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Enhancing Hispanic Participation in Mental Health Clinical Research: Development of a Spanish-speaking Depression Research Site

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Abstract

Background—Hispanics, particularly those with limited English proficiency, are underrepresented in psychiatric clinical research studies. We developed a bilingual and bicultural research clinic dedicated to the recruitment and treatment of Spanish-speaking subjects in the Predictors of Remission in Depression to Individual and Combined Treatments (PREdict) study, a large clinical trial of treatment-naïve subjects with major depressive disorder (MDD).

Methods—Demographic and clinical data derived from screening evaluations of the first 1,174 subjects presenting for participation were compared between the Spanish-speaking site (N=275) and the primary English-speaking site (N=899). Reasons for ineligibility (N=888) for the PREdict study were tallied for each site.

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Conflict of Interest:

Dr. Aponte-Rivera has salary support through an NIMH grant. Dr. Dunlop reports salary support through an NIMH K-23 award as well as grants from Forest Pharmaceuticals, Pfizer, Bristol-Myers Squibb and Glaxo Smith Kline. He is a paid consultant for Medavante, Pfizer, Roche and Bristol-Myers Squibb. Drs. Ramirez and Kelley have salary support through an NIMH grant. Rebecca Schneider, Beatriz Blastos and Jacqueline Larson have no financial interests to disclose. Dr. Mercado has salary support through an NIH grant. She also paid by the National Dairy Council for lectures, development of educational presentations and travel for such activities. Dr. Mayberg is the PI for two NIMH grants. She is a paid consultant for St. Jude Medical, Inc. and provides expert testimony through the Department of Justice. She is paid by various academic institutions for lectures, including speaker bureaus and grand rounds, and related travel accommodations. Dr. Mayberg has a patent with St. Jude Medical, Inc for an investigational product related to deep brain stimulation for depression. Dr. Craighead is the PI for an NIMH grant and has also received grants from the Realan Foundation and the Brock Family Foundation. Eli Lilly and Forest Pharmaceuticals have provided the medications used in Dr. Craighead's NIMH grant. He is a paid board member of the George West Mental Health Foundation and receives book royalties from John Wiley and Sons. Dr. Craighead has been a paid lecturer for the World Psychiatry Association and the Icelandic Association for Cognitive and Behavioral Therapies.

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Results—Compared to English-speakers, Spanish-speakers had a lower level of education and were more likely to be female, uninsured, and have uncontrolled medical conditions. Clinically, Spanish-speakers demonstrated greater depression severity, with higher mean symptom severity scores, and a greater number of previous suicide attempts. Among the subjects who were not randomized into the PRedICT study, Spanish-speaking subjects were more likely to have an uncontrolled medical condition or refuse participation, whereas English-speaking subjects were more likely to have bipolar disorder or a non-MDD depressive disorder.

Conclusion—Recruitment of Hispanic subjects with MDD is feasible and may enhance efforts at signal detection, given the higher severity of depression among Spanish-speaking participants presenting for clinical trials. Specific approaches for the recruitment and retention of Spanish-speaking participants are required.

Keywords

major depressive disorder; minority groups; Hispanic Americans; culture; research subject recruitment

INTRODUCTION

Patients of Hispanic ethnicity frequently have poorer outcomes than non-Hispanic white patients in the treatment of major depressive disorder (MDD).^{1,2} Hispanics constitute the largest and fastest growing ethnic minority group in the United States (US),^{3,4} with more than half of the US total population growth between 2000 and 2010 arising from the increase in the Hispanic population.⁵ Hispanics currently constitute 16% of the total U.S. population, and census projections estimate that by the year 2050 that number will rise to 30%.⁴ Identifying ways to maximize treatment response in Hispanic patients with MDD is an increasingly urgent concern. Currently Hispanics constitute only a small proportion of participants in psychiatric clinical research, potentially limiting the generalizability of research findings to the growingly diverse US population.

Twenty-five years ago, The National Institute of Health (NIH) developed guidelines for the inclusion of women and minorities in clinical research.⁸ These policies were made into law by Congress in 1993 through the NIH Revitalization Act.⁹ Despite some gains, minority participation in research continues to be inadequate and not representative of the population at large. In particular, recruiting Hispanic participants and preventing these participants from terminating early from treatment has been challenging.¹⁰ In a review of ethnic diversity in 379 National Institute of Mental Health (NIMH) funded clinical trials following the establishment of the NIH Revitalization Act, the mean proportion of Hispanic participants was only 9%.¹¹ The NIMH subsequently included in its strategic planning the need to further understand how cultural and ethnic factors may be involved in mental illness.¹²

Barriers to Hispanics' participation in clinical research across all fields of medicine include the non-specific challenges faced by low-income, low-education individuals, such as transportation difficulties, inability to pay for childcare and low literacy level.^{13,14} Other factors more specific to Hispanics include language barriers, acculturation issues, and distrust of medical providers.^{15–17} Acceptance of medication as treatment for psychiatric

disorders is lower among Hispanics than any other minority group.^{18–19} Even when patients do start antidepressant medication treatment the discontinuation rate is higher than in other ethnic or racial populations.²⁰ Fifty-five percent of the adult Hispanic population in the US has Limited English Proficiency (LEP).²¹ Recruitment of monolingual Hispanics is greatly affected by the lack of availability of assessment instruments in Spanish as well as the variations in regional dialects.²¹ Moreover, Hispanic health care providers are underrepresented at all levels of health care, leading to a shortage of bilingual and bicultural professionals available to conduct clinical studies.^{22,23} Although the use of Hispanic recruitment specialists,²⁴ bilingual and culturally sensitive staff,²¹ and community outreach efforts^{25,26} have produced some mild success, more substantial approaches are needed to overcome this challenge.²⁷

For mental health research, increasing Hispanic engagement faces even greater challenges, particularly for LEP patients. In an effort specifically to enhance Hispanic recruitment, the Sequenced Treatment Alternatives To Relieve Depression (STAR*D) effectiveness trial included sites with preexisting bilingual (English/Spanish) staff.²⁸ Although this trial enrolled 327 participants who self-identified as Hispanic, only 25% of these participants requested questionnaires and interviews be conducted in Spanish, suggesting a relatively high level of acculturation in the STAR*D Hispanic sample, which limits the generalizability of the study's findings to LEP Hispanics.²⁹

Strong cultural values among Hispanics with low levels of acculturation may also adversely impact Hispanic participation in mental health research. “*Familismo*” (familism) is an important Hispanic value describing the central role of the family, and the importance of family well-being above that of the individual.³⁰ Participants seeking treatment are not always supported by their family members who might not be convinced that MDD is a real disorder with effective treatments.³¹ The concept of “*fatalismo*” (fatalism) is also prominent in Hispanic culture. This belief assumes that individuals cannot control their destiny and thus have minimal control over their environment.³² Therefore, seeking mental health services can be seen as a futile action.

We describe the development of a dedicated Hispanic research site called “Clínica Latina para el Tratamiento de la Depresión” (CLTD, ‘Latin Clinic for the Treatment of Depression’) and how the emerging challenges were managed. This bilingual and bicultural site was created to enhance recruitment of Hispanic subjects for participation in a federally-funded study being conducted at Emory University School of Medicine, the ‘Predictors of Remission in Depression to Individual and Combined Treatments’ (PREdict).³³ We aimed to identify the demographic and clinical factors that differed between the Spanish-speaking Hispanics and the English-speaking potential participants screened from the start of the study in January 2007 through June 30, 2012. Due to their more limited access to medical care, we hypothesized that Hispanics would show higher rates of uncontrolled medical illnesses, greater severity of illness, and more substance abuse or dependence, than the English-speaking participants. Because there is a general paucity of published data about participants excluded from clinical trials during the screening phase, a secondary aim of this analysis was to identify clinical and demographic differences between those screened subjects who did and did not go on to be randomized into the PREdict trial.

MATERIALS AND METHODS

Study Overview

A comprehensive report of the design of the PReDICT study has been reported elsewhere,³³ and is described briefly here. The aims of PReDICT are to identify biological and psychological factors that predict differential response to pharmacotherapy or psychotherapy among treatment-naïve patients with MDD. We defined treatment-naïve as never having received either an approved antidepressant at the minimum effective dose for at least 4 weeks, or 4 sessions of an evidence-based psychotherapy for MDD. The primary predictors for the study include brain functional magnetic resonance imaging (fMRI), genetics, dexamethasone-corticotropin releasing hormone (Dex-CRH) test reactivity, genetics, clinical features, and personality disorder assessments. Participants completing these measures are randomly assigned in a 1:1:1 manner to 12 weeks of treatment with escitalopram 10–20 mg/day, duloxetine 30–60 mg/day, or 16 sessions of Cognitive Behavioral Therapy (CBT). Repeat fMRI and phlebotomy are performed after 2–4 weeks of treatment. Upon completion of the 12 weeks of treatment, subjects undergo another fMRI, phlebotomy, and Dex-CRH test. Subjects remitting from depression at the end of 12 weeks are eligible to enroll in a 21-month follow up period in which they are evaluated every 3 months for depressive recurrence. Subjects who do not remit by the end of the 12-week monotherapy phase are offered 12 additional weeks of combination treatment, in which CBT is added to medication non-remitters, and escitalopram is added to CBT non-remitters. Subjects demonstrating response at the end of the 12-week combination treatment are then offered 18 months of follow-up in which they are evaluated every 3 months for depressive relapse or recurrence. All study procedures were done in compliance with the Declaration of Helsinki and the NIMH. The Emory Institutional Review Board and the Grady Hospital Research Oversight Committee approved the study design, procedures, and recruitment strategies.

The study started recruitment in January 2007 at the English-language site on the Emory University campus. In July 2009, the CLTD was established at the International Medical Center (IMC) at Grady Hospital in downtown Atlanta and serves as a purely Spanish-speaking site.

Site selection

Options considered as potential sites for the CLTD included a free-standing clinic in rented office space in a neighborhood of high Hispanic concentration, expansion of the English-language site at Emory, and integration with an existing clinic focused on the treatment of LEP participants. Because Hispanics with mental health concerns are more likely to seek help from a general medical care provider or a primary care setting rather than a psychologist or psychiatrist,¹⁵ we selected the IMC as the CLTD site. This center offers health services, education and social services in a culturally and linguistically appropriate manner to Atlanta's growing immigrant population. Although the IMC had no previous experience with clinical research trials, the clinic and hospital are well known and trusted within the Hispanic community in Georgia and it is easily accessible by car and public transportation. Selecting this location aimed to partially offset potential distrust of Hispanics concerning participating in a depression research study.

Staff

Previous studies have reported that a fully bilingual staff is optimal for research success,²¹ so we actively sought to hire bilingual professionals who were also bicultural and had a thorough understanding of the cultural variables that influence participation in depression research. Any cultural challenges encountered were addressed during regular staff discussions. Some of the staff members also function as patient navigators, a concept previously developed to help decrease barriers to care for underserved populations.³⁴ Navigators accompany participants to the fMRI and Dex-CRH testing locations. They provide basic interpretation services and help participants decipher public transportation routes to and from CLTD. The study personnel represent six different Spanish-speaking countries. The staff works at both CLTD and the Emory English-speaking site, thereby increasing reliability across the two sites, enhancing internal validity of the project, and helping to control costs.

Study Measures

The screening assessments included a self-report intake packet, semi-structured clinical interviews, and a clinician administered 17- item Hamilton Depression Rating Scale (HAMD),^{35–37} described below. Validated Spanish translations of the measures were used for Spanish-speaking participants.

Recruitment

Initial recruitment efforts consisted of awareness-building efforts describing MDD and the study via in-person contact with trusted community agencies within the Hispanic population of Georgia; these included consulates, Spanish speaking primary care clinics, churches, Latino associations, and the primary care physicians at the IMC. Subsequently, multiple Spanish television, radio and newspaper interviews and advertisements were used, along with health fair booths and placement of flyers in areas known to have a substantial Hispanic population.

Potential study participants were initially evaluated via telephone screening. Telephone screening included: inquiring about age, level and duration of depressive symptoms, history of previous treatment for depression, alcohol and illicit substance use, and medical conditions including pregnancy. Appropriate candidates were then scheduled for a 3–4 hour in-office screening evaluation. Persons ineligible after phone screening were referred to community mental health services.

Screening Procedures

At both the English- and Spanish-language sites, subjects attending the in-office evaluation first were explained the initial screening procedures and then signed a general consent form providing permission to conduct a psychiatric interview. They also completed an intake packet for demographic data and self-reported psychiatric and medical history. The initial assessment involved a 60–90 minute intake interview, which included administration of the HAMD. Subjects then met with a study psychiatrist who performed an additional 30–60 minute diagnostic evaluation, including review of medical history and previous psychiatric treatment. At this point, the psychiatrist determined whether the subject appeared eligible for

the PReDICT study, which included having a screening HAMD score ≥ 18 . For these subjects, the psychiatrist provided a 5–10 minute verbal description of the study, emphasizing the study's rationale, procedures and the process of random assignment to treatment. Subjects were informed that although they may have a preference for a certain type of treatment, to be included in the study they had to be willing to start treatment with the intervention (medication or CBT) to which they were randomized. After the psychiatrist answered any initial questions, the subject was asked if they remained interested in the study. If so, they were given the PReDICT study written informed consent form (ICF). After reading the consent, subjects again met with the psychiatrist to answer questions, and then decided whether to sign the consent form.

Classification of screened subjects

Subjects who did not qualify to participate in the PReDICT study were classified as “screen negative,” and they were referred to community care. “Screen positive” subjects were those who were offered participation and who signed the ICF as well as those who qualified but declined to sign the ICF after reading it or hearing the verbal description of the study. These screen positive subjects went on to complete the remaining screening procedures including the Structured Clinical Interview for DSM-IV (SCID),³⁸ the Montgomery-Asberg Depression Rating Scale,³⁹ and the Hamilton Anxiety Rating Scale.⁴⁰ A physical exam, electrocardiogram, and screening laboratory tests were also performed. Early life stress was assessed via the Childhood Trauma Questionnaire (CTQ)⁴¹ and the Early Home Environment Interview.⁴² Subjects who continued to meet all eligibility criteria were scheduled to complete the biological and psychological predictors assessments. After completion of these measures, subjects who continued to be in a major depressive episode and had a HAMD score ≥ 15 at the baseline visit were randomized and treatment initiated.

To capture the full panoply of reasons for which subjects failed to proceed from the screening visit to randomization, we assessed the reasons for ineligibility for all the screen negative subjects and for the screen positive subjects who did not go on to be randomized (i.e., had abnormal physical exam finding, electrocardiogram, or laboratory test, had a baseline HAMD score <15 , or did not return after the screening visit). We categorized reasons for study ineligibility through a hierarchical ranking, as follows: 1) meets criteria for another primary psychiatric disorder (specified as a non-MDD depressive disorder, bipolar disorder, psychotic disorder, a primary anxiety disorder, primary substance abuse/dependence, or other); 2) meets MDD criteria but previously treated for MDD; 3) meets MDD criteria for primary MDD but has comorbid obsessive compulsive disorder, eating disorder, or substance abuse or positive urine drug screen; 4) imminent and high current suicide risk; 5) meets MDD criteria but HAMD <18 at screening; 6) meets MDD criteria but has severe personality disorder as determined by the psychiatrist's interview; 7) has a medical illness prohibiting participation; 8) refused participation; 9) other (e.g., legal issues, moved, randomization HAMD <15); 10) lost to follow up. Although subjects could have met more than one ineligibility criterion, they were assigned only the highest-ranking reason. This approach was used because data to evaluate all reasons was not gathered on all subjects. For example, subjects determined to have bipolar disorder would not subsequently have been carefully evaluated for medical issues.

Data Analysis

Comparisons of clinic and screen result differences were performed using univariate t-tests or chi-square test of proportions as appropriate. Clinic by screen result interactions were tested using analysis of variance on continuous variables and logistic regression on the binary variables; tests of interactions take into account the effects for main effects of clinic or screen result. We set $p < .01$ to identify significant differences; no adjustments were made for multiple comparisons because the tests are for descriptive purposes only and not hypothesis testing.⁴³

RESULTS

Screen Positive vs Screen Negative subjects

Between the two sites, 1,174 subjects had completed in-office screening evaluations by June 30, 2012. The demographic and clinical characteristics of the sample, divided into screen positive and screen negative participants, are presented in Table 1. Screen positive subjects were more likely to be married, have a previous diagnosis of substance abuse and have higher current levels of depression, as measured by HAMD scores. Screen negative subjects were characterized by a more severe psychiatric history, more suicide attempts, more previous treatments, and more alcohol consumption in the month prior to screening. There were no significant differences for age, race, gender, education, medical insurance status, or self-injurious behavior.

Spanish-speaking versus English-speaking subjects

Table 2 presents demographic and clinical categories of the entire sample divided by study site. Compared to the English-speaking subjects, Spanish-speaking subjects had lower levels of education and medical insurance, were less likely to be male or report being of white race, and were more likely to be married and have more children. These subjects had higher current depression scores, and also reported a higher rate of being previously diagnosed with MDD by a physician, more previous suicide attempts, and were less likely have received some form of psychotherapy. Subjects at the English-speaking site were more likely to report a positive family psychiatric history, more likely to be using alcohol or other drugs and less likely to have a previous substance abuse diagnosis. Subjects at both sites reported a similar history of self-injury, current antidepressant medication use, and history of previous diagnosis of bipolar disorder and anxiety disorder. To better characterize the Hispanic participants additional demographic factors were collected for the subjects at CLTD. These patients represented fourteen Spanish speaking countries and Brazil, with only four patients born in the US. Mexico was the country of origin for 64% of the subjects, El Salvador for 6% and the rest of the countries each represented less than 5% of the sample. The average length of time living in the US was 11.7 years. Spanish was the preferred language for reading (86.5%), speaking (89.3%), and writing (90.7%).

Table 3 presents the results of the site by positive/negative screen interactions. These results indicated that the finding that screen negative subjects were less likely to be married derived primarily from the English-speaking site, as these characteristics differed little among the screen positive and screen negative Spanish-speaking subjects. Spanish-speaking subjects

who reported a previous diagnosis of depression were significantly more likely to screen positive than those who did not.

Reasons for ineligibility

Of the 1,174 patients screened, 286 (24%) were randomized into PReDICT and 888 (76%) were not. The percentage of screened patients who went on to be randomized was similar between the sites [Emory: N=205 (22.8%); CLTD: N=81 (29.4%)]. Table 4 presents the reasons for failure to qualify for PReDICT randomization by screen outcome. Overall, the most common reason for ineligibility among screen negative patients was a primary psychiatric disorder other than MDD; most often an anxiety disorder, non-MDD depressive disorder, bipolar disorder or substance abuse/dependence. An additional 10.2% of patients who met criteria for MDD had a HAMD score at screen <18. For the patients who screened positive, there were three primary causes for ineligibility: loss to follow up prior to randomization, excluded medical condition, and “other”, a category that included randomization HAMD<15, plan to move, and legal problems.

Table 4 also shows that reasons for ineligibility differed by site. Among the screen negative subjects, bipolar disorder and non-MDD depressive disorder were more common reasons for exclusion among English-speaking rather than among the Spanish-speaking subjects. In contrast, the Spanish-speaking subjects were more likely to be ineligible due to excluded or uncontrolled medical conditions and refusal to participate. The reasons why patients refused to participate were not systematically collected, but in general included time commitment, difficulty getting time off work and concern about research procedures. Reasons for ineligibility did not meaningfully differ between the sites for screen positive subjects, with loss to follow-up and excluded or uncontrolled medical condition being the most common.

DISCUSSION

This analysis of nearly 1,200 subjects completing in-office screenings for a clinical trial demonstrates the feasibility of recruiting Hispanics into mental health clinical research programs. We found that Spanish-speaking subjects differed most significantly from English-speaking subjects by their greater proportion of women, lower level of education, lower rates of medical insurance. In line with our expectations, Spanish-speaking subjects had higher level of uncontrolled medical conditions and a more severe depressive illness, as evinced by their higher HAMD scores and greater number of previous suicide attempts. Contrary to our hypothesis, substance abuse rates were similar between the two populations.

On the secondary aim of comparing trial eligible versus ineligible subjects, the most notable finding was the eligible subjects were more likely to be female, married, have greater severity of illness, and report a prior history of substance abuse. The difference in severity (HAMD score) by eligibility status was driven primarily by the English-speaking subjects, as the difference in severity levels was considerably smaller among the Spanish-speaking subjects. This result suggests that, on average, Spanish-speakers with depression delay seeking help until their symptoms reach a higher level of severity than English-speakers with depression.

During the process of establishing the CLTD, careful consideration was given to known barriers limiting Hispanic participation in clinical trials. We believe that our location as well as our bilingual and bicultural staff were crucial to the success of the CLTD. The initial contacts with community agencies, consulates, community affairs shows, and primary care clinics provided a steady influx of study participants to supplement our purchased advertising efforts. Although initially more time consuming, this method proved to be very productive. The use of patient navigators greatly facilitated the timely arrival of patients to study related procedures.

Nevertheless, several challenges occurred in the development of CLTD; these challenges and how they were managed are reported to provide guidance for others who may consider establishing Hispanic-focused research clinics. Spanish-speakers who called expressing interest in the study frequently wanted to know if they were “depressed” since it was not clear to them what was meant by the term. To address this, we frequently used detailed descriptions of the symptoms of depression and used terms such as sadness or “nervios” (nerves) rather than the word “depressed”. Family members commonly called requesting an appointment for a relative, and they expressed irritation and confusion when told that the potential participant needed to be the person who called. We assured them of the availability of Spanish speaking staff as well as explained the need for the patient to be directly interviewed to ensure that they met inclusion criteria and were voluntarily participating. Consistent with the Hispanic cultural value of ‘*familismo*’, family members frequently accompanied patients to the appointments. They also at times participated, at the request of the subjects, in the discussion of the study and informed consent process. Openness to include family members in the decision process commonly increased participant’s comfort level.

Screening visits were typically longer than at the English-speaking site, mostly due to subjects spending a significant amount of time reading the consent forms and their difficulties understanding self-report scales used to assess symptom severity. Ample time was set for appointments and screening visits were sometimes conducted over two days. Instructions for the self-report scales were routinely reviewed with the patients to ensure their understanding. Some participants presented with a highly traditional view of treatment, wishing to defer to the physician and please the study team, thereby requiring an even more thorough informed consent process to ensure their understanding of the study and the voluntary nature of their participation. Any concerns about the research procedures were discussed and visual aids such as pictures of MRI machines were used.

At screening, many subjects reported using medications brought from their countries of origin; these medications are not always available in the US or approved by the Food and Drug Administration. This required careful evaluation of the medications being consumed by the subjects to make certain that they were not contributing to the presenting symptoms or were a potential source of drug interactions with the study medications. Study psychiatrists conducted detailed medication histories and inquired about natural supplements and herbs. Spanish-speaking participants rarely had a primary care provider, as evident in the higher rate of screen failure due to medical conditions amongst the CLTD participants.

Our location within a primary care clinic with Spanish speaking staff allowed for an easy referral process when uncontrolled medical conditions were identified.

Maintaining contact with participants was another challenge. Most subjects used cellular phone numbers which frequently changed or were disconnected. For this reason, multiple emergency contact numbers were obtained and the potential subjects' contact information was reviewed on every appointment. Other clinic challenges were not participant related, for example, identifying and retaining qualified bilingual and bicultural research staff.

There are limitations in this study. For example, previous psychiatric history was derived from self-report. During the initial phone interview, we explained that participants needed to be willing to be randomized to either medication or therapy, perhaps thereby selecting for people willing to take medication. Other factors related to Hispanics' mental health and possibly to study participation, such as acculturation and acculturative stress, were not directly measured in this study.^{44–46} Nevertheless, the CLTD subjects were mostly immigrants whose preferred language was Spanish and had a limited number of years living in the US, suggesting that our CLTD subjects had lower acculturation levels. The “immigrant paradox”⁴⁶ could explain why there is a significantly lower percentage of a positive family psychiatric history among the subjects at CLTD. This could also be related to the decreased awareness about mental health found among Hispanics as well as limited options for diagnosis and treatment.

CONCLUSION

The development of clinics specifically dedicated to the recruitment of minority, in particular Hispanic, populations is a feasible way to target the problem of their underrepresentation in clinical research studies and the broader issue of health disparities in the US. Our sample, primarily including Spanish speaking Hispanic immigrants with apparent lower levels of acculturation, provides insights into this understudied group. Spanish speaking participants in this study had a higher illness severity and higher rates of self-reported suicide attempts. Uncontrolled medical conditions were more prevalent in the Spanish speaking clinic. An understanding of cultural variables, the recruitment of bilingual and bicultural staff, and the development of partnerships with community agencies are essential to the success of these endeavors. Flexibility with clinic hours less time intensive study designs could help decrease patient's reluctance to participate. Strategies to decrease language, transportation and educational barriers that hinder Hispanics' participation in clinical trials are also necessary. These factors need to be taken into account when designing clinical trials and developing budgets such that appropriate clinical research clinics can be developed.

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References

1. Van Voorhees BW, Walters AE, Prochaska M, Quinn MT. Reducing health disparities in depressive disorders outcomes between non-Hispanic whites and ethnic minorities: A call for pragmatic strategies over the life course. *Med Care Res Rev.* 2007; 64:157S–194S. [PubMed: 17766647]
2. Roy-Byrne PP, Perera P, Pitts CD, Christi JA. Paroxetine response and tolerability among ethnic minority patients with mood or anxiety disorders: A pooled analysis. *J Clin Psychiatry.* 2005; 66:1228–33. [PubMed: 16259535]
3. U.S. Census Bureau. Minority population tops 100 million. May 17. 2007 <http://www.census.gov/newsroom/releases/archives/population/cb07-70.html>
4. U.S. Census Bureau, Population Division. Table 5: Percent distribution of the projected population by net international migration series, race, and Hispanic origin for the United States: 2010 to 2050. Aug 14. 2008 Available at <https://www.census.gov/population/projections/data/national/2008/summarytables.html>
5. U.S. Census Bureau. The Hispanic population 2010. 2010 census briefs. May. 2011 Available at <http://www.census.gov/prod/cen2010/briefs/c2010br-04.pdf>
6. Evelyn B, Toigo T, Banks D, et al. Participation of racial/ethnic groups in clinical trials and race-related labeling: A review of new molecular entities approved 1995–1999. *J Natl Med Assoc.* 2001; 93:18S–24S. [PubMed: 11798060]
7. Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials race-, sex- and age-based disparities. *JAMA.* 2004; 291:2720–2726. [PubMed: 15187053]
8. National Institutes of Health. NIH policy and guidelines on the inclusion of women and minorities as subjects in clinical research – Amended October, 2001. Oct 1. 2001 Available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm
9. National Institute of Health. Revitalization Act of 1993. Public Law 103-43. Jun 10. 1993 Available at <http://history.nih.gov/research/downloads/PL103-43.pdf>
10. Miranda J, Nakamura R, Bernal G. Including ethnic minorities in mental health intervention research: A practical approach to a long-standing problem. *Cult Med Psychiatry.* 2003; 27:467–486. [PubMed: 14727681]
11. Mak WWS, Law RW, Alvidrez J, Pérez-Stable EJ. Gender and ethnic diversity in NIMH-funded clinical trials: Review of a decade of published research. *Adm Policy in Ment Health.* 2007; 34:497–503.
12. National Institute of Mental Health. The National Institute of Mental Health Strategic Plan. Aug. 2008 Available at <http://www.nimh.nih.gov/about/strategic-planning-reports/index.shtml>
13. Alvarez R, Vasquez E, Mayorga C, et al. Increasing minority research participation through community organization outreach. *West J Nurs Res.* 2006; 28:541–563. [PubMed: 16829637]
14. Alegría M, Chatterji P, Wells K, et al. Disparity in depression treatment among racial and ethnic minority populations in the United States. *Psychiatr Serv.* 2008; 59:1264–1272. [PubMed: 18971402]
15. Delgado PL, Alegría M, Cañive JM, et al. Depression and access to treatment among U.S. Hispanics. *FOCUS.* 2006; IV:38–47.
16. Kouyoumdjian H, Zamboanga BL, Hansen DJ. Barriers to community mental health services for Latinos: Treatment considerations. *Clin Psychol Sci Pr.* 2003; 10:394–422.
17. Santiago-Rivera AL, Kanter JW, Busch AM, et al. An initial examination of treatment issues at a community clinic. *J Immigr Minor Health.* 2011; 13:772–779. [PubMed: 20734139]
18. Cooper LA, Gonzales JJ, Gallo JJ, et al. The acceptability of treatment for depression among African-American, Hispanic and White primary care patients. *Med Care.* 2003; 41:479–489. [PubMed: 12665712]
19. Givens JL, Houston TK, Van Voorhees BW, et al. Ethnicity and preferences for depression treatment. *Gen Hosp Psychiatry.* 2007; 29:182–191. [PubMed: 17484934]
20. Hodgkin D, Volpe-Vartanian J, Alegría M. Discontinuation of antidepressant medication among Latinos in the US. *J Behav Health Serv Res.* 2007; 34:329–342. [PubMed: 17570068]

21. Suarez-Morales L, Matthews J, Martino S, et al. Issues in designing and implementing a Spanish-language multi-site clinical trial. *Am J Addict.* 2007; 16:206–215. [PubMed: 17612825]
22. Brotherton SE, Etzel SI. Graduate medical education, 2008–2009. *JAMA.* 2009; 302:1357–1372. [PubMed: 19773575]
23. Ruiz P. Hispanic access to health/mental health services. *Psychiatr Q.* 2002; 73:85–91. [PubMed: 12025724]
24. El-Khorazaty MN, Johnson AA, Kiely M, et al. Recruitment and retention of low-income minority women in a behavioral intervention to reduce smoking, depression and intimate partner violence during pregnancy. *BMC Public Health.* 2007; 7:1–18. [PubMed: 17199891]
25. Shatell MM, Hamilton D, Starr SS, et al. A community-based participatory research project. *Issues Ment Health Nurs.* 2008; 29:351–370. [PubMed: 18382914]
26. Eakin EG, Bull SS, Riley K, et al. Recruitment and retention of Latinos in a primary care-based physical activity and diet trial: The resources for healthy study. *Health Educ Res.* 2007; 22:361–371. [PubMed: 16963726]
27. UyBico SJ, Pavel S, Gross CP. Recruiting vulnerable populations into research: A systematic review of recruitment interventions. *J Gen Intern Med.* 2007; 22:852–863. [PubMed: 17375358]
28. Lesser I, Zisook S, Flores Deborah, et al. Depression outcomes of Spanish- and English-speaking Hispanic outpatients in STAR*D. *Psychiatr Serv.* 2008; 59:1273–1284. [PubMed: 18971403]
29. Lesser IR, Castro DB, Gaynes BN, et al. Ethnicity/Race and outcome in the treatment of depression: Results from STAR*D. *Med Care.* 2007; 45:1043–1051. [PubMed: 18049344]
30. Ellington L, Wahab S, Martin SS, et al. Factors that influence Spanish- and English-speaking participants' decision to enroll in cancer randomized clinical trials. *Psychooncology.* 2006; 15:273–284. [PubMed: 15973647]
31. Alvidrez J. Ethnic variations in mental health attitudes and service use among low- income African-American, Latina and European-American young women. *Community Ment Health J.* 1999; 35:515–530. [PubMed: 10863988]
32. Neff JA, Hoppe SK. Race/ethnicity, acculturation, and psychological distress: Fatalism and religiosity as cultural resources. *J Community Psychol.* 1993; 21:3–20.
33. Dunlop BW, Binder EB, Cubells JF, et al. Predictors of remission in depression to individual and combined treatments (PReDICT): Study rationale and design. *Trials.* Jul.2012 13(1):106. [PubMed: 22776534]
34. Dohan D, Schrag D. Using patient navigators to improve care of underserved patients: Current practices and approaches. *Cancer.* 2005; 104:848–855. [PubMed: 16010658]
35. Hamilton M. Development of a rating scale for primary depressive illness. *Br J Soc Clin Psychol.* 1967; 6:278–96. [PubMed: 6080235]
36. Williams JB. Standardizing the Hamilton Depression Rating Scale: past, present future. *Eur Arch Psychiatry Clin Neurosci.* 2001; 251(Suppl 2):II/6–II/12.
37. Williams JB. A structured interview guide for the Hamilton Depression Rating Scale. *Arch Gen Psychiatry.* 1989; 45:742–747. [PubMed: 3395203]
38. First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JB. Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-I/P, Version 2.0). Biometrics Research Department, New York State Psychiatric Institute; New York: 1995.
39. Montgomery SA, Åsberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry.* 1979; 134:382–389. [PubMed: 444788]
40. Hamilton M. The assessment of anxiety states by rating. *Br J Med Psychol.* 1959; 32:50–55. [PubMed: 13638508]
41. Bernstein DP, Ahluvalia T, Pogge D, Handelsman L. Validity of the Childhood Trauma Questionnaire in an adolescent psychiatric population. *J Am Acad Child Adolesc Psychiatry.* 1997; 36:340–348. [PubMed: 9055514]
42. Lizardi H, Klein DN, Ouimette PC, et al. Reports of the childhood home environment in early-onset dysthymia and episodic major depression. *J Abnorm Psychol.* 1995; 104:132–139. [PubMed: 7897035]

43. Streiner DL, Norman GR. Correction for multiple testing: is there a resolution? *Chest*. 2011; 140:16–18. [PubMed: 21729890]
44. Hovey JD, King CA. Acculturative stress, depression, and suicidal ideation among immigrant and second-generation Latino adolescents. *J Am Acad Child Adolesc Psychiatry*. 1996; 5:1183–1192. [PubMed: 8824062]
45. Escobar JI, Nervi CH, Gara MA. Immigration and mental health: Mexican Americans in the United States. *Harv Rev Psychiatry*. 2000; 8:64–72. [PubMed: 10902095]
46. Torres L. Predicting levels of Latino depression: Acculturation, acculturative stress and coping. *Cultur Divers Ethnic Minor Psychol*. 2010; 16:253–263.

Table 1

Screening visit clinical and demographic data by PREdict eligibility.

Variable	Screen negative (n=597)	Screen positive (n=513)	All Subjects (n=1110)	Test Statistic	DF	Screen-pos p-value
Age, yrs (SD)	37.7 (11.5)	39.4 (11.3)	38.5 (11.4)	7.2 ^a	1/1060 ^c	0.012
Gender (% Male)	46.8	39.4	43.3	6.2 ^b	1	0.013
Race (% Non-white)	63.3	60.9	62.2	0.7 ^b	1	0.401
Married (%)	33.5	46.9	39.7	20.4 ^b	1	<0.0005
No. children (SD)	1.3 (1.5)	1.6 (1.5)	1.4 (1.5)	2.0 ^a	1/1083 ^c	0.001
Education (% Less than 12 yrs)	10.9	13.9	12.3	2.3 ^b	1	0.132
Medical Insurance (%)	39.8	38.4	39.1	0.22 ^b	1	0.642
HAMD total (SD)	17.9 (6.4)	21.6 (3.3)	19.8 (5.4)	64.6 ^a	1/1011 ^c	<0.0005
History of suicide attempt (%)	14.9	8.9	12.1	9.3 ^b	1	0.002
History of self-injury (%)	7.6	4.6	6.2	3.9 ^b	1	0.049
Current antidepressant medication (%)	2.8	0.8	1.8	5.9 ^b	1	0.015
Any previous psychotherapy (%)	33.8	25.6	30.0	8.6 ^b	1	0.003
Previous depression diagnosis (%)	15.4	19.5	17.3	3.2 ^b	1	0.074
Previous bipolar disorder diagnosis (%)	1.4	0.6	1.0	1.7 ^b	1	0.194
Previous anxiety disorder diagnosis (%)	10.7	8.1	9.5	2.1 ^b	1	0.148
Previous substance abuse diagnosis (%)	4.1	16.7	6.4	11.5 ^b	1	0.001
Past month alcohol consumption (%)	60.0	51.4	55.9	8.05 ^b	1	0.005
Past month substance use (%)	12.8	10.5	11.7	1.42 ^b	1	0.234
Family history of psychiatric illness (%)	73.8	69.3	71.6	2.3 ^b	1	0.129

DF: Degrees of freedom

SD: Standard Deviation

HAMD: Hamilton Depression Rating Scale, 17-item

^aF Statistic

^bChi-Square Statistic

Numerator DF/Denominator DFs

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Table 2

Screening visit clinical and demographic data by clinic.

Variable	Emory (n=834)	CLTD (n=276)	Test Statistic	DF	Clinic p-value
Age, yrs (SD)	38.7 (11.9)	37.6 (9.6)	3.3 ^a	1/1060 ^c	0.069
Gender (% male)	49.0	26.3	44.7 ^b	1	< 0.0005
Race (% non-white)	50.0	99.3	215.0 ^b	1	< 0.0005
Married (%)	35.1	52.9	27.5 ^b	1	< 0.0005
No. children (SD)	1.1 (1.4)	2.2 (1.5)	109.5 ^a	1/1083 ^c	< 0.0005
Education (% <12 years)	3.1	40.3	259.5 ^b	1	< 0.0005
Medical Insurance (%)	49.8	7.8	147.7 ^b	1	< 0.0005
HAMD total score (SD)	19.2 (5.4)	21.5 (4.8)	28.9 ^a	1/1011 ^c	< 0.0005
History of suicide attempt (%)	9.9	19.0	15.0 ^b	1	< 0.0005
History of self-injury (%)	5.9	7.0	0.42 ^b	1	0.519
Current antidepressant medication (%)	1.7	2.3	0.36 ^b	1	0.549
Any previous psychotherapy (%)	34.6	15.9	33.8 ^b	1	< 0.0005
Previous depression diagnosis (%)	13.1	29.7	39.2 ^b	1	< 0.0005
Previous bipolar disorder diagnosis (%)	1.2	0.4	1.4 ^b	1	0.231
Previous anxiety disorder diagnosis (%)	8.3	13.3	4.9 ^b	1	0.027
Previous substance abuse diagnosis (%)	4.1	32.0	29.7 ^b	1	< 0.0005
Past month alcohol consumption (%)	67.4	21.5	172.9 ^b	1	< 0.0005
Past month substance use (%)	15.4	0.4	45.1 ^b	1	< 0.0005
Family history of psychiatric illness (%)	77.6	55.6	42.6 ^b	1	< 0.0005

DF: Degrees of freedom

SD: Standard Deviation

HAMD: Hamilton Depression Rating Scale, 17-item

^aF Statistic

^bChi-Square Statistic

χ^2 Numerator DF/Denominator DF

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Table 3

Interactions of clinic by screening outcome eligibility.

Variable	Emory (n=834)		CLTD (n=276)		Test Statistic	DF	Clinic *screen-pos p-value
	Screen negative (n=486)	Screen positive (n=348)	Screen negative (n=111)	Screen positive (n=165)			
Age, yrs (SD)	38.0 (11.7)	39.7 (12.0)	35.8 (9.8)	38.7 (9.3)	0.51 ^a	1/1060 ^c	0.476
Gender (% male)	51.3	46.0	27	25.5	0.18 ^b	1	0.669
Race (% non-white)	54.9	42.8	100	98.8	0.0 ^b	1	0.997
Married (%)	28.7	44.3	54.5	52.1	7.3 ^b	1	0.007
No. children (SD)	1.1 (1.4)	1.2 (1.4)	2.2 (1.5)	2.3 (1.5)	0.14 ^a	1/1083 ^c	0.712
Education (% <12 years)	4.2	1.7	41.1	39.6	2.5 ^b	1	0.115
Medical Insurance (%)	46.7	54.2	9.4	6.8	1.9 ^b	1	0.171
HAMD Total score (SD)	17.4 (6.3)	21.2 (3.1)	20.3 (6.1)	22.3 (3.6)	6.2 ^a	1/1011 ^c	0.013
History of suicide attempt (%)	13.4	5.0	21.5	17.0	3.6 ^b	1	0.059
History of self-injury (%)	7.5	3.8	7.9	6.5	0.71 ^b	1	0.400
Current antidepressant medication (%)	2.7	0.3	3.0	1.9	1.8 ^b	1	0.178
Any previous psychotherapy (%)	37.6	30.6	17.4	15.2	0.15 ^b	1	0.699
Previous depression diagnosis (%)	14.8	10.9	17.9	37.7	13.6 ^b	1	0.000
Previous bipolar disorder diagnosis (%)	1.7	0.6	0.0	0.6	0.0 ^b	1	0.997
Previous anxiety disorder diagnosis (%)	10.7	5.1	10.7	14.4	5.5 ^b	1	0.019
Previous substance abuse diagnosis (%)	4.1	3.4	—	32.0	—	—	—
Previous eating disorder diagnosis (%)	0.2	0.6	4.5	8.3	0.072 ^b	1	0.789
Past month alcohol consumption (%)	68.7	65.8	22.9	20.9	0.001 ^b	1	0.977
Past month substance use (%)	15.7	15.2	0.0	0.6	0.0 ^b	1	0.997
Family history of psychiatric illness (%)	79.2	75.4	52.6	57.5	1.7 ^b	1	0.197

DF: Degrees of freedom

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SD: Standard Deviation

HAMD: Hamilton Depression Rating Scale, 17-item

^dF-Statistic

^bChi-Square Statistic

^cNumerator DF/Denominator DF

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Table 4

Reasons for PRedICT study ineligibility by screening phase and site.

Reason for Ineligibility	SCREEN NEGATIVE						SCREEN POSITIVE						ALL INELIGIBLE SUBJECTS (n=824)	
	Emory (n=541)	Clinica Latina (n=150)	Total (n=691)	Emory (n=88)	Clinica Latina (n=45)	Total (n=133)	Emory (n=541)	Clinica Latina (n=150)	Total (n=691)	Emory (n=88)	Clinica Latina (n=45)	Total (n=133)	N	%
Exclusionary Diagnosis														
Non-MDD depressive disorder	99	13	112	0	0	0	99	13	112	0	0	0	112	13.6
Bipolar disorder	85	2	87	0	0	0	85	2	87	0	0	0	87	10.6
Psychotic disorder	23	2	25	0	1	1	23	2	25	0	1	1	26	3.2
Primary anxiety disorder	107	31	138	1	4	5	107	31	138	1	4	5	143	17.4
Other exclusionary diagnosis*	9	3	12	0	0	0	9	3	12	0	0	0	12	1.5
Previous AD treatment	18	8	26	2	0	2	18	8	26	2	0	2	28	3.4
Substance Abuse/Dependence	54	9	63	5	0	5	54	9	63	5	0	5	68	8.3
Acute suicide risk	6	2	8	1	0	1	6	2	8	1	0	1	9	1.1
HAMD<18 at screening	58	18	76	0	0	0	58	18	76	0	0	0	76	9.2
Personality disorder	6	2	8	0	0	0	6	2	8	0	0	0	8	1.0
Medical condition	15	14	29	22	10	32	15	14	29	22	10	32	61	7.4
Refused participation	55	41	96	0	0	0	55	41	96	0	0	0	96	11.7
Other reason ⁺	6	5	11	7	5	12	6	5	11	7	5	12	23	2.8
Lost to follow up	0	0	0	50	25	75	0	0	0	50	25	75	75	9.1

MDD: Major Depressive Disorder

AD: antidepressant

HAMD: Hamilton Depression Rating Scale, 17-item

* Other exclusionary psychiatric diagnosis include: obsessive compulsive disorder, eating disorder, somatoform disorders.

⁺ Other reasons include: plan to move, legal issues and randomization HAMD score <15