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# Depression remission rates among older black and white adults: Analyses from the IRL-GREY trial

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## Abstract

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**Objective—**This study explored whether older black and white adults with major depressive disorder differ in rates of remission or attrition during open-treatment with venlafaxine and supportive care.

**Methods—**47 black (10%) and 412 white (90%) adults ≥ age 60 were treated using open-label venlafaxine extended-release (up to 300mg/day) for 12-14 weeks during the initial phase of an NIMH-sponsored, multisite, randomized, placebo-controlled augmentation trial. Participants were help-seeking elders with non-psychotic major depressive disorder (single or recurrent episode) referred from specialty mental health clinics, primary care practices, advertisements and research programs. Remission was defined as a Montgomery-Asberg Depression Scale score of ≤10 for two consecutive assessments at the end of 12 weeks. Kaplan-Meier curves were employed to display time to drop out and time to initial remission. Cox Proportional Hazard models were used to assess differences in attrition and remission rates.

**Results—**Black participants had greater baseline medical comorbidity, worse physical-health related quality of life and poorer cognitive function compared with white participants. Whites were more likely than blacks to have received an adequate trial of antidepressant and psychotherapy before entering the study. Baseline depression severity, duration of depression, age of onset, and recurrence history did not differ between the two groups. Blacks and whites had similar final doses of venlafaxine, rates of attrition and remission. Side effect profiles were comparable between the two groups.

**Conclusion—**Despite greater medical comorbidity, lower cognitive function, and less adequate prior antidepressant and psychotherapy exposure, black participants were no more likely to discontinue antidepressant pharmacotherapy, and experienced a rate of remission comparable to white participants.

## Introduction

### Disparities faced by older black adults

Many older black adults are at risk for depression due to social stressors (including poverty, low education attainment, exposure to violence, discrimination[1]), and health problems (including high rates of obesity, substance use disorders[2], and dementia[3]). Older blacks tend to endorse a greater number of depressive symptoms than older whites[4]. However, blacks often have limited access to and underutilize mental health services[5,6,7,8]. The underutilization may be explained, in part, by stigma surrounding mental illness, mistrust of mental health care practitioners and a preference for non-pharmacological treatment strategies[9,10]. As a result, black individuals are often under diagnosed and under-treated when they are depressed[11,12]. One barrier to reducing these disparities is the lack of evidence on interventions and outcomes (e.g., remission rates to antidepressants), particularly in diverse aging populations.

### Antidepressant outcome studies among black adults

Studies evaluating antidepressant outcomes in middle-aged black adults have yielded mixed results. Some studies[13,14,15] suggest that blacks have worse antidepressant treatment outcomes compared to whites. A number of studies using older antidepressants have even shown that blacks respond more quickly than whites[16,17]. Other studies[18,19,20,] have shown

similar remission rates in black and white participants, including those adjusting for baseline clinical and sociodemographic variables[21,22,23]. Likewise, pooled analyses[24,25] from pharmacy-sponsored databases have shown similar remission rates between minorities and whites.

Studies comparing antidepressant outcomes have focused on middle-aged adults. Similar investigations have been largely unstudied in later-life. Investigating antidepressant remission among aging minority populations is important since both older age[26,27] and race-ethnicity may alter antidepressant remission rates. Studies investigating treatment outcomes in older black adults have been performed in the context of collaborative care models of depression treatment. One such study[28] showed that older black adults respond at similar rates to older white adults, while another[29] showed less benefit for older blacks compared to older whites. To our knowledge, no studies have looked at differences in remission rates among older black and white adults using antidepressants alone.

### Study aims

Using data from an NIMH-sponsored multisite trial, this report aims to explore whether older black and white participants with major depressive disorder differ in rates of attrition and remission during open-treatment with venlafaxine and supportive care. We also explore differences in clinical features, rates of medical and psychiatric co-morbidity (including cognitive function and obesity), outside psychotherapy and adequacy of prior trials of antidepressants between the two groups.

## Methods

### Primary study description

Data originated in an NIMH-sponsored multicenter (Pittsburgh, St. Louis, and Toronto) trial entitled “Incomplete Response in Late-Life Depression: Getting to Remission” (IRL-Grey; ClinicalTrials.gov Identifier: NCT00892047). In the initial phase of IRL-GREY, older adults with major depressive disorder were treated openly with venlafaxine extended-release for 12-14 weeks. Participants who did not respond to venlafaxine extended-release at a maximum daily dose of 300 mg were randomized to venlafaxine extended-release plus aripiprazole or venlafaxine extended-release plus placebo. A very small percentage of participants were treated for up to 24 weeks for feasibility reasons (e.g., transportation/travel difficulties) in order to achieve the maximum dose of venlafaxine and to determine definitively whether or not they qualified for the subsequent double-blind, randomized, placebo-controlled trial of augmentation pharmacotherapy with aripiprazole. This analysis examines only data from the open-treatment phase with venlafaxine extended-release .

Inclusion criteria required participants to be aged 60 or older, have a diagnosis of major depressive disorder (single or recurrent episode), meet criteria for a current non-psychotic major depressive episode as diagnosed by the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) [30], and a Montgomery-Asberg Depression Scale (MADRS) score of ≥ 15. Exclusion criteria included presence of clinical dementia, history of a bipolar or a psychotic disorder, current psychotic symptoms, alcohol or substance abuse or dependence

within the past 3 months, high suicide risk and refusing to be hospitalized, an unstable medical illness, inability to safely taper or discontinue psychotropic medications before study initiation, and a contraindication to venlafaxine extended-release or aripiprazole.

## Participants

Between July 20, 2009, and December 30, 2013, we screened 1,098 depressed individuals aged 60 and older; 490 were excluded because of failure to satisfy all eligibility criteria. Of the 608 eligible participants who consented to participate, 140 withdrew before starting treatment. The remaining 468 participants started treatment. We excluded from this analysis 8 Asian/Pacific and 1 Native American participants and included 47 black and 412 white participants (N=459). They were recruited based on referrals from mental health facilities and clinics (N= 161; 35%), advertisements (radio, newspaper, staff presentations, etc) (N=118; 26%), research programs (N =81; 18%); referrals from primary care or non-psychiatrist physicians (N=66; 14%); and other miscellaneous referral sources (N= 33; 7%). There was no difference in referral sources with respect to the proportion of black and white participants. The protocol was approved by the three local institutional review boards. All participants gave written informed consent.

## Measures

We assessed depression severity using the MADRS[31], a ten-item clinician administered rating scale (score range: 0-60). Depression remission is the outcome variable for this analysis. Remission was defined as a MADRS score of ≤10 for two consecutive assessments at the end of the open label treatment phase. Depression severity was also assessed at baseline using the 17-item Hamilton Rating Scale for Depression (HDRS-17)[32] in order to allow camparison of our data with other trialsSuicidal ideation was assessed using the 21-item scale for suicide ideation (SSI),[33] and a score of 1 or greater indicated the presence of current suicidal ideation.

Medical comorbidity and burden were assessed using the Cumulative Illness Rating Scale for Geriatrics (CIRS-G)[34] which rates each organ system from 0 (no problem) to 4 (end organ failure/ severe functional impairment) (total score range: 0-52; number of organ systems with a score greater than zero: range 0-13). Quality of life was measured using the short-form 36-item Measures of Quality of Life Core Survey (MOS)[35]. The Antidepressant Treatment History Form (ATHF) [36] was used to assess the adequacy of previous trials of antidepressants or electroconvulsive therapy on a scale of 0-5 with a score of ≥3 representing an adequate trial.

We measured general anxiety symptoms using the Brief Symptom Inventory (BSI-anxiety) [37]. The BSI-anxiety is a 6-item self-report questionnaire rated on a 5-point scale (0: not present, 4: extremely severe). Anxiety sensitivity (fear of symptoms of anxiety and panic) was measured using the Anxiety Sensitivity Index (ASI)[38].The ASI is a 16-item self-report questionnaire rated on a 5-point scale (0: a little, 4: very much).

The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)[39] was used to evaluate global cognitive functioning, as well as delayed memory ability. Executive functioning was evaluated using the combined mean of two tests (Color-Word Interference

Inhibition and Trail Making) on the Delis-Kaplan Executive Function Scale (D-KEFS)[40]. All scores were age-normed. Current or past anxiety disorders and drug or alcohol use were evaluated using the SCID.

Other pre-treatment assessments focused on basic demographic information (age, sex, race, education) and clinical variables (age at onset of first lifetime depressive episode, duration of current episode, receiving any psychotherapy outside of the trial, history of substance abuse, and body mass index (BMI)).

### Treatment protocol

Venlafaxine extended-release was initiated at 37.5 mg/day and titrated (in 37.5 mg increments separated by at least 3 days) to a target dose of 150 mg/day. At the end of week-6, non-remitters had their dose increased further (in 37.5–75 mg increments separated by at least 3 days) to a target dose of up to 300 mg/day. The dose could be reduced at any time if participants experienced adverse effects. Lorazepam (up to 2 mg/day) could be prescribed for sleep or anxiety. Participants could also continue using some other medications for sleep (zolpidem, zopiclone, trazadone, low-dose amitriptyline) or participate in outside psychotherapy if it had started prior to study entry and could not be discontinued.

Throughout the study, pharmacotherapy was embedded in a model of depression care management (i.e., supportive clinical care focusing on psychoeducation about depression and its treatment, depressive symptoms, suicidal ideation, countermeasures for medication adverse effects, and treatment adherence, but *not* incorporating any depression-specific psychotherapy[41]). Participants were seen once a week for the first 2 weeks and then every 2 weeks by study clinicians under the supervision of physician investigators. During each of these visits, the research team assessed depressive symptoms (MADRS), suicidal ideation (SSI), vital signs, and adverse effects (UKU side effects rating scale[42])[43].

### Statistical analysis

Baseline demographics of black and white participants were compared using analysis of covariance (ANCOVA) for continuous variables or logistic regression for categorical variables. Analyses controlled for site differences after testing verified there were no site by race interactions. For categorical variables, if rates were small, the Exact Logistic regression was used. Age-normed cognitive measures were analyzed controlling for site, education, sex, medical burden, and severity of depression. Kaplan-Meier curves[44] were employed to display time to drop out and time to initial remission for the black and white participants classified as remitters at end of treatment. Formal inference for differences in attrition and remission rates used Cox Proportional Hazard models controlling for site[45].

## Results

### Participant sociodemographics

Of the 459 participants, 10% (N=47) of the sample were black and 90% (N=412) were white. The Toronto site had a lower proportion of black participants (7/120; 6%) than Pittsburgh (20/199; 10%) or St. Louis (20/140; 14%) but the differences were not

significant. Participant characteristics are summarized in Table 1: black participants differed from whites in having fewer males and fewer years of formal education. They did not differ in age or proportion of subjects living at home alone (as sole occupant of household).

### Medical comorbidity and health-related quality of life

Black participants had greater medical comorbidity as evidenced by a greater number of affected organ systems on the CIRS-G. They also endorsed worse physical-health related quality of life, but scored higher on the mental component of the MOS. Black and white participants were comparable in terms of their mean BMI and the percentage of individuals who were obese (BMI ≥ 30). There were no differences in rates of diabetes; however, black participants had higher rates of hypertension.

### Depression severity and psychiatric comorbidity

Black and white participants had similar baseline depression severity as reflected by their HDRS-17 or MADRS scores (Table 2). They did not differ in their mean age of onset of depression, percentage having recurrent episodes of depression, or duration of the current depressive episode, percentage having suicidal ideation, prior suicide attempts, number of co-morbid anxiety disorders or self-reported anxiety symptoms (BSI). However, blacks reported a higher rate of self-reported anxiety sensitivity (ASI).

### History of pharmacotherapy and psychotherapy

White participants were more likely than black participants to have received an adequate trial of antidepressant before enrolling in the study and to have received psychotherapy.

### Cognitive Function

Controlling for age, site, years of education, sex, medical burden (CIRS-G total scores), and depression severity (HDRS-17), black participants had lower RBANS total score, delayed memory scores, and D-KEFS executive functioning scores.

### Attrition

Over the course of treatment, 94/459 (20%) participants withdrew from treatment: 11/47 (23%) black participants and 83/412 (20%) white participants (OR: 1.15[95 % CI=.61-2.17). Participants withdrew because of: adverse effects (n=31); preference for other treatment (n=26); non-compliance/non-adherence with study medication or appointments (n=11); supervening medical problems (n=10); or other reasons (n =16) such as relocation, cognitive impairment, worsening of depression, onset of psychosis, use of alcohol, drugs, or death. Kaplan-Meier survival curve shows that black and white participants had similar time to dropout (Figure 1).

### Tolerability

The final daily dose of venlafaxine did not differ between the two groups (blacks: 225.8 (74.4) mg, median =225; whites: 222.0 (82.3), median=225). Black and white participants reported comparable side effects (Table 3).

### Remission

With open venlafaxine extended-release treatment and supportive care, 189/459 (41%) participants reached depression remission (blacks: 19/47 (40%); whites: 170/412 (41%); OR:1.12 [.70-1.81]). The Kaplan-Meier survival curve shows that black and white participants had similar time to remission (Figure 2).

## Discussion

This study investigated potential differences in major depressive disorder remission rates among black and white elders utilizing venlafaxine. Despite greater medical comorbidity, lower performance on cognitive tests, and less adequate prior antidepressant and psychotherapy exposure, black participants were no more likely to discontinue antidepressant pharmacotherapy and experienced a rate of remission comparable to white participants. One might have anticipated that black participants would have a lower rate of remission given that they had less education and showed worse cognitive performance. In other studies, impairment in executive function, response inhibition[46,47], and verbal memory[48] have been associated with worse outcomes to antidepressants in late-life depression.

### Comparison to previous literature

Comparing the results of this analysis to other studies investigating antidepressant outcomes among diverse racial groups is difficult because of the differences in recruitment strategies, study design and interventions used. Nevertheless, the results of this analysis are similar to studies showing little difference in treatment outcomes between middle-aged blacks and whites[49,50,51,52] including results from pooled analyses [53,54]. A number of studies[55,56,57,58] showed poorer outcomes in black participants, but when adjusting for baseline sociodemographic and clinical variables no difference was found. Our analysis did not control for baseline differences. Therefore we cannot rule-out the possibility that blacks may have responded better than whites as was seen in studies utilizing older antidepressants[59,60]. The current results stand in contrast to results of studies showing worse outcomes to for black participants. In addition to differing recruitment strategies, and antidepressant classes used, results may have also differed because of the very different populations studied. For example, one study[61] investigated HIV positive individual with depression and another study[62] focused on the characteristics of participants whose depression worsened throughout the course of treatment.

The majority of studies accessing outcomes among minorities have been in middle-aged populations. Very few have focused on older adults. Those that have are in the context of collaborative care models which include antidepressants, psychotherapy, education, and case management. The current results are in agreement with one collaborative care study[63]showing comparable rates of depression remission between whites and blacks but in disagreement with another collaborative care study[64]. Although important, these analyses provide us with little information about remission rates to antidepressant intervention alone. This is important since antidepressant monotherapy is often used as a first-line treatment for late-life depression.

Despite this and previous analyses, the role of race-ethnicity in antidepressant outcomes, especially among older adults, remains inconclusive; however, the bulk of this work suggest that treatment outcomes are similar between blacks and whites. Additional research in this area is warranted to facilitate appropriate care to an aging and increasingly diverse population, as noted by the Surgeon General's report[65]. Our analysis represents one of the very few studies exploring treatment outcomes in older minorities. To our knowledge it is the only analysis investigating remission via antidepressants alone among older black adults.

## Study Strengths/ Limitations

The strengths of this study include a large total sample size, the use of structured interviews and validated measures to assess outcomes, a supportive clinical environment, and relatively low attrition rates. The tables show we had the power to detect clinically meaningful effect sizes . Limitations include an analysis of open treatment data from a trial that was not designed to specifically assess racial-ethnic differences in antidepressant response. We also cannot rule out the possibility that white participants were more treatment-resistant than black participants as evidenced by a history of more prior adequate trials of antidepressants and psychotherapy. Thus, it is plausible that most of our black participants had been undertreated at the point when they enrolled in this study.[66] Participants self-identified their racial-ethnic backgrounds. Grouping participants into categories of race is problematic since such groupings do not imply sociocultural or genetic homogeneity. Differences in antidepressant treatment outcomes among racial-ethnic groups may be due to pharmacokinetic factors such as differing polymorphisms of cytochrome P450 enzymes, which may lower enzymatic activity in certain ethnicities[67]. We also cannot be certain whether the baseline differences among ethnic-racial groups represent an accurate picture of help-seeking older adults in the general population or if they only relate to the participating sites. Additionally, many older blacks do not seek out mental health services for their depressive symptoms and when they do, they are under-diagnosed for depression. Therefore, our study sample may not reflect community-dwelling black elders with major depressive disorder.

There is a need for additional studies of more broadly representative samples recruited by systematic screening, as we have elsewhere reported[68].

## Conclusion

Our study suggests that with adequate treatment it is possible to mitigate the disparity in antidepressant outcomes between older black and white adults. With appropriate pharmacotherapy embedded in good supportive care, black and white older adults with major depressive disorder can do equally well. However, this is often not seen because of numerous barriers to recruitment[69], retention[70], and adherence[71] confronting black people and others living with socioeconomic adversity. We acknowledge that treatment outcome differences are not limited to the effects of race (although some variability may be accounted for by genetically mediated pharmacokinetic and possibly pharmacodynamics differences), but include a myriad of sociocultural and socioeconomic barriers (including poverty, violence, low education attainment, limited access to mental health services, and discrimination) to effective antidepressant treatment. In this context we recognize that our

black participants were recruited by traditional means which often fail to result in a true representation of the older black population; thus, our study was limited to help-seeking seniors. Although this is clinically meaningful, it falls short of true generalizability. Finally, given that the majority of participants in both groups did not remit future studies need to compare the outcomes of second-line antidepressant treatment in black and whites elders.

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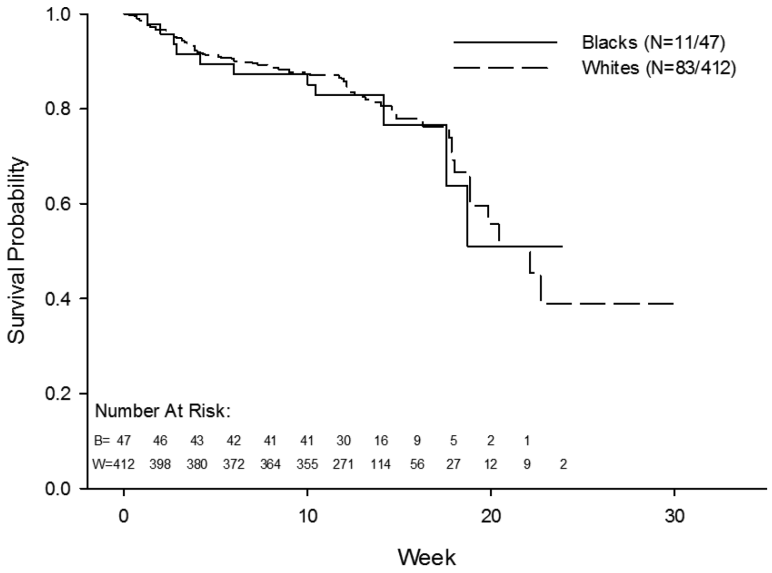


**Figure 1. Time to Dropout**

Cox Proportional Hazard Model controlling for site: Hazard Ratio (black vs. white) = 1.15 [95% CI = .61-2.17], Wald Chi-square=.18, df=1, p=.67

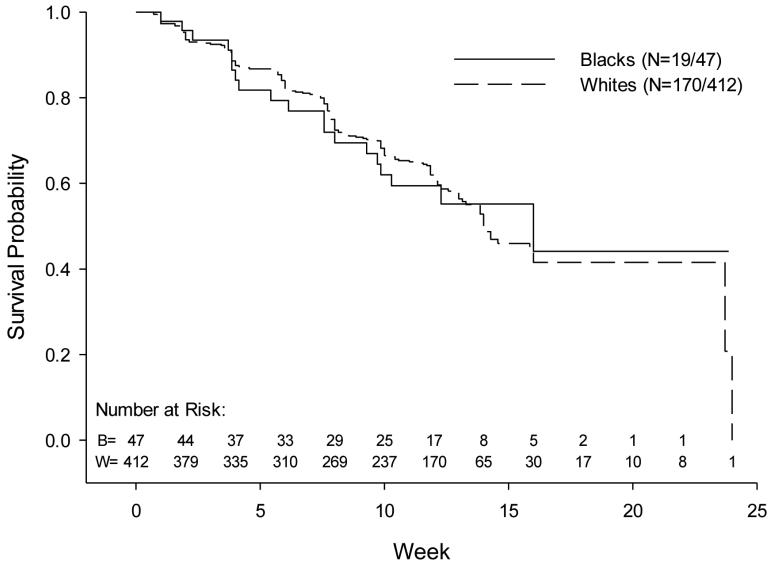


**Figure 2. Time to Remission**

Blacks and whites did not differ in rates of remission (blacks = 40.43% (n=19/47), whites= 41.26% (n=170/412)).

Cox proportion hazard model controlling for site showed both groups were equally likely to remit. (Wald chi-square=.23, df=1, p=.63, Hazard Ratio (black vs. white)=1.12 [95%CI=. 70-1.81]). Results similar if you drop subjects who came in on venlafaxine (black remission =42.22% (n=19/45) vs. white remission=42.26% (n=161/381)).

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**Table 1**

Baseline demographic and clinical variables.[a]

| | All Subjects (N=459) | | Black (N=47) | | White (N=412) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | Test statistic | df | p | Effect size *d* | 95% CI |
| Age (M±SD) | 69.04± 7.22 | | 67.32± 6.73 | | 69.23± 7.26 | | 2.69 | 1,455 | .10 | .006 | |
| Gender (reference: white) | | | | | | | 5.25 | 1 | .02 | 2.42 | 1.14-5.16 |
| Female (event) | 299 | 65 | 38 | 81 | 261 | 63 | | | | | |
| Male | 160 | 35 | 9 | 19 | 151 | 37 | | | | | |
| Education (M±SD) | 14.37± 2.84 | | 13.09± 2.57 | | 14.52± 2.83 | | 13.98 | 1,455 | <.001 | .03 | |
| Living Status (reference: white) | | | | | | | | | .99[b] | 1.12 | .32-3.97 |
| Home alone (event) | 394 | 92 | 38 | 93 | 356 | 92 | | | | | |
| Other | 35 | 8 | 3 | 7 | 32 | 8 | | | | | |
| Cumulative Illness Rating Scale | | | | | | | | | | | |
| Total (M±SD) | 9.88± 4.43 | | 11.13± 3.99 | | 9.74± 4.46 | | 2.76 | 1,454 | .10 | .006 | |
| Count (M±SD) | 6.17± 2.35 | | 6.98± 2.05 | | 6.08± 2.37 | | 4.21 | 1,454 | .04 | .008 | |
| Medical Outcomes Survey | | | | | | | | | | | |
| Physical Component (M±SD) | 42.65± 11.61 | | 36.14± 11.03 | | 43.39± 11.45 | | 16.66 | 1,477 | <.001 | .04 | |
| Mental Component (M±SD) | 27.36± 8.92 | | 30.55± 9.01 | | 27.00± 8.84 | | 6.10 | 1,477 | .02 | .01 | |

| | All Subjects (N=459) | | Black (N=47) | | White (N=412) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | Test statistic | df | p | Effect size[d] | 95% CI |
| BMI[c] (M±SD) | 29.88± 6.85 | | 31.95± 8.23 | | 29.64± 6.64 | | 3.27 | 1,451 | .07 | .007 | |
| BMI categorical (reference: white) | | | | | | | .99 | 1 | .32 | 1.36 | .74-2.52 |
| ≥ 30 (event) | 193 | 42 | 24 | 51 | 169 | 41 | | | | | |
| < 30 | 262 | 58 | 23 | 49 | 239 | 59 | | | | | |
| Diabetes (reference: white) | | | | | | | 1.49 | 1 | .22 | 1.57 | .76-3.24 |
| Yes (event) | 77 | 18 | 12 | 27 | 65 | 17 | | | | | |
| No | 349 | 82 | 33 | 73 | 316 | 83 | | | | | |
| Hypertension (reference: white) | | | | | | | 7.24 | 1 | .007 | 2.64 | 1.30-5.34 |
| Yes (event) | 215 | 50 | 33 | 73 | 182 | 48 | | | | | |
| No | 211 | 50 | 12 | 27 | 199 | 52 | | | | | |

[a] Means were compared by ANOVA and proportions were compared by logistic regression. All analyses controlled for site.

[b] Exact probability.

[c] Mean and standard deviations reported in original units. Transformation used in the analyses.

[d] Eta-squared report for continuous measures and odds ratio for the logistic regression.

**Table 2**

Baseline neuropsychiatric variables

| | All Subjects (N=459) | | Black (N=47) | | White (N=412) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | Test statistic | df | p | Effect size[d] | 95% CI |
| Hamilton Rating Scale – 17 item (M±SD) | 19.97± 4.95 | | 21.30± 4.54 | | 19.81± 4.98 | | 3.38 | 1,455 | .07 | .007 | |
| MADRS (M±SD) | 26.64± 5.72 | | 27.64± 6.05 | | 26.53± 5.68 | | 1.10 | 1,445 | .29 | .002 | |
| MADRS at end of open label treatment phase[c] (M±SD) | 13.73± 10.59 | | 12.31± 9.90 | | 13.88± 10.65 | | .92 | 1,384 | .34 | .002 | |
| Depression Type (reference: white) | | | | | | | .78 | 1 | .38 | .75 | .39-1.43 |
| Recurrent (event) | 326 | 71 | 30 | 64 | 296 | 72 | | | | | |
| Single Episode | 133 | 29 | 17 | 36 | 116 | 28 | | | | | |
| Age of Onset (first lifetime episode) (M±SD) | 42.28± 21.45 | | 45.47± 22.00 | | 41.91± 21.39 | | 2.70 | 1,454 | .10 | .006 | |
| Duration of Current Episode (weeks)[c] (M±SD, median) | 292.76± 614.1 | Med = 74 | 192.34 ±206.2 | Med = 104 | 304.28 ±643.8 | Med = 68 | .04 | 1,453 | .85 | .0001 | |
| Suicidal ideation (reference: white) | | | | | | | 1.87 | 1 | .17 | .62 | .32-1.23 |

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| | All Subjects (N=459) | | Black (N=47) | | White (N=412) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | Test statistic | df | p | Effect size[d] | 95% CI |
| SSI >0 (event) | 184 | 40 | 14 | 30 | 170 | 41 | | | | | |
| SSI = 0 | 274 | 60 | 32 | 70 | 242 | 59 | | | | | |
| History of suicide attempts (reference: white) | | | | | | | .73 | 1 | .39 | 1.43 | .63-3.26 |
| Yes (event) | 60 | 13 | 8 | 17 | 52 | 13 | | | | | |
| No | 397 | 87 | 39 | 83 | 358 | 87 | | | | | |
| SCID diagnosis Anxiety (reference: white) | | | | | | | 2.29 | 1 | .13 | 1.61 | .87-2.98 |
| Yes (event) | 191 | 42 | 25 | 53 | 166 | 40 | | | | | |
| No | 268 | 58 | 22 | 47 | 246 | 60 | | | | | |
| BSI Anxiety[c] (M±SD) | 1.49± .93 | | 1.39± .94 | | 1.50± .92 | | .19 | 1,449 | .66 | .0004 | |
| Anxiety Sensitivity Index (ASI)–self report (M±SD) | 25.51± 12.75 | | 30.41± 14.78 | | 24.96± 12.39 | | 10.10 | 1,449 | .002 | .02 | |
| ATHF – Strength of highest rated trial of depression (reference: white) | | | | | | | 8.63 | 1 | .003 | .39 | .21-.73 |
| Yes (≥3) (event) | 278 | 61 | 18 | 39 | 260 | 64 | | | | | |
| No (<3) | 177 | 39 | 28 | 61 | 149 | 36 | | | | | |
| Outside psycho- | | | | | | | 4.30 | 1 | .04 | .22 | .05-.92 |

| | All Subjects (N=459) | | Black (N=47) | | White (N=412) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | Test statistic | df | p | Effect size[d] | 95% CI |
| therapy (reference: white) | | | | | | | | | | | |
| Yes (event) | 76 | 17 | 2 | 4 | 74 | 18 | | | | | |
| No | 383 | 83 | 45 | 96 | 338 | 82 | | | | | |
| RBANS | | | | | | | | | | | |
| Delayed Memory Index Score[e] (M±SD) | 96.38± 15.53 | | 89.19± 15.31 | | 97.12± 15.38 | | 7.35 | 1,440 | .007 | .02 | |
| Total index score[e] (M±SD) | 94.89± 15.88 | | 82.93± 13.97 | | 96.11± 15.57 | | 20.72 | 1,437 | <.001 | .04 | |
| DKEFS – Executive Domain[e] (M±SD) | 9.16± 2.84 | | 7.53± 3.13 | | 9.34± 2.76 | | 10.80 | 1,437 | .001 | .02 | |

a Means were compared by ANOVA and proportions were compared by logistic regression, both controlling for site.

b Exact probability.

[c] Mean and standard deviations reported in original units. Transformation used in the analyses.

[d] Eta-squared report for continuous measures and odds ratio for the logistic regression.

[e] Means(STD) age adjusted. Analyses controlled additionally for education, sex, CIR and HRS17

## Table 3

Increase in side effects severity during open label treatment phase from baseline (Max score during open label treatment phase > baseline score)

| | All Subjects (N=459) | | Black (N=47) | | White (N=412) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | Exact p | Effect size[d] | 95% CI |
| Sleepiness/ sedation (reference: white) | | | | | | | .14 | 2.05 | .79-5.35 |
| Yes (event) | 40 | 11 | 6 | 18 | 34 | 10 | | | |
| No | 341 | 89 | 28 | 82 | 333 | 90 | | | |
| Reduced duration of Sleep (reference: white) | | | | | | | .24 | .47 | .14-1.59 |
| Yes (event) | 62 | 16 | 3 | 9 | 59 | 17 | | | |
| No | 319 | 84 | 31 | 91 | 288 | 83 | | | |
| Orthostatic dizziness (reference: white) | | | | | | | .63 | .74 | .25-2.20 |
| Yes (Event) | 55 | 14 | 4 | 12 | 51 | 15 | | | |
| No | 326 | 86 | 30 | 88 | 296 | 85 | | | |