Purpose of the Study and Background

Purpose of the Study

Migraine is a significant public health problem worldwide, and migraine has considerable personal and social costs, greater healthcare utilization, work absenteeism. Cognitive behavioral therapy, biofeedback and progressive muscle relaxation therapy for migraine are level A evidence-based behavioral treatments for migraine, yet attrition and suboptimal adherence may diminish its impact. Surprisingly little attention has been devoted to understanding factors associated with following physician recommendation to be treated by a therapist trained in these interventions and the role of adherence with these treatments. This study will evaluate factors associated with adherence to referral to behavioral treatment.

Selected References

-Trautmann E, Kroner-Herwig B. A randomized controlled trial of internet-based self-help training for recurrent headache in childhood and adolescence. Behav Res Ther. 2010;48:28-37.

-Huguet A, Stinson J, MacKay B, et al. Bringing psychosocial support to headache sufferers using information and communication technology: Lessons learned from asking potential users what they want. *Pain Res Mana*g. 2014;19:e1-e8.

-Donovan E, Mehringer S, Zeltzer LK. Assessing the feasibility of a web-based self-management program for adolescents with migraines and their caregivers. Clin Pediatr. 2013;52:667-670.

-Day MA, Thorn BE, Ward L, et al. Mindfulness-based cognitive therapy for the treatment of headache pain: A pilot study. Clin J Pain. 2014;30:152-161.

-Matchar DB, Harpole L, Samsa GP, et al. The headache management trial: A randomized study of coordinated care. *Headach*e. 2008;48(9):1294-1310.

-Holroyd KA, Cottrell CK, O'Donnell FJ, et al. Effect of preventive (beta blocker) treatment, behavioural migraine management, or their combination on outcomes of optimised acute treatment in frequent migraine: Randomised controlled trial. *BMJ*. 2010;341:c4871. doi: 10.1136/bmj.c4871 [doi].

-Powers SW, Kashikar-Zuck SM, Allen JR, et al. Cognitive behavioral therapy plus amitriptyline for chronic migraine in children and adolescents: A randomized clinical trial. *JAM*A. 2013;310(24):2622-2630. doi: 10.1001/jama.2013.282533 [doi].

-Campbell J, Penzien D, Wall E. Evidence-based guidelines for migraine headache: Behavioral and physical treatments.1999. http://tools.aan.com/professionals/practice/pdfs/gl0089.pdf

-Andrasik F, Blanchard EB, Neff DF, Rodichok LD. Biofeedback and relaxation training for chronic headache: A controlled comparison of booster treatments and regular contacts for long- term maintenance. *J Consult Clin Psycho*l. 1984;52(4):609-615.

-Schafer AM, Rains JC, Penzien DB, Groban L, Smitherman TA, Houle TT. Direct costs of preventive headache treatments: Comparison of behavioral and pharmacologic approaches. *Headach*e. 2011;51(6):985-991. doi: 10.1111/j.1526-4610.2011.01905.x [doi].

-Janssen K, Neutgens J. Autogenic training and progressive relaxation in the treatment of three kinds of headache. *Behav Res The*r. 1986;24(2):199-208. doi: 0005-7967(86)90091-4 [pii].

-Daly EJ, Donn PA, Galliher MJ, Zimmerman JS. Biofeedback applications to migraine and tensi n headaches: A double-blinded outcome study. *Biofeedback Self Regu*l. 1983;8(1):135-152.

Study Design

This is a prospective study to examine factors associated with adherence to referral for migraine behavioral treatment.

Patients will be recruited from the New York University Medical Outpatient Setting (both in the FGP Neurology Group by neurologists who have large headache practices and in the private practice office). Consecutive subjects presenting with a chief complaint of headaches with migrainous features will be recruited.

Drs. Minen, Ashina, Berk, Halpern, Newman, Levitan and Jann will be the neurologists recruiting for the study. Dr. Minen will begin recruitment on 5/27/16.

All of these neurologists are part of the NYU Langone Headache Center, and are knowledgeable about the study. No printed information will be given to these doctors.

Characteristics of the Research Population

Number of Subjects

2000 total subjects; We expect that 200 subjects will be referred to behavioral treatment.

We are requesting to extend enrollment to 2000 people as fewer enrolled participants are being referred for behavioral treatment than was originally anticipated. Those who are not referred for behavioral treatment are no longer eligible, as that is what is being studied.

*Of note, as of 12/10/19 only about 150 subjects who have been enrolled have been referred for behavioral therapy. We hope to have a total of 60 subjects who are referred to biofeedback (one of the forms of behavioral therapy) take part in this study.

Gender of Subjects

Both genders will be included.

Age of Subjects

16+

Racial and Ethnic Origin

No enrollment restrictions.

Inclusion Criteria

Inclusion criteria are: a) age 16+ years of age; b) primary diagnosis of migraine based on the

International Classification of Headache Disorders 3 beta criteria (documentation of migraine confirmed by Board Certified Neurologist)

Patients will be screened for migraine diagnosis on the questionnaire but the diagnosis will be a clinical diagnosis of migraine based on the ICHD 3 beta criteria made by the neurologist during the patient visit.

Exclusion Criteria

Exclusion criteria are: a) No phone number to receive a follow-up call.

Vulnerable Subjects

We are including age 16+. These treatments are appropriate for children and without significant side effects. A recent paper by Scott Powers et al in JAMA showed that the combination of amitriptyline and CBT resulted in the most favorable reduction in headache days.

Methods & Procedures

Methods & Procedures

Please note that "RA" stands for study research team member. We carefully select from a group of specially selected group of CUNY students who are part of the highly coveted S Jay Levy Fellowship. These students are pre-selected by CUNY for their professionalism and top
grades and then the students undergo a very selective interview process by Dr. Minen. We also take high achieving Barnard students who are pre-health who have high grades and many of whom are part of the Barnard Summer Research Institute. Dr. Minen has been a mentor as part of this program for several years, and the students in this program are supposed to learn research methods from start to finish, culminating in a poster presentation at a minimum. All study team members will have undergone a one week training intensive to understand the screening process, recruitment process, informed consent process and enrollment process (as described throughout this IRB). In brief, research volunteers will be trained during an intense one week training on study procedures including an emphasis on how to screen, recruit, consent, and enroll the participants. This is a no risk/very low risk study
unlike other interventional studies. It is similar to many of the hundreds of commercial apps available on the market that people use every day. Thus, it is appropriate for trained research volunteers to consent these participants just as they would be able to do so for survey type studies. They study team members will be carefully observed during the initial consent process to ensure that they are doing it correctly.

When patients check in and complete their regular intake questionnaire:

1. They will be approached by research assistants based on their indicated chief complaint. Patients presenting with headache will be informed about the study and consented (as described below). Using the information obtained during the visit (clinical history, physical exam and any additional medical records), the Neurologist will confirm after the visit that the diagnosis is migraine. Participants will complete the initial questionnaires on paper or electronically directly into REDCap using an iPad. The questionnaires include: the Migraine Disability Assessment Scale (Lipton et al, 2001), the Migraine Quality of Life (MSQ v2), the Patient Health Questionnaire-8 (PHQ-8), Generalized Anxiety Disorder 7-item (GAD-7) and the Insomnia Sleep Index (ISI), and a brief series of questions regarding the headache frequency and intensity and history of which types of providers were previously consulted for treatment of the headaches. (All questions are attached). The Neurologist or research assistants will record whether the patient was referred for behavioral treatment. Data will then be entered into RedCap by the PI (Dr. Minen) or research assistant(s) (who will be listed on the IRB at a later date) if the diagnosis is confirmed to be migraine.

2. Participants will be told that they will receive a series of follow up calls or REDCap emails regarding their treatment. The PI (Dr. Minen) or research assistant(s) who will be listed on the IRB at a later date will be the person to make the telephone call/send the email.

Ten call attempts will be made for each participant for each f/u period (month 1, month 2, month 3). If subjects cannot be reached by phone or text, they will be emailed to set up a convenient time for the follow-up phone call or they will be sent the follow-up survey directly via REDCap. The survey will be emailed a second time if the subject does not respond – 5 days after the first attempt.

Separate documents include scripts of any messages or emails for subjects.

Data Analysis and Data Monitoring

Analysis Plan

Descriptive statistics for all variables will be reported. We will will evaluate differences between people who did and did not follow through on behavioral treatment referrals for normally distributed, rank, and nominal psychosocial and migraine-related variables, respectively, and we will examine whether they chose to pursue behavioral therapy with a therapist (Master's or Doctorate level psych trained therapist or a physical therapist trained in biofeedback). The study does not involve us contacting or working with the PTs for the treatment. We will just collect the data from the questionnaire regarding the subjects' perceptions/decision making of whom to see for behavioral therapy. The physical therapists/psychologists may be outside of NYU. Power analysis suggests we have a power of .80 to detect a medium effect size, with a two-sided test and alpha set at .05. Qualitative analysis will include a grounded theory evaluation of responses to open-ended questions regarding adherence to behavioral treatment referral.

Data Storage and Confidentiality

Data from the questionnaires will be entered into REDCap. The questionnaires will be stored in a locked cabinet in the new office Dr. Minen will be in as part of the Department of Neurology on 41st Street, in a locked cabinet later on in Dr. Halpern's private outpatient office, and in a locked cabinet in the Men's Health Center Headache Center Office. Any emails sent from the provider to the PI or research volunteer (to be added at a later date) about any study participants needing follow-up telephone calls will be sent via the HIPAA compliant NYUMC webmail system to only those with an NYU email address.

Risk/Benefit Assessment

Risk

There is minimal harm in asking patients about their thought processes regarding behavioral treatments for migraine, which have very minimal risk to patients. Patients do not need to answer any questions which may cause anxiety or discomfort.

Breach of confidentiality is also a risk, which will be minimized by use of the NYU email system only and by use of REDCap.

Protection Against Risks

As stated above, data will be appropriately secured. Patients will be instructed that they can leave the study at any time.

Potential Benefits to the Subjects

Patients may reconsider the possibility of doing evidence based behavioral treatment for their headaches.

Investigator's Qualifications & Experience

Please see the attached CV.

Subject Identification, Recruitment and Consent/Assent

Method of Subject Identification and Recruitment

Patients will be recruited from the New York University Medical Outpatient Setting during their standard Neurology medical appointment (in the FGP Neurology Group by neurologists who have large headache practices, in the private practice office, and Men's Health Center Headache Center).

Process of Consent

MDs (or IRB approved RAs) participating in the study will obtain consent from potential subjects at their Neurology standard medical appointment. Patients will be told that we are doing a study examining their opinions and practices regarding some migraine treatment recommendations. The initial questionnaire is composed of several questionnaires and then there are brief serial follow-up calls in the MI group and one call in the TAU group. Participation is voluntary and will not affect their care whether or not they elect to participate in the study. If patients are uncertain and want to think about it, they can decide to come back within 48 hours to complete the study questionnaire.

In those ages 16-17, the patient will be provided with the consent form along with the parent due to the age of the child. The purpose of the study, risk, benefits, description of the study, subjects right to withdraw and confidentiality will be discussed with the all subjects before consent is obtained.

Subjects will be given an opportunity to ask questions and have their questions answered. Once the subject signs consent the subject will receive a copy of the signed consent form.

To monitor for treatment fidelity, we are requesting to record phone conversations during which motivational interview techniques are employed. The PI will be reviewing these recordings to account for consistency across interviewers. An A/V consent form has been submitted.

Subject Capacity

Only patients with capacity will be asked to participate in the study.

Subject/Representative Comprehension

Patients will be asked to explain that they understand that the purpose of the study.

Debriefing Procedures

N/A

Consent Forms

Consent forms provided to the patient follow standard IRB guidelines and all subjects who agree to participate will receive a copy of the signed consent form.

Documentation of Consent

The documentation will be kept in a locked storage unit in Dr. Minen's office on 41st St, in a locked cabinet later on in Dr. Halpern's private outpatient office, and in a locked cabinet in the Men's Health Center Headache Center Office. In the case a potential subject is 16 or 17 years of age, the parent grants permission. Consent will be documented by the signature of the parent after review of all consent information and questions addressed. The neurologist will also review the assent form with the child. Questions will be answered and a statement of assent will be confirmed with the signature from the child. A copy of the consent will be provided to the parent and child.

Costs to the Subject

There is no cost to the subjects.

Payment for Participation

There is no payment for participating in the study.