using trial data from the Establishing Moderators and Biosignatures of Antidepressant Response in Clinical Care† (EMBARC) study. The primary objective of the algorithm is to switch treatment in patients who will not reach clinical effectiveness by the end of the stage, and the secondary objective is to avoid accidentally switching treatment in patients who will reach clinical effectiveness by the end of the stage. †Trivedi et al. Journal of Psychiatric Research 78 (2016) 11-23 METHODS/STUDY POPULATION: First, the algorithm was derived assuming a linear or non-linear trajectory. Next, performance of the algorithm was assessed using data from the Establishing Moderators and Biosignatures of Antidepressant Response in Clinical Care† (EMBARC) study. This two-stage SMART design measured the effectiveness of sertraline in 242 patients with non-psychotic Major Depressive Disorder (MDD). The algorithm was applied to baseline and interim measurements from the EMBARC study to predict end-stage Hamilton Depression (HAMD17) scores, the primary outcome of the study. True positive rate (TPR) and false positive rate (FPR) were used to measure respectively the primary study objective (switching treatment in patients who will not reach clinical effectiveness by the end of the stage), and the secondary study objective (avoiding accidentally switching treatment in patients who will reach clinical effectiveness by the end of the stage). TPR and FPR were calculated for the following prediction scenarios: (1) three separate two-point predictions: Baseline and Week 2, Baseline and Week 4, Baseline and Week 6, and (2) a single three-point prediction: Baseline and Weeks 2 and 6. †Trivedi et al. Journal of Psychiatric Research 78 (2016) 11-23 RESULTS/ANTICIPATED RESULTS: When using two-point prediction, we found TPR to increase and FPR to decrease as the interim measurements approached closer to the end of the stage. We also found TPR to increase when using a three-point prediction, but at the expense of FPR also increasing. Across these scenarios, TPR ranged between 70 and 90%, and FPR ranged between approximately 20 and 50%. DISCUSSION/SIGNIFICANCE OF IMPACT: Although SMART designs ultimately assign patients to more effective treatments, this process can take time and leave a patient (currently on an ineffective treatment) waiting until the end of a stage to try a potentially superior treatment. This disadvantage of the SMART design is currently addressed by this algorithm. By introducing a regression and likelihood approach to predict whether a patient should switch or stay on their current treatment, we move closer to the goal of designing rigorous, patient-centered studies. This work has the potential to improve individual clinical outcomes for patients enrolled in pragmatic clinical trials.

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Increased Monounsaturated Fat Consumption is Associated with Improved Body Composition in Subjects with Obesity and Heart Failure with Preserved Ejection Fraction

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OBJECTIVES/SPECIFIC AIMS: We hypothesized that increasing percent calories from MUFA (%MUFA) would be associated an increased FFM/FM index. METHODS/STUDY POPULATION: Nine consecutive HFpEF patients with obesity participated in a 12-week pilot feasibility trial of UFA supplementation (NCT03310099).

Subjects were educated at baseline by a dietitian on UFA rich foods including high MUFA choices such as extra-virgin olive oil, canola oil and avocados. Participants were given a list of items, corresponding serving sizes and asked to eat at least one serving of these UFA rich foods per day for 12 weeks. Adherence was encouraged through weekly phone calls by the dietitian. Standardized 5-pass 24-hour dietary recall was performed by a dietitian at baseline and 12 weeks. The recalls were analyzed to establish intake of MUFA in percent calories (%kcals) with Nutrition Data Systems for Research software (NDSR). Body composition including FM%, fat free mass percent of body weight (FFM%) and ratio of FFM to FM (FFM/FM Index) was measured with bioelectrical impedance analysis (RJL systems) at baseline and 12 weeks. Statistical analysis was performed with SPSS (24.0). Spearman rank test was used for correlations. Values are expressed as numbers and percentages or as median and interquartile range (IQR). RESULTS/ANTICIPATED RESULTS: Subjects were mostly female (56%) with a median age 56 (IQR 50-59). Baseline median body mass index (kg/m2) was 36.7 (36.2-48.0), median FM% was 44.5 (IQR 32.5-53.4), median FFM% was 55.5 (IQR 46.7-67.5) and median FFM/FM Index was 1.25 (IQR 0.88-2.1). The only significant change was an increase in %MUFA from baseline 12.4% (IQR 6.9-14.3) to 12 weeks 21.8% (17.6-36.9) ($p = 0.008$). Increased %MUFA was highly associated with increased FFM% ($r = 0.783$, $p = 0.013$) (Figure 1A), decreased FM%($r = -0.783$, $p = 0.013$)(Figure 1B) and increased FFM/FM index ($r = 0.800$, $p = 0.010$) (Figure 1C). All correlations remained statistically significant after adjustment for changes in energy intake. DISCUSSION/SIGNIFICANCE OF IMPACT: Increasing dietary %MUFA is protective against negative changes in body composition in patients with obesity and HFpEF, independent of changes in caloric intake. Future work should focus on whether the correlation found in this pilot study translate in improved body composition and finally, exercise tolerance and clinical outcomes.

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Intermittent Theta Burst Stimulation to Relieve Depression and Executive Function impairment in older adults

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OBJECTIVES/SPECIFIC AIMS: The objective of the study is to examine the ability of iTBS to improve depression and executive impairment in depressed older adults. If effective, this treatment will have the potential to improve the quality of life in LLD. METHODS/STUDY POPULATION: From 12- 2016 to date older adults (60 – 85 y/o) in a major depressive episode, with evidence of executive dysfunction (on the NIH Tool Box battery) were enrolled. iTBS protocol: This brief paradigm (3 min 9 seconds duration) was administered on weekdays for four weeks (20 sessions total). Stimulation intensity was set up to 120% of the observed motor threshold. Depression primary outcome: Change in the Montgomery Asberg Depression Rating Scale (MADRS) from baseline to the end of iTBS course. Executive function primary outcome: Change in executive measures from the electronic NIH Tool Box cognitive domain battery8. Executive secondary outcome: Change in scores from baseline to the end of iTBS on the Frontal Systems Behavior Scale (FrSBe), this self reported instrument measures dys-executive behavior. Statistical Analysis: paired t-test examined changes in depression and executive variables from baseline to post iTBS. Pearson correlation examined

the association between degree of mood improvement and degree of improvement in executive function. SPSS v 24 was used for all analyses. RESULTS/ANTICIPATED RESULTS: We examined 11 subjects. Primary outcomes: Patients showed a significant decrease in scores on the Montgomery Asberg Depression Rating Scale (MADRS) from baseline Mean (M) = 27.73, Standard Deviation (SD) 8.2 to the end of 4 weeks of iTBS: M = 15.91, SD = 10.05, t = 7.4, p < .001. The Flanker Inhibitory Control and attention test significantly improved from baseline M = 91.0, SD = 7 to the end of iTBS M = 98.7, SD = 12.8, t = −2.9, p = .014 (higher scores at week 4 denote improvement). The List Sorting Working Memory test and the Dimensional Change Card sort a measure of cognitive flexibility improved but did not reach statistical significance. The self reported executive measure improved from baseline M = 48.6, SD = 9.4 to post iTBS M = 39.4, SD = 8.5, t = 3.8, p = .003 (lower scores at week 4 denote improvement). We also examined whether the degree of improvement in depression related to the degree of improvement in executive function. We found positive correlations between change in mood scores with iTBS with change in executive scores with iTBS, with a strong relationship with working memory r = 0.34. Tolerability and Side effects: Common side effects were twitching in facial muscles during the stimulation (n =11), headaches (n =10) and pain or discomfort at the stimulation site and face (n =4). One participant withdrew due to intolerance to the stimulation. DISCUSSION/SIGNIFICANCE OF IMPACT: The iTBS paradigm was effective in improving mood and executive function in older adults. Both the psychometric measure and the self reported executive function measure (indicative of dysexecutive behavior) reflected improvements post iTBS. Improvement in executive function was correlated with depression improvement. We targeted the Dorso Lateral Prefrontal cortex, which exhibits decreased connectivity with the dorsal anterior cingulate in depressed elderly and is a key in orchestration of executive function. Our findings are consistent with the conceptualization of depression as a circuit level disorder affecting interconnected networks involving mood and cognition. Although we demonstrated potential therapeutic effects, the mechanism of action of iTBS remains unknown. We are presently conducting a randomized controlled trial to examine the effects of iTBS on brain connectivity using functional MRI. Results of this study underway will hopefully demonstrate engagement of the TMS target and contribute to a neurocircuitry based approach treatment of geriatric depression.

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Maximizing the Value of Your Trial Innovation Network Hub Liaison Team

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OBJECTIVES/SPECIFIC AIMS: The University of Washington (UW) CTSA Hub Liaison Team has directed and facilitated work required to bring TIN multisite trials to the CTSA hub and its affiliates by: (1) Connecting hub and affiliate investigators with the services offered by the Trial and Recruitment Innovation Centers, (2) identifying investigators at academic and non-academic institutions to act as co-investigators on multisite trials, (3) supporting the local and affiliate human research protection programs and investigators throughout the life-cycle of the study, (4) maximizing CTSA and local study team resources to develop and monitor study-specific

volunteer recruitment and retention plans. The UW CTSA TIN Hub Liaison Team has worked to achieve these objectives via the following methods designed for generalization and dissemination. METHODS/STUDY POPULATION: (1) Providing consultations to investigators interested in the services offered by the Trial and Recruitment Innovation Centers. (2) Hub and affiliate investigators at academic and non-academic institutions are identified by a variety of approaches, including the engagement of existing CTSA hub regional collaboration networks, utilizing EHR data from CTSA developed phenotypes and targeted "Investigator Engagement Packets". (3) Ensuring regulatory oversight and compliance is challenging in the new age of single IRB review. Establishing a flexible reliance office, engaging with the central TIN IRBs and providing guidance and resources to local study teams ensures investigator confidence in the integrity of the protocol approval and study activity processes. (4) The CTSA Hub Liaison team has developed a Recruitment and Retention Plan template and holds recruitment and retention planning meetings with the CTSA study teams engaging in TIN studies. RESULTS/ANTICIPATED RESULTS: It is anticipated that The Hub Liaison Team: (1) Will contribute to the TIN's process improvement to bring regionally appropriate studies to the CTSA hub and affiliates. (2) Identify ideal investigators to engage both in proposal submission and co-investigating multisite trials. (3) Collect, compare and improve regulatory and contract approval cycle times. (4) Monitor and support screening, accrual and retention of study volunteers. DISCUSSION/SIGNIFICANCE OF IMPACT: Due to low prevalence of disease, challenges related to identifying and randomizing study volunteers and urgency to address clinical and public health issues, multisite study design is an essential option for NCATS. The Trial Innovation Network is an exciting approach to leverage local and national resources to provide infrastructure to improve multisite clinical and observational trial conduct. The University of Washington CTSA hub has developed and piloted methods to achieve the mission of the TIN, by recruiting investigators and realizing trial objectives, with the hope that these methods could be utilized by other CTSA TIN Hub Liaison Teams.

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Measuring Fluid Compartments Before and After Rapid Saline Infusion

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OBJECTIVES/SPECIFIC AIMS: To evaluate the ability of various techniques to track changes in body fluid volumes before and after a rapid infusion of saline. METHODS/STUDY POPULATION: Eight healthy participants (5M; 3F) completed baseline measurements of 1) total body water using ethanol dilution and bioelectrical impedance analysis (BIA) and 2) blood volume, plasma volume and red blood cell (RBC) volume using carbon monoxide rebreathe technique and I-131 albumin dilution. Subsequently, 30mL saline/kg body weight was administered intravenously over 20 minutes after which BIA and ethanol dilution were repeated. RESULTS/ANTICIPATED RESULTS: On average, 2.29±0.35 L saline was infused with an average increase in net fluid input-output (I/O) of 1.56±0.29 L. BIA underestimated measured I/O by −3.4±7.9%, while ethanol dilution did not demonstrate a measurable change in total body water. Carbon monoxide rebreathe differed from