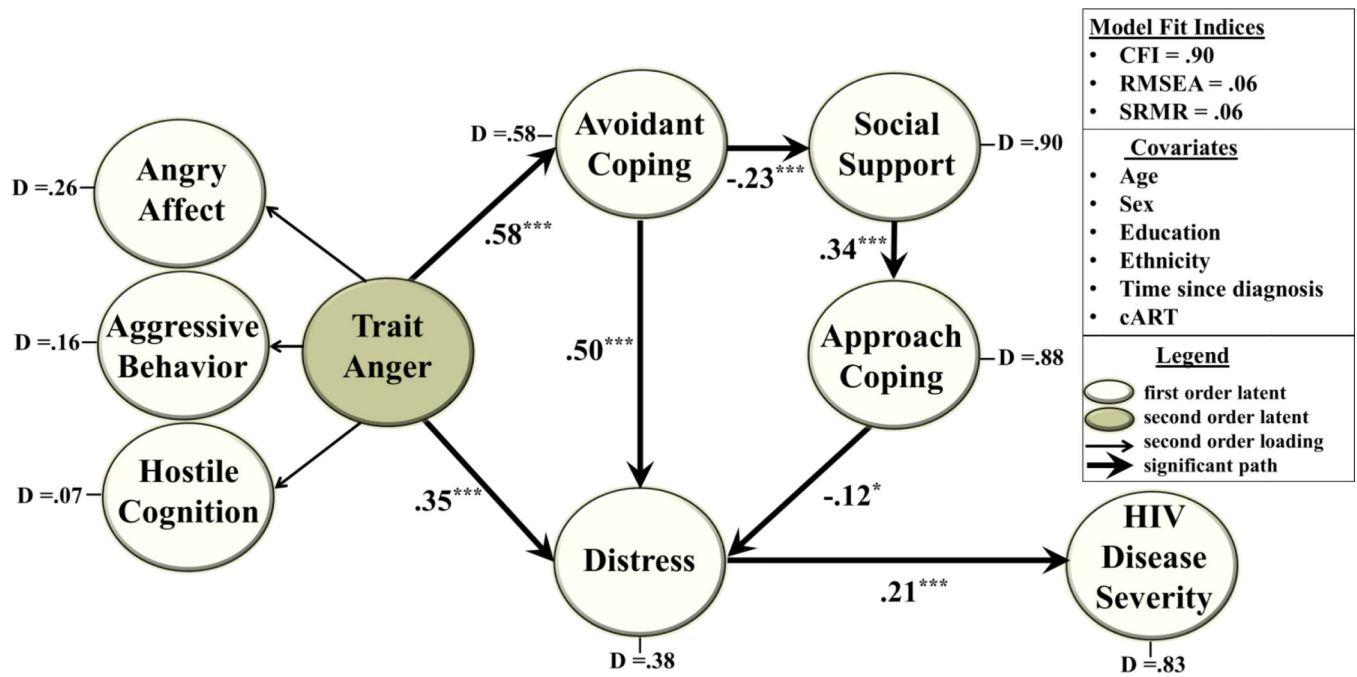
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**Figure 1. Hypothesized Model**

Model depicting hypothesized interrelationships among anger (comprised of indices of angry affect, aggressive behavior, and hostile cognition), approach coping, social support, avoidant coping, psychological distress and HIV disease severity. Open ovals represent first-order latent factors. The second order latent factor, Trait Anger, is depicted by a shaded oval. Positive hypothesized associations are indicated by “+” and inverse associations indicated by “-”.



**Figure 2. Final Model**

The final trimmed model derived using structural equation modeling methodology is depicted. The open ovals represent first-order latent factors and the shaded oval depicts the second-order latent factor, Trait Anger. The model shows that greater trait anger was linked in a direct path with elevated distress and HIV-disease severity, and in two indirect paths via increased avoidance coping, and via increased avoidance coping to decreased social support to decreased approach coping. Path coefficients are standardized  $\beta$  weights. Solid arrows depict statistically significant associations ( $***p < .001$ ;  $**p < .01$ ). Non-significant paths are not shown. Disturbance (D) terms reflect the proportion of unexplained variance in each latent factor after accounting for all other latent variables and covariates. The model has good fit to the data as indicated by the fit indices.

**Table 1**

Demographic and disease-related characteristics of the cohort (N = 377)

<b>Characteristics</b>	<b>Mean</b>	<b>(SD)</b>
Age (years)	41.4 ±	7.4
Sex (%)		
Men	68.9	
Women	30.3	
Ethnicity (%)		
African American	60.5	
Hispanic	26.0	
Non-Hispanic White	6.9	
Other	6.6	
Socioeconomic status		
Education (years)	12.3 ±	2.7
Household income (\$/year)	8,640.1 ±	10,075.7
Time since HIV diagnosis (months)	111.4 ±	70.0
CD4+ count nadir (cells/ $\mu$ l)	421.1 ±	267.9
Undetectable HIV viral load (%) <sup>a</sup>	46.2	
HIV disease stage classification (%)		
HIV asymptomatic	27.3	
HIV symptomatic	7.2	
AIDS asymptomatic	22.8	
AIDS symptomatic	42.7	
Hepatitis C Virus seropositive (%)	23.6	
Antiretroviral medication regimen (%)		
cART treatment	82.3	
Adherence (4-day)	91.1	

Abbreviations: cART, combination antiretroviral therapy.

<sup>a</sup>Below 50 HIV-1 RNA copies/ml

**Table 2**

Means, standard deviations and factor loadings for first-order latent variables.

<b>First-Order Factors and Indicators</b>	<b>Mean</b>	<b>SD</b>	<b>Factor Loading</b>
<b>Angry Affect</b>			
Angry temperament	6.2	2.7	.79
Angry reactivity	7.7	2.8	.79
<b>Aggressive Behavior</b>			
Antagonism	9.1	3.7	.56
Anger out	14.7	4.2	.58
<b>Hostile Cognitions</b>			
Cynicism	14.1	5.8	.54
Paranoid alienation	4.5	3.1	.65
<b>Avoidant Coping</b>			
Self-blame	3.7	1.8	.59
Denial	6.4	2.9	.72
Behavioral disengagement	6.2	2.5	.61
<b>Social Support</b>			
Attachment	11.4	2.4	.79
Social integration	11.9	2.4	.87
Reassurance of worth	11.8	2.4	.87
Guidance	12.3	2.6	.84
Nurturance	11.2	2.7	.68
<b>Approach Coping</b>			
Positive reappraisal	12.9	3.2	.81
Acceptance	13.1	2.9	.68
Active	11.6	3.0	.64
<b>Distress</b>			
Impact of events	21.7	14.8	.65
Beck depression inventory	7.6	8.1	.69
Perceived stress	22.0	7.5	.63
<b>HIV-Disease Severity</b>			
HIV-1 viral load (copies/ml)	15,050.1	54,788.3	.93
T helper cell count (cells/ $\mu$ l)	450.9	321.0	-.49

**Table 3**

Correlations among factor indicators used in the modeling analyses.

Variables	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
1. Angry temperament (TAS-T)	1.00																					
2. Angry reactivity (TAS-R)	.62**	1.00																				
3. Antagonism (CM-A)	.29***	.37***	1.00																			
4. Anger out (AX-Out)	.51***	.37***	.31***	1.00																		
5. Cynicism (CM-C)	.28***	.35***	.87***	.34***	1.00																	
6. Paranoid alienation (CM-PA)	.42***	.38***	.68***	.34***	.59***	1.00																
7. Positive reappraisal (COPE)	-.05	.05	-.01	.02	.03	-.23**	1.00															
8. Acceptance (COPE)	-.04	.06	.01	.10	.05	-.21**	.55***	1.00														
9. Active (COPE)	.02	.05	.04	.03	.01	-.09	.54***	.45***	1.00													
10. Self-blame (COPE)	.20***	.20***	.28***	.18***	.27***	.35***	-.01	.03	.04	1.00												
11. Denial (COPE)	.30***	.24***	.29***	.18***	.27***	.40***	-.01	-.11*	.07	.41***	1.00											
12. Behavioral disengagement (COPE)	.19***	.11*	.16**	.04	.13*	.35***	-.07	-.14**	-.02	.34***	.48***	1.00										
13. Attachment (SPS)	-.11*	-.01	-.08	.03	-.01	-.16**	.19***	.15**	.16**	-.17**	-.08	-.17**	1.00									
14. Social integration (SPS)	-.11*	-.03	-.06	.07	.02	-.17**	.25***	.25***	.15**	-.16**	-.16**	-.15**	.69***	1.00								
15. Reassurance of worth (SPS)	-.22***	-.12*	-.18**	-.07	-.09	-.27***	.26***	.23**	.15**	.20***	-.22**	-.18	.69***	.75***	1.00							
16. Guidance (SPS)	-.19***	-.04	-.06	.04	-.01	-.19**	.24***	.25**	.16**	-.12*	-.09	-.13*	.75***	.73***	.73***	1.00						
17. Nurturance (SPS)	-.08	-.02	-.01	.07	.07	-.13*	.22**	.18**	.18**	-.05	.01	-.10	.54***	.69***	.58***	.59***	1.00					
18. HIV-related Anxiety (IES)	.19***	.22***	.27***	.21***	.26***	.30***	.06	.04	.04	.34***	.43***	.30***	-.09	-.03	-.09	-.07	-.01	1.00				
19. Depressive symptoms (BDI)	.28***	.24***	.25***	.26***	.25***	.37***	-.13*	-.13*	-.06	.40***	.31***	.25***	-.14**	-.18**	-.23***	-.19**	-.05	.45***	1.00			
20. Perceived stress (PSS)	.28***	.16**	.16**	.24***	.21***	.35***	-.18	-.17**	-.20**	.30***	.23***	.24***	-.08	-.10	-.19**	-.18**	-.06	.38***	.48***	1.00		
21. HIV-1 viral load	.07	.09	.08	.06	.10	.08	-.04	-.02	-.07	.02	.06	.05	-.01	.01	-.05	-.02	-.04	.07	.05	.03	1.00	
22. T helper cell count	-.02	-.06	-.08	-.01	-.13*	-.08	.03	.10*	.03	-.10	-.09	-.07	.07	.06	.10	.07	.06	-.07	-.08	-.01	-.27***	1.00

Abbreviations: TAS-T = Trait Anger Scale-temperament; TAS-R = Trait Anger Scale-reactivity; CM-A = Cook-Medley Hostility Scale-antagonism; AX-Out = Anger Expression Scale-out; CM-C = Cook-Medley Hostility Scale-cynicism; CM-PA = Cook-Medley Hostility Scale-paranoid alienation; COPE = Coping Inventory; SPS = Social Provisions Scale; IES = Impact of Events Scale; BDI = Beck Depression Inventory; PSS = Perceived Stress Scale.

\* P < .05



1000 > d  
\*\*\*  
10 > d  
\*\*

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