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An Exploratory Study of Responses to Low-Dose Lithium in African Americans and Hispanics

Jodi Gonzalez Arnold, PhD[1], **Stephanie Salcedo, BA**[2], **Terrence A. Ketter, MD**[3], **Joseph R. Calabrese, MD**[4], **Dustin J. Rabideau, MS**[2], **Andrew A. Nierenberg, MD**[2], **Melissa Bazan, MA**[1], **Andrew C. Leon, PhD**[2], **Edward S. Friedman, MD**[5], **Dan Iosifescu, MD**[6], **Louisa G. Sylvia, PhD**[2], **Michael Ostacher, MD**[3], **Michael Thase, MD**[7], **Noreen A. Reilly-Harrington, PhD**[2], and **Charles L. Bowden, MD**[1]

[1] University of Texas Health Science Center San Antonio

[2] Massachusetts General Hospital - Bipolar Clinic and Research Program

[3] Stanford University School of Medicine

[4] Case Western Reserve University

[5] University of Pittsburgh School of Medicine

[6] Mount Sinai School of Medicine

[7] University of Pennsylvania School of Medicine

Abstract

Objectives—Few prospective studies examine the impact of ethnicity or race on outcomes with lithium for bipolar disorder. This exploratory study examines differences in lithium response and treatment outcomes in Hispanics, African Americans, and non-Hispanic Whites with bipolar disorder in the Lithium Treatment Moderate Dose Use Study (LiTMUS).

Methods—LiTMUS was a six-site randomized controlled trial of low-dose lithium added to optimized treatment (OPT; personalized, evidence-based pharmacotherapy) versus OPT alone in outpatients with bipolar disorder. Of 283 participants, 47 African Americans, 39 Hispanics, and 175 non-Hispanic whites were examined. We predicted minority groups would have more negative medication attitudes and higher attrition rates, but better clinical outcomes.

Results—African Americans in the lithium group improved more on depression and life functioning compared to whites over the 6 month study. African Americans in the OPT only group had marginal improvement on depression symptoms. For Hispanics, satisfaction with life did not significantly improve in the OPT only group, in contrast to whites and African Americans who improved over time on all measures. Attitudes toward medications did not differ across ethnic/racial groups.

Conclusions—African Americans show some greater improvements with lithium than non-Hispanic whites, and Hispanics showed more consistent improvements in the lithium group. The impact of low-dose lithium should be studied in a larger sample as there may be particular benefit for African Americans and Hispanics. Given that the control group (regardless of ethnicity/race) had significant improvements, optimized treatment may be beneficial for any ethnic group.

One aim of personalized medicine is to incorporate research on medication efficacy and tolerability differences by ethnicity/race (1). For bipolar disorder, there is limited information on whether medication responses are influenced by ethnic background. In studies assessing lithium red blood cell to plasma ratio in Caucasians and African Americans, African Americans had a higher lithium red blood cell to plasma ratio and also reported more side effects, suggesting African Americans may need lower doses to have better lithium tolerability (2,3). Degenhardt et al. (4) studied olanzapine to treat bipolar mania and found no differences in dosing or outcomes for African Americans compared to Caucasians; however, African Americans were more likely to discontinue treatment early and had some side effects at higher rates (4). No studies have specifically investigated lithium red blood cell to plasma ratios or response to lithium in U.S. Hispanics. Studies of mania and depression suggest Hispanics may have better (5) or similar (6) responses than whites (i.e. non Hispanic) to antipsychotics. African Americans and Hispanics may have more negative attitudes toward taking psychiatric medication (7,8) which may account for early study termination (9-12).

The Lithium Treatment Moderate Dose Use Study (LiTMUS) examined the efficacy of adding low to moderate doses of lithium to personalized, guideline-based optimized pharmacological treatment. The LiTMUS main outcomes reported no differences on psychiatric or global symptom ratings when low-dose lithium was added to optimized treatment (13). In this exploratory study, we examined whether African Americans or Hispanics had differential clinical outcomes to add-on lithium as compared to whites.

We predicted African Americans and Hispanics would discontinue add-on lithium (600mg) sooner than whites and that their attitudes toward mood stabilizers would mediate this earlier discontinuation. We predicted that African Americans and Hispanics who remained in the lithium arm of the study would have greater improvement than whites on manic and depressive symptom severity, overall bipolar illness severity, life functioning, and quality of life.

Methods

Procedure

LiTMUS was a six-site randomized 6-month clinical trial conducted from April 2008 to March 2010. LiTMUS examined the efficacy of adding low to moderate doses of lithium (averaging 600 mg) to optimized treatment (OPT; personalized, guideline-based pharmacological treatment as indicated by the Texas Implementation of Medical Algorithm (14). Participants were randomized to lithium plus OPT versus OPT without lithium. Participants attended biweekly the first two months and then monthly for four months. In the lithium plus OPT group, lithium dosages were 600 mg/day for the first two months, and

individual clinical adjustments were permitted thereafter. The full study details, design, and rationale have been described elsewhere (15). This study was approved by the Institutional Review Boards at each participating institution, in accordance with the Helsinki Declaration of 1975. Subjects provided verbal and written informed consent prior to participation.

Participants

Two hundred eighty three adult participants were randomized. Participants met DSM-IV criteria for bipolar disorder, were currently symptomatic (as indicated by a Clinical Global Impression of Severity for Bipolar Disorder (CGI-BP-S) score ≥ 3, and had not taken lithium for at least 30 days. Primary exclusion criteria were (1) contraindication to lithium; (2) requiring acute inpatient hospitalization; (3) requiring current detoxification from opiates, barbiturates, or alcohol; (4) history of lithium intolerance; (5) renal impairment; (6) thyroid stimulating hormone > 20% over the upper normal limit; or (7) unwilling to comply with study requirements and procedures.

Ethnicity/Race—Participants were asked to report their ethnicity (Hispanic/Latino, not Hispanic/Latino, or unknown). Separately, they reported their race and could indicate any of the following that applied: White, African American/black, Asian/Asian American, Native American/American Indian, or Native Hawaiian/Pacific Islander. Those reporting any Hispanic/Latino background were classified as Hispanic regardless of race. Subjects were not asked country of Hispanic/Latino origin. Those noting white and not Hispanic were classified as white, and African American/black and not Hispanic were classified as African American. Due to small sample sizes, subjects reporting other or multiple ethnic/racial groups were not included in this analysis. The six sites contributed to the ethnic/race sample as follows: Massachusetts General Hospital – 14% of African Americans and 7% of Hispanics; Case Western Reserve – 28% of African Americans and no Hispanics; Stanford University School of Medicine – 4% of African Americans and 21% of Hispanics; University of Pennsylvania – 28% of African Americans and no Hispanics; University of Pittsburgh Medical Center – 19% of African Americans and 10% of Hispanics; University of Texas Health Science Center San Antonio – 9% of African Americans and 62% of Hispanics.

Measures

At the baseline visit, participants' demographics (e.g., age, gender, number of children, education, employment status, marital status, birthplace, income) were collected. To determine current and lifetime DSM-IV diagnoses, participants were interviewed using the clinician-rated Extended Mini-International Neuropsychiatric Interview (16) and the SCID DSMIV Substance Use Disorder Module.

Participants also reported their attitudes towards mood stabilizers, bipolar disorder, medication side effects and stigma using the Attitudes toward Mood Stabilizer Medication Questionnaire (AMSQ), a modified version of the of the Lithium Attitudes Questionnaire (17). Higher scores indicate more negative attitudes towards mood stabilizers.

Mood symptoms, functioning and side effects were assessed at every study visit. Blinded clinician raters assessed manic symptoms using the Young Mania Rating Scale (YMRS) (18) and depressive symptoms using the Montgomery Asberg Depression Rating Scale (MADRS) (19); higher scores on these scales indicate greater symptom severity. The Clinical Global Impression of Severity for Bipolar Disorder (CGI-BP-S) was used to assess overall bipolar symptom severity (20).

At baseline, as well as weeks 12 and 24, participants rated their overall functioning and life satisfaction using the LIFE-Range of Impaired Functioning Tool (LIFE-RIFT) (21) and quality of life was assessed using the Quality of Life, Enjoyment, and Satisfaction Questionnaire - Short Form (Q-LES-Q-SF) (22). Lower scores indicate better functioning on the LIFE-RIFT and higher scores indicate better quality of life on the QLES-Q-SF.

Statistical Methods

We provide descriptive statistics of ethnicity/race by treatment group in the entire LiTMUS cohort (N=283). For the remainder of our analysis, we considered only those subjects who self-identified as African American/Black (N=47), Hispanic (N=39), and white (non-Hispanic) (N = 175) as defined above.

First, we compared African Americans and Hispanics to whites on various baseline demographic and clinical variables using two-sample t-tests for continuous variables and chi-square tests for categorical variables. Mixed-effects regression models were used to see whether there were improved outcomes over time between African Americans and Hispanics compared to whites. We considered whether ethnic/racial group improved on each outcome within each treatment group and whether there was a differential effect of ethnicity/race between treatment groups. Due to the non-linear nature of response in LiTMUS, log(time) was used in the mixed effects models.

We produced Kaplan-Meier plots and log-rank tests to determine whether African Americans and Hispanics were more likely to have shorter time to lithium discontinuation compared to whites. We defined discontinuation as either discontinuation of lithium (prior to 6 months) *or* loss to follow-up. Patients who completed on protocol were censored at study exit. We looked within the lithium group only. A significance level of 0.05 was used to test each hypothesis and, due to the exploratory nature of this paper, no adjustment for multiple hypothesis testing was made.

Results

At baseline, African Americans reported more children, lower incomes (<25K) and less employment and education compared to whites. Hispanics were marginally more likely to be in the lowest income category and were more likely to be born outside of the U.S. compared to whites (12.8% versus 4.6%) (see Table 1). Baseline clinical characteristics and attitudes were similar across ethnic/racial groups (Table 1). However, African Americans were much less likely to report a prior suicide attempt compared to whites (34% versus 60%).

Early discontinuation of lithium was somewhat less frequent among African Americans compared to whites (21% versus 37%) ($p = 0.11$, log-rank chi-square = 2.61, df = 1). Hispanics and whites did not differ in discontinuation rates (44% Hispanics versus 37% whites). Given the lack of baseline group differences on attitudes, no analyses were conducted examining whether attitudes mediated discontinuation rates.

As for improvement within groups, African Americans and whites improved significantly over time on each of the outcome measures – in the experimental and control conditions. Hispanics generally improved as well on most measures, except in the OPT only group Hispanics did not improve significantly on satisfaction with life (QLESQ) ratings (Table 2).

Between group clinical outcomes. There were no group differences in our main hypotheses regarding Clinical Global Impression overall severity and mania ratings (data not shown). However, in the lithium group, African Americans had greater improvement on depression symptoms (MADRS) compared to whites ($p = 0.04$, $t = -2.03$, df = 1305), and, similarly, had improved quality of life (LIFE-RIFT) scores over time compared to whites ($p = 0.03$, $t = -2.16$, df = 171). Improvement on depression scores (MADRS) in the OPT only group was marginally better for African Americans compared to whites ($p = 0.05$, $t = -1.96$, df = 1305). None of the clinical outcomes differed between Hispanics and whites over the course of the study in the low dose or OPT only group.

Discussion

In this exploratory analysis of add-on low-dose lithium to treat bipolar disorder, African Americans and Hispanics did not have more negative attitudes toward mood stabilizers, in contrast to our hypothesis. Encouragingly, African Americans and Hispanics did not discontinue lithium more frequently compared to whites. Our collaborative group has addressed approaches to improve engagement of ethnic minorities in clinical research studies for over a decade (23). Whereas in the STEP-BD program the African American and Hispanic participants comprised was 8% of the sample, in this study they comprised 31%, a substantial and meaningful improvement.

Ethnic groups in both arms improved on outcomes, with the exception of life satisfaction for Hispanics not taking lithium. These results suggest that high quality of care provided in a clinical trial can confer meaningful clinical improvements. Although specific medication or psychological treatment responses may differ, when ethnic/racial minority groups have high quality care, outcomes can be similar to whites (24-26).

We found, as predicted, that African Americans prescribed lithium improved more over the study duration compared to whites, but only for depressive symptoms and overall quality of life. And that Hispanics had more robust within group improvements on outcomes when prescribed lithium. However, although there may be a small signal suggestive of better response to lithium in the two minority groups than whites, the evidence is insufficient to make conclusions regarding clinical care differences. An additional research question is whether higher doses of lithium would result in stronger responses, although most studies on this question have not reported greater benefits with increased dosage (27).

There are limitations to this study. The statistically significant findings were for exploratory hypotheses, and thus should be addressed in future studies using a correction for multiple comparisons and larger sample sizes. This study can help generate a priori hypotheses for treatment outcome studies. We did not assess the country of ethnic origin for the Hispanic subjects, which could aid in better understanding the sample.

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Appendix

Contributors

Jodi Gonzalez Arnold wrote initial drafts of the manuscript and collaborated with the statistician on the study hypotheses. Stephanie Salcedo wrote the Methods section and collaborated with the statistician in developing the Results. Terrence A. Ketter has expertise in minority issues in bipolar disorder and reviewed all versions of the manuscript. Joseph R. Calabrese reviewed all versions of the manuscript, Dustin J. Rabideau carried out all statistics for the manuscript. Andrew A. Nierenberg oversaw the LiTMUS clinical trial and reviewed all versions of the manuscript. Melissa Bazan participating in data collection and reviewed all versions of the manuscript. Andrew C. Leon helped develop the study design and statistical approach for the trial. Edward S. Friedman participated in data collection and reviewed all versions of the manuscript, Dan Iosifescu participated in data collection and reviewed all versions of the manuscript. Louisa G. Sylvia provided extensive feedback on each version of the manuscript. Michael Ostacher provided extensive feedback on the manuscript and particularly the Discussion. Michael Thase oversaw clinical data collection at a study site and reviewed the manuscript. Noreen A. Reilly-Harrington was involved in overseeing the LiTMUS study data rating and collection and reviewed versions of the manuscript. Charles L. Bowden assisted in developing exploratory hypothses, interpreting results, writing the Discussion and reviewed all versions of the manuscript.

Conflict of interest

Disclosures:

Dr. Gonzalez Arnold has no relationships to disclose.

Ms. Salcedo has no relationships to disclose.

Dr. Ketter had the following financial interests/arrangements or affiliations that could be perceived as real or apparent conflicts of interest in the past three years: Grant/Research Support from the AstraZeneca Pharmaceuticals LP, Cephalon Inc., Eli Lilly and Company, Pfizer Inc., and Sunovion Pharmaceuticals; Consultant Fees from Allergan, Inc., Avanir

Pharmaceuticals, Bristol-Myers Squibb Company, Cephalon Inc., Forest Pharmaceuticals, Janssen Pharmaceutica Products, LP, Merck & Co., Inc., Sunovion Pharmaceuticals, Teva Pharmaceuticals; Lecture Honoraria from Abbott Laboratories, Inc., AstraZeneca Pharmaceuticals LP, GlaxoSmithKline, and Otsuka Pharmaceuticals; and Publication Royalties from American Psychiatric Publishing, Inc. In addition, Dr. Ketter's spouse is an employee of and holds stock in Janssen Pharmaceuticals.

Dr. Calabrese Dr. Calabrese has received federal funding from the Department of Defense, Health Resources Services Administration and National Institute of Mental Health and research support from Abbott, AstraZeneca, Bristol-Myers Squibb, Cephalon, Cleveland Foundation, Eli Lilly, GlaxoSmithKline, Janssen, Lundbeck, NARSAD, Repligen, Stanley Medical Research Institute, Takeda, and Wyeth. Dr. Calabrese consulted to or served on advisory boards of Abbott, AstraZeneca, Bristol-Myers Squibb, Cephalon, Dainippon Sumitomo, EPI-Q, Inc., Forest, France Foundation, GlaxoSmithKline, Janssen, Johnson and Johnson, Lundbeck, Merck, Neurosearch, OrthoMcNeil, Otsuka, Pfizer, Repligen, Schering-Plough, Servier, Solvay, Supernus, Synosia, Takeda, and Wyeth. He has provided CME lectures supported by AstraZeneca, Bristol-Myers Squibb, France Foundation, GlaxoSmithKline, Janssen, Johnson and Johnson, Merck, Sanofi Aventis, Schering-Plough, Pfizer, Solvay, and Wyeth.

Mr. Rabideau has no relationships to disclose.

Dr. Nierenberg is a consultant for Abbott Laboratories, Astra Zeneca, Basilea, BrainCells Inc., Brandeis University, Bristol-Myers Squibb, Cephalon, Corcept, Eli Lilly & Co., Forest, Genaissance, GlaxoSmithKline, Innapharma, Janssen Pharmaceutica, Jazz Pharmaceuticals, Lundbeck, Merck, Novartis, PamLabs, PGx Health, Pfizer, Ridge Diagnostics, Roche, Sepracor, Schering-Plough, Shire, Somerset, Sunovion, Takeda, Targacept, and Teva. He is a stakeholder in Appliance Computing, Inc. (MindSite); Brain Cells, Inc., InfoMed (potential share of income). He receives research support from AHRQ, Bristol-Myers Squibb, Cederroth, Cyberonics, Elan, Forest Pharmaceuticals, GlaxoSmithKline, Janssen Pharmaceutica, LichtwerPharma, Eli Lilly, Mylin (formerly Dey Pharmaceuticals), NARSAD, NIMH, Pamlabs, Pfizer, Shire, Stanley Foundation, and Wyeth-Ayerst. Honoraria include MGH Psychiatry Academy in the past 3 years (Prior to 3 years ago, honoraria from Bristol-Myers Squibb, Cyberonics, Forest Pharmaceuticals, GlaxoSmithKline, Eli Lilly, Shire, Wyeth-Ayerst). Dr. Nierenberg receives other income from legal case reviews for CRICO, MBL Publishing for past services as Editor-in-chief of CNS Spectrums, Slack Inc. for services as Associate Editor of Psychiatric Annals, and Editorial Board, Mind Mood Memory, Belvior Publications. He has copyright joint ownership with MGH for Structured Clinical Interview for MADRS and Clinical Positive Affect Scale and additional honoraria from ADURS, American Society for Clinical Psychopharmacology and Zucker Hillside Hospital and Forest and Janssen, Biomedical Development, Boston Center for the Arts, University of Pisa, University of Wisconsin at Madison, University Texas Southwest at Dallas, Health New England and Harold Grinspoon Charitable Foundation and Eli Lilly and AstraZeneca, Brandeis University, International Society for Bipolar Disorder, 2nd East Asian Bipolar Forum, Mid-Atlantic Permanente Research Institute, Up-to-Date.

Ms. Bazan has no relationships to disclose.

Dr. Leon served on independent Data and Safety Monitoring Boards for AstraZeneca, Sunovion, and Pfizer and as a Consultant/Advisor to: FDA, NIMH, MedAvante and Roche. He had equity in MedAvante.

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Dr. Sylvia was a shareholder in Concordant Rater Systems and serves as a consultant for United Biosource Corporation and Clintara. She receives royalties from New Harbinger.

Dr. Ostacher has no relationships to disclose.

Dr. Thase has been an advisor/consultant: to Alkermes, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Forest Laboratories, GlaxoSmithKline, Janssen Pharmaceuticals, Lundbeck, MedAvante, Merck, Mylan, Neuronetics, Otsuka, Pamlab, PharmaNeuroboost, Pfizer, Rexahn, Roche, Shire, Sunovion, Supernus, Takeda, and Teva, as well as the US Food and Drug Administration and the National Institute of Mental Health. During the same time frame, Dr. Thase has received honoraria for talks from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Merck, and Pfizer and he has received research grants from Alkermes, AstraZeneca, Eli Lilly, Forest, GlaxoSmithKline, Otsuka, PharmaNeuroboost, and Roche, as well as the National Institute of Mental Health and the Agency for Healthcare Research and Quality.

Dr. Reilly-Harrington was a shareholder in Concordant Rater Systems and serves as a consultant for Clintara and United Biosource Corporation. She receives royalties from the American Psychological Association, New Harbinger, and Oxford University Press.

Dr. Bowden is a research collaborator with Elan and a consultant with Teva, He has no participation with speaker bureaus, nor does he or his wife hold any equity position in any biomedical or pharmaceutical corporation.

Reference List

1. Murphy E, McMahon FJ. Pharmacogenetics of antidepressants, mood stabilizers and antipsychotics in diverse human populations. Discovery Medicine. 2013; 16:113–122. [PubMed: 23998447]
2. Strickland TL, Lin K, Fu P, et al. Comparison of lithium ratio between African-American and Caucasian bipolar patients. Biological Psychiatry. 1995; 37:325–330. [PubMed: 7748984]
3. Strickland, TL.; Lawson, W.; Lin, K.; Fu, P. Interethnic variation in response to lithium therapy among African-American and Asian-American populations, in Psychopharmacology and psychobiology of ethnicity. Lin, K.; Poland, RE.; Nakasaki, G., editors. American Psychiatric Association; Washington DC: 1993. p. 107-121.
4. Degenhardt DK, Tamayo JM, Jamal HH, et al. Rlationship between African-American or Caucasian origin and outcomes in the olanzapine treatment of acute mania: a pooled analysis of three adult studies conducted in the United States of America. International Clinical Psychopharmacology. 2011; 26:141–145. [PubMed: 21164352]

5. Tamayo JM, Mazzotti G, Tohen M, et al. Outcomes for Latin American versus White patients suffering from acute mania in a randomized, double-blind trial comparing olanzapine and haloperidol. Journal of Clinical Psychopharmacology. 2007; 27:126–134. [PubMed: 17414234]

6. Tamayo JM, Sutton VK, Mattei MA, et al. Effectiveness and safety of the combination of fluoxetine and olanzapine in outpatients with bipolar depression: An open label randomized, flexible dose study in Puerto Rico. Journal of Clinical Psychopharmacology. 2009 in press.

7. Cooper LA, Gonzales JJ, Gallo JJ, et al. The acceptability of treatment for depression among African-American, Hispanic, and white primary care patients. Medical Care. 2003; 41:479–489. [PubMed: 12665712]

8. Nadeem E, Lange JM, Miranda J. Mental health care preferences among low-income and minority women. Arch Womens.Ment.Health. 2008; 11:93–102. [PubMed: 18463940]

9. Arnold JG, Miller AL, Canive JM, et al. Comparison of outcomes for African Americans, Hispanics and non-Hispanic whites in the CATIE study. Psychiatric Services. 2013; 64:570–578. [PubMed: 23494108]

10. Sanchez-Lacay JA, Lewis-Fernandez R, Goetz D, et al. Open trial of nefazodone among Hispanics with major depression: efficacy, tolerability, and adherence issues. Depression and Anxiety. 2001; 13:118–124. [PubMed: 11387731]

11. Gonzalez JM, Bowden CL, Berman N, et al. One-year treatment outcomes of African-American and Hispanic patients with bipolar I or II disorder in STEP-BD. Psychiatr Serv. 2010; 61:164–172. [PubMed: 20123822]

12. Stauffer V, Case M, Kollack-Walker S, et al. Trajectories of response to treatment with atypical antipsychotic medication in patients with schizophrenia pooled from 6 double-blind, randomized clinical trials. Schizophrenia Research. 2011; 130:11–19. [PubMed: 21489754]

13. Nierenberg AA, Friedman ES, Bowden CL, et al. Lithium treatment moderate-dose use study (LiTMUS) for bipolar disorder: a randomized comparative effectiveness trial of optimized personalized treatment with and without lithium. American Journal of Psychiatry. 2013; 170:102–110. [PubMed: 23288387]

14. Suppes T, Dennehy EB, Hirschfeld RM, et al. The Texas implementation of medication algorithms: Update to the algorithms for treatment of bipolar I disorder. Journal of Clinical Psychiatry. 2005; 66:870–886. [PubMed: 16013903]

15. Nierenberg AA, Sylvia LG, Leon AC, et al. Lithium treatment-moderate does use study (LiTMUS) for bipolar disorder: Rationale and design. Clinical Trials. 2009; 6:637–648. [PubMed: 19933719]

16. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. Journal of Clinical Psychiatry. 1998; 59(Suppl 20):22–33. [PubMed: 9881538]

17. Harvey NS. The development and descriptive use of the Lithium Attitudes Questionnaire. Journal of Affective Disorders. 1991; 22:211–219. [PubMed: 1939930]

18. Young RC, Biggs JT, Ziegler VE, et al. A rating scale for mania: reliability, validity and sensitivity. British Journal of Psychiatry. 1978; 133:429–435. [PubMed: 728692]

19. Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. British Journal of Psychiatry. 1979; 134:382–9. [PubMed: 444788]

20. Spearing MK, Post RM, Leverich GS, et al. Modification of the Clinical Global Impressions (CGI) Scale for use in bipolar illness (BP): the CGI-BP. Psychiatry Research. 1997; 73:159–171. [PubMed: 9481807]

21. Leon AC, Solomon DA, Mueller TI, et al. A brief assessment of psychosocial functioning of subjects with bipolar I disorder: the LIFE-RIFT. Longitudinal Interval Follow-up Evaluation-Range Impaired Functioning Tool. J Nerv.Ment.Dis. 2000; 188:805–812. [PubMed: 11191580]

22. Endicott J, Nee J, Harrison W, et al. Quality of Life Enjoyment and Satisfaction Questionnaire: A new measure. Psychopharmacology Bulletin. 1993; 29:321–326. [PubMed: 8290681]

23. Kogan JN, Bauer MS, Dennehy EB, et al. Increasing minority research participation through collaboration with community outpatient clinics: the STEP-BD Community Partners Experience. Clin Trials. 2009; 6:344–354. [PubMed: 19587069]

24. Miranda J, Bernal G, Lau A, et al. State of the science on psychosocial interventions for ethnic minorities. Annual Review of Clinical Psychology. 2005; 1:113–142.

25. Ngo VK, Asarnow JR, Lange J, et al. Outcomes for youths from racial-ethnic minority groups in a quality improvement intervention for depression treatment. Psychiatr Serv. 2009; 60:1357–1364. [PubMed: 19797376]

26. Santiago CD, Kaltman S, Miranda J. Poverty and mental health: How do low-income adults and children fare in psychotherapy? Journal of Clinical Psychology. 2013; 69:115–126. [PubMed: 23280880]

27. Severus WE, Kleindienst N, Seemuller F, et al. what is the optimal serum lithium level in the long-term treatment of bipolar disorder-a review? Bipolar Disord. 2008; 10:231–237. [PubMed: 18271901]

Table 1

Baseline Demographics and Clinical Characteristics.

	Selected Race/Ethnicity Group			Pairwise Comparisons	
	White NH N=175	AA/Black N=47	Hispanic N=39	AA vs NH White	Hispanic vs White NH
Continuous Variable	**Mean ± SD (N)**	**Mean ± SD (N)**	**Mean ± SD (N)**	**p-value**	**p-value**
Age	38.8 ± 12.6 (175)	40.8 ± 12.4 (47)	38.5 ± 11.7 (39)	.339	.910
# of children	1.3 ± 1.6 (175)	1.9 ± 1.7 (47)	1.4 ± 1.4 (39)	.029	.736
AMSQ	4.3 ± 3.2 (161)	4.8 ± 2.7 (43)	4.1 ± 2.8 (39)	.415	.642
CGI-BP Overall Severity	4.3 ± 0.9 (174)	4.3 ± 1.0 (47)	4.3 ± 1.0 (39)	.887	.711
CGI-BP Mania	2.8 ± 1.4 (174)	2.9 ± 1.4 (47)	3.0 ± 1.2 (39)	.797	.384
CGI-BP Depression	3.7 ± 1.4 (174)	3.9 ± 1.4 (47)	3.9 ± 1.1 (39)	.576	.453
YMRS	12.4 ± 8.3 (174)	13.7 ± 8.9 (47)	12.4 ± 7.4 (39)	.338	.953
MADRS	22.1 ± 9.8 (174)	25.1 ± 10.3 (47)	20.8 ± 11.7 (39)	.066	.479
LIFE-RIFT	13.1 ± 3.7 (174)	13.9 ± 3.7 (47)	14.0 ± 3.7 (39)	.163	.167
Q-LES-Q	46.1 ± 18.3 (172)	44.4 ± 19.4 (47)	47.5 ± 20.3 (39)	.563	.678

Categorical Variable	**% (n)**	**% (n)**	**% (n)**	**p-value**	**p-value**
Female (vs. male)	53.1% (93)	61.7% (29)	61.5% (24)	.295	.341
At least some college (vs. none)	78.3% (137)	51.1% (24)	64.1% (25)	<.001	.062
Employed/student (vs. not)	50.3% (87)	34.0% (16)	38.5% (15)	.048	.182
Income				<.001	.056
<25K	41.1% (72)	72.3% (34)	64.1% (25)		
25 to <50K	20.6% (36)	17.0% (8)	15.4% (6)		
50K to <75K	16.0% (28)	4.3% (2)	5.1% (2)		
>=75K	22.3% (39)	6.4% (3)	15.4% (6)		
Married/living as married (vs. not)	29.7% (52)	19.1% (9)	28.2% (11)	.150	.852
Born in USA (vs. not)	95.4% (167)	100.0% (47)	87.2% (34)	.135	.051
Previously hospitalized for psychiatric reasons (vs. not)	41.0% (71)	50.0% (22)	37.8% (14)	.284	.719
Prior suicide attempt (vs. not)	59.6% (28)	34.1% (59)	50.0% (19)	.002	.066

NH=non-Hispanic; AA=African American; CGI=Clinical Global Impression; QLESQ = Quality of Life, Enjoyment, and Satisfaction Questionnaire- Short Form; LIFE RIFT = LIFE-Range of Impaired Functioning Tool; MADRS=Montgomery Asberg Depression Rating Scale; YMRS = Young Mania Rating Scale; Li = lithium; OPT = optimized personalized treatment.

P-values are based on two-sample t-test for continuous variables and chi-square test for categorical variables.

Table 2

Model-based 6-month outcomes by ethnicity/race and randomized treatment group.

Variable	Estimated 6-month change from baseline [95% CI]		
Li+OPT group	**White NH**	**AA/Black**	**Hispanic**
CGI-BP Severity	−.97 [−1.29,−.66]	−1.27 [−1.85,−.69]	−1.12 [−1.83,−.40]
CGI-BP Mania	−.99 [−1.30,−.68]	−.70 [−1.28,−.12]	−.72 [−1.40,−.04]
CGI-BP Depression	−.60 [−.99,−.22]	−1.22 [−1.94,−.51]	−.94 [−1.80,−.08]
Q-LES-Q SF	9.43 [4.59,14.26]	15.43 [6.69,24.17]	11.67 [0.24,23.11]
LIFE-RIFT	−1.62 [−2.65,−.60]	−3.95 [−5.81,−2.08]	−3.72 [−5.94,−1.50]
MADRS	−4.91 [−7.63,−2.19]	−10.89 [−15.92,−5.86]	−8.11 [−14.23,−1.98]
YMRS	−5.86 [−7.85,−3.87]	−4.52 [−8.24,−.79]	−4.46 [−8.90,−.02]
OPT only group	**White NH**	**AA/Black**	**Hispanic**
CGI-BP Severity	−1.21 [−1.53,−.89]	−1.75 [−2.36,−1.13]	−1.22 [−1.82,−.63]
CGI-BP Mania	−.88 [−1.20,−.56]	−1.43 [−2.03,−.82]	−.73 [−1.30,−.16]
CGI-BP Depression	−.88 [−1.27,−.48]	−1.24 [−1.99,−.48]	−1.08 [−1.79,−.36]
Q-LES-Q SF	8.79 [3.93,13.63]	9.68 [.39,18.97]	**8.00 [−2.01,18.00]**
LIFE-RIFT	−2.12 [−3.15, −1.10]	−2.22 [−4.20,−.24]	−2.70 [−4.58,−.82]
MADRS	−7.16 [−9.94,−4.39]	−13.07 [−18.36,−7.77]	−5.35 [−10.45,−.26]
YMRS	−6.06 [−8.10,−4.02]	−8.55 [−12.44,−4.65]	−4.23 [−7.93,−.53]

NH=non-Hispanic; AA=African American; CGI=Clinical Global Impression; QLESQ = Quality of Life, Enjoyment, and Satisfaction Questionnaire- Short Form; LIFE RIFT = LIFE-Range of Impaired Functioning Tool; MADRS=Montgomery Asberg Depression Rating Scale; YMRS = Young Mania Rating Scale; Li = lithium; OPT = optimized personalized treatment.

All groups improved significantly over time with the exception of the bolded 6 month change for Hispanics on the Q- LES-Q-SF