NIH Collaboratory Rethinking Clinical Trials®

Health Care Systems Research Collaboratory

Ethics and Regulatory Core Consultation Call:

Fibromyalgia TENS in Physical Therapy Study (FM TIPS)

Friday, December 20, 2019

Meeting Participants

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Overview of Demonstration Project	• **Overview:** The FM TIPS study is testing the effectiveness of transcutaneous electrical nerve stimulation (TENS) nonpharmacologic treatment for pain and fatigue in patients with fibromyalgia (FM) in a real-world, physical therapy practice setting. FM is a chronic condition characterized by widespread musculoskeletal pain, tenderness, and stiffness associated with fatigue and sleep disturbance. While physical therapists are trained in TENS, it is underused in primary care. A recent study has shown that with repeated use it can be effective at reducing pain with movement and resting pain compared with placebo or no treatment. The goal of this study is to assess the feasibility of adding TENS to the		• The collaborative network partners have changed. BenchMark Physical Therapy was replaced with Advanced Physical Therapy and Sports Medicine. Results Physical Therapy and Vanderbilt Physical Therapy will not be used. The University of Illinois Chicago has been added. • There are 5 healthcare systems as collaborative network partners: ○ Advanced Physical Therapy and Sports Medicine ○ Genesis Healthcare Systems ○ Kepros Physical Therapy and Performance ○ Rock Valley Physical Therapy ○ University of Illinois Chicago

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	treatment of patients with FM in a real-world, physical therapy setting, and to determine if the addition of TENS to physical therapy reduces pain, increases adherence to physical therapy, and allows patients with FM to reach their specific functional goals with less medication use. • **Collaborative network partners:** ○ Kepros Physical Therapy and Performance ○ Genesis Healthcare Systems ○ Vanderbilt University Physical Therapy Services ○ BenchMark Physical Therapy ○ Rock Valley Physical Therapy ○ Results Physical Therapy • **NIH Institute:** National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) • **Study design:** FM TIPS is designed as a cluster-randomized pragmatic trial conducted with approximately 600 patients across 20-25 physical therapy clinics within 6 healthcare systems in both rural and urban settings in Iowa, Illinois, Kentucky, and Tennessee. All individuals with physician-diagnosed FM (around the trunk area, shoulder or hip) and who do not have		• Clinics are located in Iowa, Illinois, Michigan and Wisconsin.

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	contraindication to TENS will be eligible to participate. In the intervention clinics, TENS will be administered along with standard exercise and physical therapy in the clinic, and then patients will be sent home with TENS units to administer at home. In the non-intervention clinics, patients will receive standard exercise and physical therapy in the clinic and will be offered TENS units and electrodes after completion of the study to enhance recruitment. • **Primary and secondary outcomes:** The primary outcome for the study is movement-evoked pain, a primary symptom of FM and one that interferes with adherence to physical therapy and patient-specific functional goals. Assessments will be both in-home and in-clinic. The team will provide all clinics with TENS units and electrodes as well as electronic tablets to facilitate data collection. • **Other important notes about the study:** ○ The study team expects that clinics will not already be using TENS. They will interview physical therapy clinics before initiating the study intervention to gain insight on providers' perceptions of TENS efficacy, current use of TENS and other PT interventions	Tammy sent the 2015 ethics paper to those on the call on December 20: Anderson ML, Griffin J, Goldkind SF, et al. The Food and Drug Administration and pragmatic clinical trials of marketed medical products. Clin Trials. 2015;12:511-9. doi: 10.1177/1740774515597700. The Core and NIH Project Officers can provide help to the team when evaluating this issue with the FDA.	

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	for FM, and perceptions about use of medications in treating FM. ○ There was discussion about discouraging crossovers for those participants not randomized to TENS, particularly because the same consent process will be used for all participants. It was suggested that the consent form should include information that, based on treatment guidelines, all patients regardless of randomization will receive physical activity as treatment and will be offered a TENS unit by the end of the study. ○ The study team believes there is equipoise in providing/withholding TENS. ○ The study team expects it will be within the budget to use study funds to provide the TENS units to all participants. The study team is in discussion with TENS manufacturers to obtain the units at low cost or through manufacturer donation. Of note, TENS units are widely available over the counter. ○ Patients will use TENS equipment at home, with data collected through a patient portal. Some data will be		• All subjects will be receiving TENS units along with standard physical therapy treatment. This information was included in the consent form. • TENS units will be purchased at cost from the manufacturer and provided to participants.

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	extracted via the electronic health record (EHR) or REDCap portal. Patient-reported outcomes (PROs) will not be populated in the EHR. The team will use what is in the EHR, or create a template to unify scales across systems. • The study team indicated that TENS is currently approved for relief of chronic intractable pain and as adjunctive treatment of post-surgical and posttraumatic acute pain. As mentioned earlier, the primary outcome of this study is improvement of movement-evoked pain. Consequently, those on the call asked whether this was an extension of the current indication for the device, and whether an Investigational Device Exemption (IDE) would be required to use the device for this purpose in this study. The team stated they did not believe an IDE was required for the primary pain outcome; however, the study outcomes for fatigue relief may need closer assessment. The Core members asked that the study team review a paper related to FDA-regulated products and PCTs that was prompted by the need to consider similar issues in other PCTs. The team agreed to review and assess these considerations. Although the team had not planned on		• The FDA was not consulted since the TENS units are being used under the current FDA indication for chronic pain.

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	collecting data for a new indication, the TENS manufacturers might be interested in using the study results as grounds for an extended indication for functional improvement. The team was strongly encouraged to consult with FDA on the use of TENS in this study.		
Status of IRB approval	• The University of Iowa has agreed to serve as the single IRB of record. • It is expected that most participating health systems will not have much experience with clinical research and will need GCP and human subjects research training. They will need to enter a reliance agreement with University of Iowa. The team is still in the process of identifying physical therapy clinics, but those who have agreed to participate understand the single IRB requirement.		• The Human Subjects Office at the University of Iowa provided sites with human subjects training which included parts of Good Clinical Practice (consent process, enrollment procedures, recruitment and safety). Sites with IRBs have agreed to rely on the University of Iowa, and those without IRBs have had a separate agreement to rely on the University of Iowa. The project team has worked closely with each clinic and healthcare system to complete the paperwork required to get IRB approval. IRB approval for one healthcare system to start recruiting has been approved; requests for approval for 2 more systems are being resubmitted. All systems are expected to be trained and ready to start recruitment by the end of February 2021.
Risk classification	• The University of Iowa IRB does not make a formal risk determination until the full project is submitted, but through preliminary discussions, it is expected that the study will be deemed minimal risk.		• The IRB determined that the study is minimal risk.

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	• Those on the call agreed that the study appears to be minimal risk.		
Consent	• The study team has not yet drafted a consent form. • The study team is considering using the same consent form for both study arms. The team plans to obtain electronic consent using tablets available at each clinic. Eligible patients will self-enroll. Someone on site will be available to answer questions about the study and ensure the informed consent process is followed. • Since everyone will get a TENS unit at some point during the study, those on the call suggested that the team include this information in the consent form. • Although plans have not been finalized, the study team expects that information about the study will be provided via a YouTube video as part of the consent process, allowing the main PI to share information about the study in a uniform way. It was suggested that simple videos can be done and include a mock consent conversation. • The goal is to automate consent as much as possible and have a person affiliated with study available, or have a contact number for questions, to avoid disrupting the clinical practice schedule.	Joe Ali will provide the study team with information on video consent creation (completed 1/28/2020)	• Consent will be obtained using an e-consent platform. In lieu of a video, a website (https://www.fmtips.org/) with information for potential participants to review has been developed. This process has been reviewed and approved by the IRB.

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	• The IRB will want to evaluate both the video script and the video. • The study team asked for a reference on e-consent, as it is an acceptable alternative under both FDA and the revised Common Rule. It was suggested that the team look at the ADAPTABLE trial (PCORnet) for information on its e-consent process. • FDA also has a good guidance on e-consent and the team can look at that.		
Privacy/HIPAA	• The study team will contact stakeholders about the EHR at each health system. • The University of Iowa is the data coordinating center and has a process for HIPAA compliance. • The study needs to establish a patient portal. The team will be sensitive to potential issues of privacy with REDCap (e.g., inadvertent HIPAA violations). The Vanderbilt team members have experience and expertise with REDCap and can help with any issues.		• A REDCap data collection system is in production. The system has been pilot-tested and reviewed by local REDCap personnel. All data will be entered by participants at home through a personal REDCap link sent to a personal email.
Monitoring and oversight	• NIAMS, which holds the grant for this study, expects to charter a DSMB and takes responsibility for this. • In the previous TENS study by this team, which was determined to be minimal risk, the DSMB did both data monitoring and	Martha Matocha (NINR) will contact Jim Witter to follow up (2/18/2020 update provided by Martha Matocha: (1) Charles Washabaugh has	• A DSMB has been constituted by NIAMS through its vendor KAI to provide data monitoring and oversight. The first DSMB meeting was in September 2020, and the DSMB made some useful recommendations that have been implemented.

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	advising. For example, the DSMB looked at the randomization to ensure an even distribution and hitting targets, and gave suggestions for improvements.	replaced Jim Witter as Program Officer; and (2) NIAMS confirmed that it will convene the DSMB for the study)	
Issues beyond the study	• A certificate of confidentiality will be automatically provided per recent NIH policy. This certificate adds provisions for future research uses and confidentiality obligations for future data sharing.		
Additional follow-up information			• The team had a recent additional call with the Ethics and Regulatory Core regarding DSMB recommendations and HEAL-mandated Common Data Element (CDE) questionnaires. This included discussion about how to monitor psychiatric comorbidities as well as the responsibility of the study team regarding patient safety particularly given the pragmatic and minimal risk nature of the trial, the fact that the study team has no relationship with the participants or their providers and, the relationship between the participants and the physical therapist is likely to conclude before the end of the study. Subsequently the team has developed a plan to monitor participant safety and will monitor how the plan works in real time. • The team would like to continue the conversation around study team

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			responsibilities in pragmatic minimal risk trials with respect to information provided that is outside the scope of primary study aims, but that might require action for patient safety.