Effective Treatment of Depressive Disorders in Medical Clinics for Adolescents and Young Adults living with HIV: A controlled trial

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Abstract

Objective—Preliminary test of a manualized, measurement-guided treatment for depression for adolescents and young adults in care at four sites of the Adolescent Trials Network for HIV/AIDS Interventions (ATN).

Design—The U.S. sites were randomly assigned to either a 24-week, combination cognitive behavioral therapy and medication management algorithm (COMB) tailored for youth living with HIV (YLWH) or to treatment as usual (TAU).

Methods—Youth at TAU sites had access to therapists and medication management as needed. COMB site clinicians were trained in the manualized intervention and participated in supervision calls to monitor intervention fidelity.

Results—Over the course of the study with 44 participants, those in COMB, compared to those in TAU, reported fewer depressive symptoms, p<0.01 (as measured by the Quick Inventory for Depression Symptomatology) and were more likely to be in remission, p<0.001, (65% vs.10% at week 24 end of treatment, and 71% vs. 7% at week 48 final follow-up). A greater proportion of

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COMB participants received psychotherapy (95% vs. 45%, p<0.001) and attended more sessions (12.6 vs. 5, p<0.001) than those in TAU. Viral load decreased in both groups and was associated (p<0.05) with reduction in depressive symptoms.

Conclusions—A 24-week manualized, measurement-guided psychotherapy and medication management algorithm tailored for YLWH was more effective in achieving and sustaining remission from depression than treatment as usual at HIV care clinic sites. Given observed treatment efficacy, this structured combination treatment could be disseminated to medical clinics in order to successfully treat YLWH, who are at particular risk for depression.

Introduction

Depression is prevalent among youth living with HIV (YLWH) [1]. In a study of 2,032 YLWH in medical care, 21% reported depression, which is higher than the general prevalence [2]. Other studies report depression rates in YLWH as high as 50% [3,4]. Depression increases morbidity and mortality for YLWH. It interferes with adherence to HIV treatment, increases caregiver burden, increases healthcare costs, and decreases quality of life [5,6]. Thus, treatment of depressive disorders is essential for improving both psychiatric and medical outcomes for YLWH, especially since effective antiretroviral treatments have dramatically increased life expectancy [5].

Prior reports indicate serotonin reuptake inhibitors (SSRIs) are generally safe and effective in the treatment of depression in adults with HIV [7,8], and that these treatments not only improve depression outcomes, but also are associated with greater adherence and increased CD4 T-cell counts [9]. No studies have addressed the efficacy of SSRIs in YLWH, how to proceed after no or minimal response to treatment, or examined the effectiveness of treatment guided by measures of symptomatology.

Several psychotherapies have been shown to be effective in treating depression. However, YLWH present unique issues, including chronic illness, loss, stigmatization, and cultural and sexual diversities. Motivational interviewing (MI) and Cognitive Behavior Therapy (CBT) have been shown to improve adherence to antiretroviral medications, as well as to improve depressive symptoms and life satisfaction [10]. CBT has been used successfully with diverse populations [11,12], including lesbian, gay and bisexual clients and adults living with HIV [13,14]. Despite its perceived effectiveness, there has not been a controlled trial of CBT in depressed adolescents or young adults living with HIV.

HIV clinic prescribers commonly use SSRIs, although many are not psychiatrists, and clinic therapists use a wide variety of therapies such as CBT, interpersonal therapy, general supportive therapy, mindfulness and relation relaxation training. Because of their training and work in HIV-care settings, their treatment is tailored for the needs of individual patients, although there is no systematic description of the treatment options, decision points, or

measurement that guides treatment. Practice guidelines suggest that a combination of medication management and an evidenced-based psychotherapy, such as CBT, show a more rapid reduction in depressive symptoms than a single treatment modality (i.e., either psychotropic medication *or* psychotherapy) for depression [15,16,17]. Additionally, other studies show that measured-care treatment (care decisions are guided by measures of symptomatology) is even more effective [18]. Therefore, in this study, a combined, measured-care treatment approach was chosen, within which both CBT and the medication management algorithm (MMA) were adapted for use in YLWH to be compared with treatment as usual (TAU) at participating Adolescent Trials Network for HIV/AIDS Interventions (ATN) sites [19,20].

STUDY AIMS

This is the first study to adapt and preliminarily test a measured-care combined treatment strategy that included psychopharmacology and psychotherapy for YLWH with depression in the medical care setting. Investigators predicted that, based on previous research, participants in the 24 week combined treatment (COMB) would have fewer depressive symptoms, a greater rate of response to treatment, and a greater rate of remission from depression than those receiving treatment as usual (TAU), despite the HIV experience of TAU providers and their current use of SSRIs and CBT. In addition, it was hypothesized that COMB participants would show, over the course of the study, less hopelessness and greater life satisfaction, constructs frequently associated with depression [21,22]. Also, it was predicted that COMB would be associated with greater use and better adherence to antiretroviral treatment, and better HIV health status outcomes (CD4+ T-cell count (CD4) and HIV RNA viral load (VL)) because of the known association of depression and these health indicators.

Method

PARTICIPANTS

Participants were ages 18–24 years, engaged in care at participating U.S. ATN sites, with documented HIV confirmed by medical records, and a diagnosis of nonpsychotic depression, either Major Depressive Disorder (MDD), Depression NOS, or Dysthymia as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), with significant symptomatology at entry (as defined by a Quick Inventory of Depressive Symptomatology-Self-Report (QIDS-SR) scores 7). Participants were excluded from the study if they had a history of any psychosis/psychotic disorders or Bipolar I or II Disorder, had a first degree relative diagnosed with Bipolar I Disorder, had a diagnosis of alcohol or substance dependence according to DSM-IV in the last 6 months, and/or if they were in imminent danger to themselves or others.

PROCEDURES

Four ATN sites were randomly assigned to either COMB or TAU so that TAU clinicians were not exposed to the manualized CBT and/or medication management algorithm. Sites were chosen by the ATN Site Selection Committee based on their capacity to enroll at least ten eligible participants within the period of study, the availability of staff, and ATN work

load. Study procedures were approved by Institutional Review Boards at all participating organizations. YLWH who were referred to a mental health professional for evaluation for depression, or who were in treatment but still symptomatic, were approached for participation in the study. Informed consent was obtained per local institutional guidelines. A project-trained mental health clinician confirmed that participants had QIDS-SR scores 7, and no exclusionary condition.

Combined CBT and MMA (COMB) [24-week intervention]—The Medication Management Algorithm (MMA) was developed by incorporating current practice parameters for depression [15,23,24] and HIV treatment in adults [23,24], recent data from adult and adolescent depression trials [25,26], and previously used algorithmic designs [27,28]. Modifications included rescue treatments for the onset of new disorders and symptoms specific to chronic illness or HIV (e.g., sleep disturbance, weight loss). The MMA includes strategies and considerations in treating depression for YLWH such as drug-drug interactions and side effects. The algorithm specifies the order and doses of antidepressant medications at each stage taking into consideration prior psychotropic medication history and measurement of current symptoms (see Table 1). After four to six weeks, doses could be increased as shown, or antidepressants augmented with lithium, bupropion, or an atypical antipsychotic. [A general overview of the treatment stages, doses for augmentation, and common medications to treat associated symptoms are found in the Figure and Tables in the Supplemental Digital Content.] The MMA was implemented by site prescribing clinicians who received a one-day training and participated in twice monthly monitoring and supervision calls.

Health and Wellness Cognitive Behavioral Therapy (herein referred to as CBT) decreases negative mood and unhealthy cognitions, while simultaneously enhancing strengths, positive experiences, and healthy cognitions [29]. CBT was adapted for YLWH to address factors such as medical symptoms, poverty, stigma, and alienation from families. It also integrated motivational interviewing (MI) skills in order to engage patients in treatment [30,31]. The development and feasibility of the manual for YLWH was reported previously [32]. The study CBT is comprised of three stages of treatment. Stage 1: Psychoeducation and Motivation for Treatment addresses the numerous psychosocial stresses of HIV infection, as well as treatment of current depressive symptoms. Participants may be uninterested in treatment for depression because of the seriousness of their medical condition or may be avoidant of all medical care. The therapy is non-confrontational and includes MI. Stage 2: Reducing Depressive Symptoms has six CBT sessions that teach core skills of mood monitoring, behavioral activation, reducing negative thinking, and problem-solving. Symptom reports guide the use of additional modules. Stage 3: Achieving and Maintaining Wellness identifies areas of strength and techniques to promote continued wellness because YLWH can become entrenched in the "patient" mode. All site therapists possessed either a clinical Master's or Doctoral degree. COMB therapists received a two-day CBT training (e.g. didactic instruction, role plays, and vignettes), 4 hours of training and 3 "booster" training from MI network trainer, and participated in weekly supervision calls. A random sample of 40% of CBT sessions were rated by the CBT supervisor and 95% were of acceptable quality using the Cognitive Therapy Rating Scale [33].

MEASURES

Assessments—All participants provided self-report assessments via an audio computer-assisted self-interview [at baseline and weeks 6, 12, 24 (end of treatment), 36, and 48 (end of follow-up)]. The baseline assessment included demographic information. Health data were abstracted from medical records. Also, a mental health clinician trained in the Quick Inventory of Depressive Symptomology-Clinician Rating (QIDS-C) [34] assessed baseline and end of treatment (week 24) symptoms at all sites. Also, at the COMB sites, the QIDS-C was used to guide treatment decisions 6 and 12 week medication visits.

Primary outcome measures—Participants completed the Quick Inventory of Depressive Symptomatology-Self-Report (QIDS-SR), a 16-item scale assessing 9 depressive symptoms. QIDS-SR is a reliable and valid measure of depression in adults and adolescents [34,35]. Total scores range from 0–42, whereby scores of 6–10 reflect mild symptoms, 11–15 moderate, and 16 severe. Score range and symptom severity categories are the same for the QIDS-C. QIDS-SR scores over time were used in two binary outcomes. Response to treatment was defined as a 50% decrease from baseline, and remission from depression was defined as a QIDS-SR score <5.

Secondary outcome measures—Adherence to antiretroviral medications was assessed using items from the Adherence Module developed by the ATN Adherence Workgroup [31]. Hopelessness was measured with the Beck Hopelessness Scale (BHS) [36]. This scale has been shown to predict dropout from psychosocial treatment and poorer treatment response [37] and has been used with adolescent psychiatric outpatients [38]. Life satisfaction was measured with the Multidimensional Student's Life Satisfaction Scale (MSLSS) [39], which examines five domains (Friends, Family, School, Self, and Living Environment) and general (total) life satisfaction. It has acceptable psychometric properties [40]. The Child and Adolescent Services Assessment (CASA) [41], a semi-structured face-to-face interview, obtained information about service use for mental health problems. Adequate reliability has been demonstrated (ICCs=.74 –.76). Each participant's biomarker values (CD4 and VL) within the past three months were abstracted from the medical chart.

DATA ANALYSIS

Chi-square or Fisher's exact tests were used to examine the visit-specific differences in proportions between study groups (COMB vs. TAU) for categorical outcomes. The two-sample t-test or non-parametric test was used to assess the visit-specific mean differences between study groups.

The univariate and multivariable mixed effects models with repeated measurements for continuous outcomes (QIDS-SR, QIDS-C, BHS, MSLSS, $\log_{10}$ VL, and CD4 absolute counts) and the generalized linear models with generalized equation estimation (GEE) approach for categorical outcomes (remission, response to treatment, and antidepressant medication) were used to examine the intervention effect over time while adjusting for site as a cluster effect. Additional analytic covariates considered included study visit, interaction of intervention and visit, study site, value of outcome measure at baseline, birth gender, and mode of HIV transmission. The relationship of HIV health status outcomes (CD4 counts and

log$_{10}$ VL) and depression status (QIDS-SR, response and remission status) also were examined. Covariates with p-value < 0.2 were entered in the initial multivariable full model for model selection. Backward elimination and stepwise model selection were used to choose the best final model.

The SAS MIXED procedure was used to adjust for site effects; this method also accommodates missing data [42] by using the likelihood-based approach. Generalized linear models can estimate the working correlations from the data containing missing values by using the "all available pairs" method, in which all non-missing pairs of data are used in estimating the working correlation parameters defined previously. These procedures have the capability of using all available data even for subjects who have missing observations.

Results

The 44 participants were mostly male (69%); Black/African-American (83%), and non-Hispanic (79%), with a mean age of 21.5 years. Table 2 shows significant differences between the COMB and TAU groups at baseline based on gender and transmission category. The COMB group was comprised of a significantly greater proportion of males (96% vs. 40%, p<0.001) and those who had acquired HIV via behavioral contact (95% vs. 85%, p<0.001). There were no differences at baseline between groups based on age, Hispanic ethnicity, CD4, VL, or drug and alcohol use. The CONSORT is shown in Figure 1 with 42 participants allocated to COMB (n=22) or TAU (n=20) based on random assignment of the four sites and 95% of the sample was assessed at week 24 (end of treatment) and 76% at week 48. Over the study period, five subjects prematurely discontinued (COMB, n=3; and TAU, n=2) because of a move out of state (2), loss to follow-up (2) or incarceration (1). Baseline QIDS-SR scores were compared between subjects with and without missing scores at follow-up, and there were no significant differences except Week 48 where missing subjects reported more depressive symptoms at baseline (18.5 (4.4) vs. 14.4 (4.0), t=2.74, p=0.009). Proportions of missing QIDS-SR scores by treatment condition at each study visit were not significantly different.

DEPRESSION SEVERITY

The unadjusted mean QIDS-SR and QIDS-C for both groups over time are shown in Figure 2 and Table 3 (significance tests over time adjusted for site and for covariates with p<0.2). At baseline, the groups did not differ and were moderately to severely depressed as reflected by QIDS-SR mean scores of 15. By the end of treatment (week 24), COMB participants, compared to TAU, reported significantly fewer depressive symptoms (4.3 vs. 11.1, p<0.001) and this effect was maintained at week 48 (4.1 vs. 10.2, p<0.001). Clinician symptom ratings (QIDS-C) reflected a similar pattern of a greater reduction in depressive symptoms for COMB at week 24. The relationship between QIDS-SR scores and condition (COMB or TAU) for each assessment time-point is shown in Table 3 and demonstrates that the COMB group reported significantly fewer symptoms at all time-points after baseline.

RESPONSE RATES (Table 3)

Those in COMB were significantly more likely to respond (QIDS-SR decrease 50% from baseline) at week 24 (end of treatment), compared to those in TAU (85% vs. 20%, p<0.001) and the pattern was maintained at week 48 (88% vs. 33%, p<0.001).

REMISSION RATES (Table 3)

Those in COMB, compared to those in TAU were significantly more likely to be in remission (QIDS-SR <5) over the course of the study, p<0.001. Week-specific rate differences were not calculated due to the few TAU cases in remission but the pattern was evident from week 24, (65% vs. 10%) to week 48 (71% vs. 7%).

SECONDARY OUTCOMES (Table 3)

The COMB group, relative to TAU reported significantly less hopelessness (BHS) at all visits after baseline. There was no change in life satisfaction reports over the course of the study. Similarly, CD4 counts and ARV adherence (approximately 80% at all visits (data not shown)) did not differ between groups during the study. HIV $\log_{10}$ VL decreased for the entire sample (main effect for time at weeks 36 and 38, p<0.01), but groups did not differ in the rate of change. A post hoc analysis of variance, accounting for baseline viral load, found an association between reduction in QIDS-SR scores and the final $\log_{10}$ viral loads (F=4.37, p<.05) among the entire sample.

TREATMENT CHARACTERISTICS

Participants in COMB were more likely to receive psychotherapy than in TAU (95% vs. 45%, X^2=12.44, p<0.001) and attended more sessions over the 24 weeks treatment period (12.6 (SD=3.1) vs. 5.0 (SD=2.2), t=9.01, p<0.001). There was no difference in the rate of antidepressant use between the COMB and TAU groups over the course of the study (see Table 3) and the complex details of medication usage in each condition will be reported subsequently. No significant adverse effects attributable to treatment medications were reported in either group.

Discussion

Combined cognitive behavioral therapy and medication management algorithm (COMB) delivered in HIV medical care sites by existing staff out-performed mental health treatment as usual (TAU) and resulted in a large and sustained reduction in depressive symptoms in youth living with HIV. The clinical improvement was reported by the participants and the change was confirmed by structured assessments by mental health clinicians. In addition to COMB significantly reducing the number of reported depressive symptoms, 70% of youth in the combined treatment achieved a period of symptom free functioning at the end of one year, compared to less than ten percent of the group receiving standard care who also had access at their sites to mental health treatment and psychopharmacological management. Similar, clinically meaningful reductions in depressive symptoms have been associated with improvement in other measures of health and wellness over time [43,44]. This study demonstrates that combining manualized CBT with MI skills and medication algorithms guided by symptom measurement is a highly effective intervention for depression in

YLWH. Existing staff can deliver these interventions successfully after training and with continued off-site supervision by an experienced interventionist.

Remission rates in this study are somewhat higher (71%) than reported in other clinical trials of combined CBT and medication management with non-medically ill youth, where remission rates were between 37–45% at week 24 [45,46,47,48]. Several factors could account for the excellent rates observed in this study. Collaboration between the mental health therapist and medication prescriber has been shown to be a particularly effective approach in treating depression among adolescents in medical treatment settings and the COMB treatment may have prompted increased collaboration [18]. Also, the CBT and MMA were tailored for the unique issues of those YLWH, perhaps increasing the appeal, engagement, and efficacy of the treatments over and above TAU.

COMB was more effective than TAU in engaging youth in psychotherapy (95% vs. 45%) and delivering more sessions (12 vs. 5). COMB asked youth to attend 14 CBT treatment sessions. This increased therapeutic contact could have resulted in a greater impact, irrespective of its content. MI was emphasized in COMB training and supervision to help engage and retain youth, particularly those who were withdrawn, reluctant, or skeptical of therapy and/or psychotropic medication. It is possible that YLWH who suffer from depression respond uniquely well to a time-specified, collaborative, non-confrontational treatment approach because of their experienced stigma, economic stress, somatic symptoms, and cognitive distortions. Although we do not know which aspects of the psychotherapy sessions account for its impact, the data suggests that COMB was able to address the complex psychosocial issues inherent for depressed YLWH, if they are retained in mental health care and COMB appears to have engaged and retained youth. It is important to note, many in COMB did not receive psychotropic medications and most showed improvement, despite being moderately to severely depressed at baseline. This finding suggests that the greater impact of COMB, relative to TAU, was not simply due a greater use of psychotropic medication. COMB also resulted in decreased hopelessness, consistent with the reduction in depressive symptoms, which was expected given the strong relationship between the two constructs and their responsiveness to CBT and medication.

Reduction in VL were observed over time, but was unrelated to treatment condition. Rather, reduced VL was significantly associated with reduced depression in the entire sample, confirming the general relationship between improvement in depression and better health. The lack of COMB impact on health indices could be due to the relatively small sample and associated lack of statistical power. Further, participants were receiving care in HIV-specialty clinics whereby many participants were taking antiretroviral medications at baseline with relatively good adherence reported at the outset; as a result, there may have been less room for improvement.

Despite the strengths of this study, there are a number of limitations. The sample was recruited from HIV clinical care sites and youth with substance abuse disorders were excluded, so results may not be generalizable to all YLWH. Also, the results may not be generalizable to sites outside of the U.S. or those without trained mental health professionals. Depressive symptoms were not measured by a "blind" rater but the reports of

clinicians and participants were similar. Only four clinical sites were selected for randomization, therefore site-specific characteristics (participants and staff) may have contributed to the outcomes. COMB sites enrolled a smaller proportion of eligible participants, possibly introducing group differences. In fact, COMB and TAU groups differed by gender and transmission category, although these factors were not found to affect study outcomes. Previous research has found that gender does not predict acute response, although it may impact relapse [49,50]. Although youth with perinatal transmission may differ from those with other modes in their extent of medical care and neuropathology, which could impact psychiatric treatment, the small number of perinatal youth (four) precludes examination of this important issue. COMB sites implemented structured treatment with supervision to assure treatment fidelity but treatment at TAU sites was not monitored. Inherent differences in skill or impact of providers cannot be ruled out. Nonetheless, once enrolled, sites in both conditions did equally well in retaining youth for study assessments, so, by that measure, the relationship between the sites and participants appears comparable. Data on the mental utilization at sites was not obtained after the end of treatment, limiting our understanding of the reason for the sustained remission rate in COMB.

This preliminary trial found that combined cognitive behavioral therapy with MI skills and stepped-care medication management algorithm guided by symptom measures resulted in a significant reduction in depressive symptoms for YLWH. The combined intervention was delivered in the medical care setting by existing staff, suggesting that COMB, tailored for YLWH is feasible in other U.S. medical care sites. The improvement in depression was maintained for an additional 24 weeks beyond the 24 week intervention period, suggesting that COMB could have a lasting impact. It is left to future research to confirm these findings in other sites, examine the moderating impact of factors such as gender, age, or route of transmission, and any sustained changes in treatment delivery by sites. The extension of efficacious interventions for depression to centers outside of the U.S., where the burden of HIV is greater, is also imperative.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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                          ┌─────────────────────┐
                          │ 4 Adolescent Trial  │
                          │ Network (ATN) Sites │
                          └─────────────────────┘
                           ╱                     ╲
          ┌─────────────────────┐         ┌─────────────────────┐
          │  2 ATN COMB Sites   │         │  2 ATN TAU Sites    │
          └─────────────────────┘         └─────────────────────┘
                    │                                 │
          ┌─────────────────────┐         ┌─────────────────────┐
          │     48 Screened     │         │     21 Screened     │
          └─────────────────────┘         └─────────────────────┘
                    │                                 │
          ┌─────────────────────┐         ┌─────────────────────┐
          │     34 Eligible     │         │     20 Eligible     │
          └─────────────────────┘         └─────────────────────┘
                    │                                 │
          ┌─────────────────────┐         ┌─────────────────────┐
          │     22 Enrolled     │         │     20 Enrolled     │
          └─────────────────────┘         └─────────────────────┘
                    │                                 │
          ┌─────────────────────┐         ┌─────────────────────┐
          │  6 week follow-up   │         │  6 week follow up   │
          │ completers (n = 20) │         │ completers (n = 19) │
          └─────────────────────┘         └─────────────────────┘
                    │                                 │
          ┌─────────────────────┐         ┌─────────────────────┐
          │  12 week follow-up  │         │  12 week follow up  │
          │ completers (n = 19) │         │ completers (n = 19) │
          └─────────────────────┘         └─────────────────────┘
                    │                                 │
          ┌─────────────────────┐         ┌─────────────────────┐
          │  24 week follow-up  │         │  24 week follow up  │
          │ completers (n = 20) │         │ completers (n = 20) │
          └─────────────────────┘         └─────────────────────┘
                    │                                 │
          ┌─────────────────────┐         ┌─────────────────────┐
          │  36 week follow-up  │         │  36 week follow up  │
          │ completers (n = 12)*│         │ completers (n = 11)*│
          └─────────────────────┘         └─────────────────────┘
                    │                                 │
          ┌─────────────────────┐         ┌─────────────────────┐
          │  48 week follow-up  │         │  48 week follow up  │
          │ completers (n = 17) │         │ completers (n = 15) │
          └─────────────────────┘         └─────────────────────┘
```
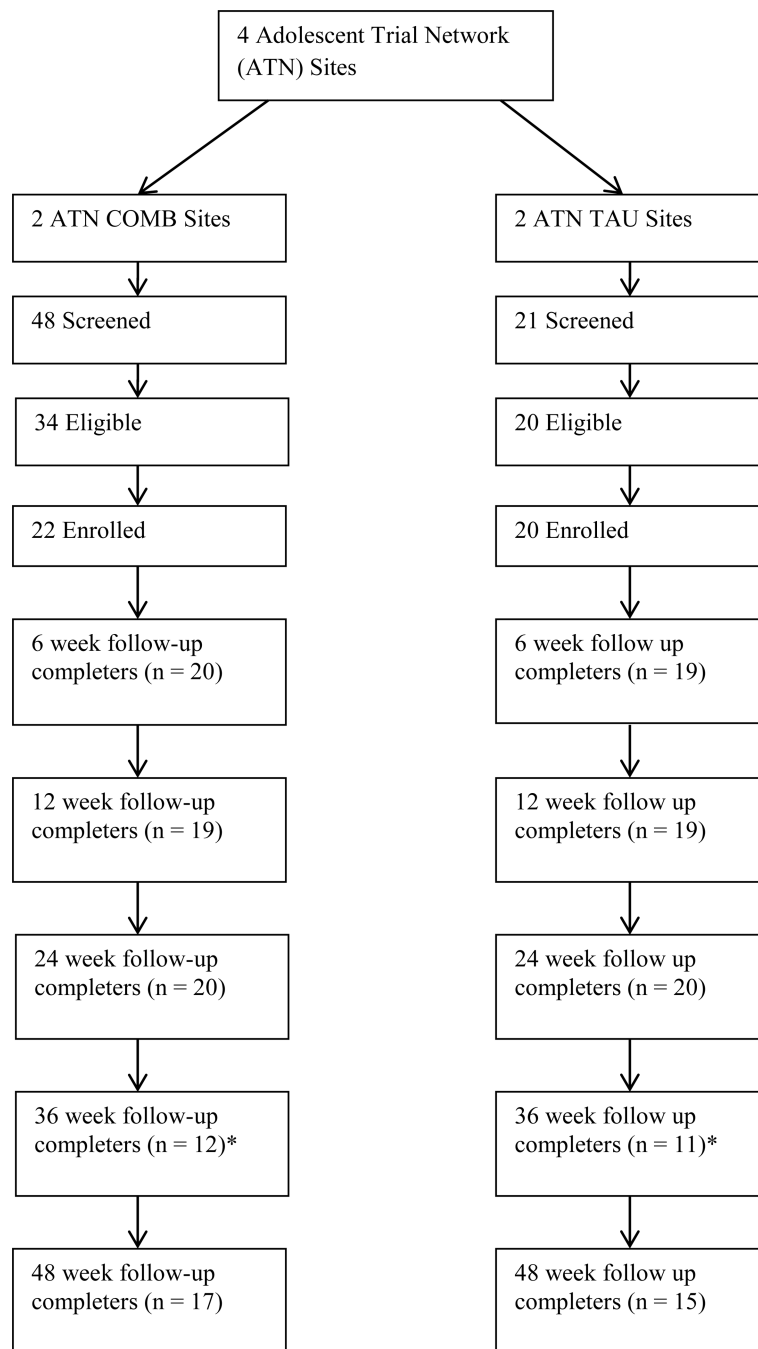
Figure 1.
Participant consent, randomization, and retention (CONSORT Flowchart)
*Delay in site approval for 36 week follow-up reduced eligible participant
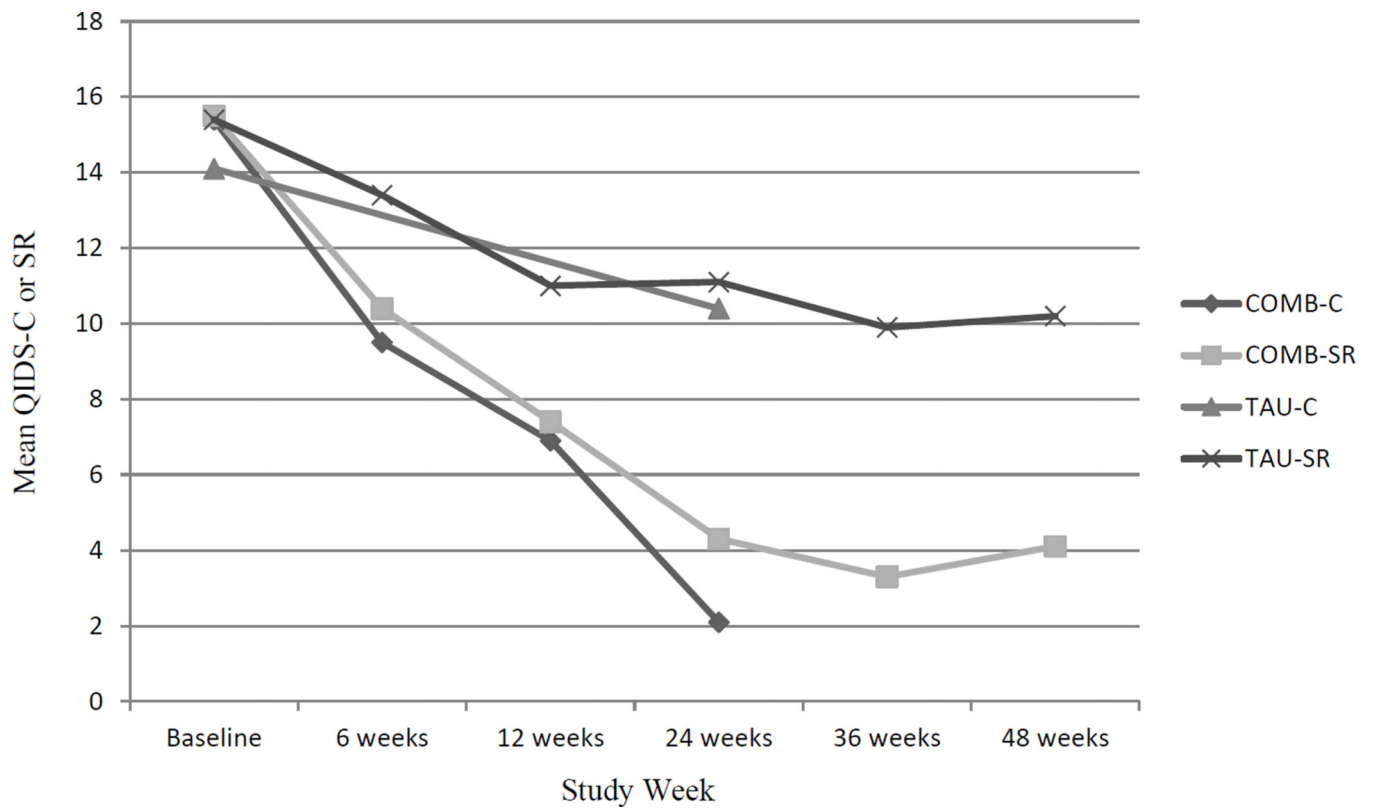
Figure 2.
Quick Inventory of Depression Symptomatology (QIDS) over Time* and by Condition
*Note: QIDS-C not administered at 36 and 48 weeks

Table 1

a. Medication Algorithm

Stage	Treatment
Stage 0	No medication
Stage 1	Monotherapy with SSRI
Stage 2	Monotherapy with 2nd SSRI
Stage 3	Monotherapy with non-SSRI
Stage 4	Combination Treatment

b. Antidepressant Doses for Depression

Antidepressant	Initial dose (mg/day)	Target dose to achieve by week 4 (mg/day)	Dose titration for partial or non-responders (mg/day)	Usual dose schedule
SSRIs				
Fluoxetine	10–20	20	30–60	q AM
Sertraline	25–50	100	150–200	q AM
Citalopram	10–20	20	30–60	q AM
Escitalopram	5–10	10	20–30	q AM
Paroxetine	10–20	20	30–50	q AM
Non-SSRIs				
Bupropion, Bupropion SR	75–100	75–300	450	bid-tid (150 mg/dose)
Bupropion XL	150	300–450	450	q AM
Mirtazapine	15–30	30	45	q hs
Venlafaxine-XR	37.5–75	75–150	225	q d
Duloxetine	20	40–60	60	20 mg bid 60 mg q d

Table 2

Demographic and Baseline Characteristics by Study Group

	Total N=42 n (%)	COMB* N=22 n (%)	TAU** N=20 n (%)	p-value
Age (years)				
Mean (SD) [range 18 – 24]	21.5 (1.6)	21.5 (1.6)	21.5 (1.6)	0.98
Gender				
Male	29 (69.0)	21 (95.5)	8 (40.0)	< 0.001
Ethnicity				
Hispanic or Latino	9 (21.4)	3 (13.6)	6 (30.0)	0.27
Race				
Black or African American	35 (83.3)	19 (86.4)	16 (80.0)	0.64
Mode of HIV transmission				
Perinatal transmission	4 (9.5)	1 (4.5)	3 (15.0)	< 0.001
High-risk heterosexual contact	5 (11.9)	1 (4.5)	4 (20.0)	
Male-to-male sexual contact	28 (66.7)	20 (90.9)	8 (40.0)	
Presumed heterosexual contact	5 (11.9)	0 (0.0)	5 (25.0)	
Baseline CD4 count - categorical				
< 200	6 (14.3)	4 (18.2)	2 (10.0)	0.93
200 – 350	6 (14.3)	3 (13.6)	3 (15.0)	
350 – 500	10 (23.8)	5 (22.7)	5 (25.0)	
500	20 (47.6)	10 (45.5)	10 (50.0)	
Log 10 Viral Load				
Mean (SD)	2.9 (1.4)	2.7 (1.3)	3.1 (1.5)	0.33
Baseline Viral load - categorical				
< 400	21 (50.0)	12 (54.5)	9 (45.0)	0.93
400 – 9,999	1 (2.4)	1 (4.5)	0 (0.0)	
1,000 – 9,999	9 (21.4)	4 (18.2)	5 (25.0)	
10,000 – 99,999	8 (19.0)	4 (18.2)	4 (20.0)	
100,000	3 (7.1)	1 (4.5)	2 (10.0)	
Did you drink alcohol (beer, wine or wine coolers, etc.) in the past 3 months?				
Yes	31 (86.1)	16 (84.2)	15 (88.2)	1.00
Have you smoked marijuana, other than just trying a few puffs, in the past 3 months?				
Yes	20 (55.6)	11 (57.9)	9 (52.9)	1.00
Have you used any other king of drug in the past 3 months?				
Yes	3 (8.3)	2 (10.5)	1 (5.9)	1.00

*COMB = combined manualized CBT and medication management algorithm

**TAU = treatment as usual

Table 3

Depression Status and Treatment Response by Study Group and Visit

	Baseline		Week 6		Week 12		Week 24		Week 36		Week 48		p-value[1]
	COMB	TAU	COMB	TAU	COMB	TAU	COMB	TAU	COMB	TAU	COMB	TAU	
Response to treatment[1]													
n	22	20	20	19	19	19	20	20	12	11	17	15	< 0.001
Number Yes	--	--	5	0	10	4[a]	17	4**	11	4**	15	5**	
Proportion	--	--	25.0	0.0	52.6	21.1	85.0	20.0	91.7	36.4	88.2	33.3	
Remission from depression[2]													
n	22	20	20	19	19	19	20	20	12	11	17	15	< 0.001
Number Yes	--	--	4	0	7	2	13	2	9	1	12	1	
Proportion	--	--	20.0	0.0	36.8	10.5	65.0	10.0	75.0	9.1	70.6	6.7	
Antidepressant medication use													
n	22	20	20	19	19	19	20	20	12	11	17	15	0.368
Number Yes	5	10	7	8	9	9	7	9	5	4	3	6	
Proportion	22.7	50	35	42.1	47.4	47.4	35	45	41.7	36.4	17.6	40	
Continuous Scale Outcomes													
Quick Inventory of Depressive Symptoms-Self Report (QIDS-SR)[3]													
n	22	20	20	19	19	19	20	20	12	11	17	15	0.001
mean	15.5	15.4	10.4	13.4[a]	7.4	11.0[a]	4.3	11.1**	3.3	9.9*	4.1	10.2**	
standard deviation	4.9	4.0	5.0	4.2	4.4	5.6	2.9	5.6	1.9	4.6	3.5	5.5	
Quick Inventory of Depressive Symptoms-Clinician (QIDS-C)[4]													
n	22	20	20	19	19	19	20	20	12	11	17	15	0.001
mean	15.4	14.1	9.5	--	6.9	--	2.1	10.4**	--	--	--	--	
standard deviation	4.4	4.1	3.4	--	4.3	--	2.6	5.5	--	--	--	--	
Beck Hopelessness Scale (BHS)[5]													
n	22	20	20	19	19	19	20	20	12	11	17	15	0.351
mean	10.3	8.3	7.0	7.9*	5.9	7.5*	4.8	6.1*	4.2	6.2[a]	3.6	6.0*	
standard deviation	4.1	3.8	4.2	5.3	4.5	5.7	3.6	3.3	2.4	4.0	1.8	3.7	

	Baseline		Week 6		Week 12		Week 24		Week 36		Week 48		p-value[1]
	COMB	TAU	COMB	TAU	COMB	TAU	COMB	TAU	COMB	TAU	COMB	TAU	
Multidimensional Student's Life Satisfaction Scale (MSLSS)[6]													
n	22	20	20	19	19	19	20	20	12	11	17	15	
mean	4.0	4.1	4.2	4.1	4.3	4.3	4.7	4.5	4.7	4.4	4.8	4.4	0.547
standard deviation	0.6	0.7	0.8	0.9	0.7	0.9	0.7	0.7	0.5	1.0	0.6	0.7	
CD4 count													
n	22	20	7	6	12	13	16	17	10	11	16	13	
mean	511.4	507.2	548.4	438.8	475.6	487.6	513.3	577.2	383.9	536.7	575.6	509.6	0.736
standard deviation	337.0	297.5	304.0	142.3	314.3	354.0	317.4	409.6	240.6	352.1	331.1	316.2	
Log 10 Viral Load													
n	22	20	7	6	12	14	16	17	10	11	16	13	
mean	2.6	3.0	2.3	2.6	2.1	2.6	2.2	2.9	1.3	2.5	1.7	2.7	0.104
standard deviation	1.4	1.6	1.4	1.0	1.3	1.6	1.2	1.7	0.2	1.4	0.8	1.3	

[1] p-value is of the test of intervention effect of each variable of interest over time.

[2] Quick Inventory of Depressive Symptoms – Self Report↓ 50% from baseline.

[3] Quick Inventory of Depressive Symptoms-Self Report score < 5.

[4] QIDS-SR: Higher score indicates a greater depression, range 0–27.

[5] QIDS-C: Higher score indicates a greater depression, range 0–27.

[6] BHS: Higher score reflects a higher level of hopelessness, range 0–20.

[7] MSLSS: average of items, range 1–6.

[a] p <.05 for difference between TAU and COMB in model test adjusting for baseline value and significant covariates retained in final model.

[*] p <.01 for difference between TAU and COMB in model test adjusting for baseline value and significant covariates retained in final model.

[**] p <.001 for difference between TAU and COMB in model test adjusting for baseline value and significant covariates retained in final model.