CCTS Scholar Presentation Abstracts

Abstract Title:	**The effects of preclinical AD pathology on default-mode network function and executive performance are mediated by declining white matter microstructure**
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Abstract: The default-mode network is a site of β-amyloid (Aβ) deposition and functional decline in preclinical Alzheimer's disease (AD). The DMN has also been linked with executive performance, which appears to undergo subtle decline in preclinical AD. In the present study, we will investigate whether declines in DMN function and executive performance are the direct effect of Aβ pathology or if these declines are due to the indirect effect of declining white matter (WM) microstructure. Thirty-five cognitively normal older adults underwent fMRI to assess DMN function, diffusion tensor imaging to measure WM microstructure, lumbar draw of cerebrospinal fluid (CSF) to measure Aβ pathology, and neuropsychological testing to measure executive function. Partial correlation and mediation analyses were used to examine the relationships between each of these measures. Declines in WM microstructure and increasing Aβ pathology were associated with declines in DMN function (r= -0.38, -0.37, p =.03, .04, respectively). However, mediation analyses revealed that the relationship between Aβ and DMN function was mediated by declines in WM microstructure. Declines in DMN function, WM, and increasing Aβ pathology all were associated with poorer performance on tests of executive function (r = -0.45, 0.42, 0.36, p = .01, .02, .05, respectively). However, mediation analysis revealed that the effect of Aβ pathology on executive function was mediated by WM-related declines in DMN function. The present results suggest that it is the negative effect of AD pathology on WM microstructure that indirectly contributes to declines in DMN function and executive performance. Therefore, WM microstructure may be a potential target for interventions aiming to delay the negative effects of preclinical AD pathology.

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Abstract Title:	**Serum Biomarkers in Early Detection of Diabetic Cardiomyopathy in West Virginian Population**
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Abstract: Introduction/Background: Diabetic cardiomyopathy (DCM) is an established complication of diabetes mellitus. In West Virginia, the especially high incidence of diabetes and heart failure validate the necessity of developing new strategies for earlier detection of DCM. Since most DCM patients remain asymptomatic until the later stages of the disease when the fibrotic complications become irreversible, we aimed to explore biomarkers that can identify early-stage DCM. Methods: The patients were grouped into four categories based on clinical diabetic and cardiac parameters: Control, Diabetes (DM), Diastolic dysfunction (DD), and Diabetes with diastolic dysfunction (DM+DD), the last group being the preclinical DCM group. Results: Echocardiography images indicated severe diastolic dysfunction in patients with DD+DM and DD compared to DM or control patients. In the DM and DM+DD groups, TNFα, isoprostane, and leptin were elevated compared to control ($p<0.05$), as were clinical markers HDL, glucose and hemoglobin A1C. Fibrotic markers IGFBP7 and TGF-β followed the same trend. The Control group showed higher beneficial levels of adiponectin and bilirubin, which were reduced in the DM and DM+DD groups ($p<0.05$). Discussion/Conclusions: Our results identified elevated levels of specific biomarkers, including IGFBP7 and TGF- β, in West Virginia patients with diastolic dysfunction. Therefore, this novel study support the clinical application of biomarkers in diagnosing early stage DCM, which will enable attenuation of disease progression prior to the onset of irreversible complications.

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Abstract Title:	**Identifying and Adapting a Depression Intervention for Rural Appalachian Women: Preliminary Findings from Formative Research**
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Abstract: Hypothesis: The prevalence of depression among rural women is nearly twice the national average, yet limited access to services and social barriers prevent many from receiving treatment. We hypothesized that an appropriate evidence-based intervention adapted to the needs of rural women may be more culturally acceptable and feasible than usual treatment offered by mental health providers. Procedures: Formative data were collected in two stages to identify a potential evidence-based intervention to be implemented in accordance with local preferences. First, interviews were conducted with Appalachian women with depression (N=28) and diverse health professionals who serve them (N=11) to identify local needs and barriers to treatment. Second, in 4 focus groups and ongoing interviews with these two groups (N=14), we are examining how the evidence-based intervention should be adapted, focusing on participant engagement and location of intervention delivery. Results: Barriers to treatment among Appalachian women included limited treatment options; depression stigma; competing comorbid health conditions and social responsibilities; and the value of self-reliance. To reduce these barriers, we identified a peer recovery intervention—Wellness Recovery Action Planning (WRAP)—that can be implemented outside traditional treatment settings, focuses on overall health rather than solely mental health, and builds on self-reliance. Participants recommended that WRAP be delivered through community health workers, and that implementing the intervention in a medical rather than community setting would improve retention. Conclusions: Adapted, non-clinical interventions hold promise for engaging rural women in depression self-management by addressing their barriers to obtaining treatment and their mental health needs.

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CCTS Scholar Presentation Abstracts

Abstract Title:	**Prevalence and Predictors of Chronic Opioid Use In a Nationally Representative Sample of Newly Diagnosed Chron's Disease Patients**
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Abstract: Background Chronic pain is a common complication of Crohn's disease (CD). Clinicians frequently resort to opioids analgesics to treat chronic pain in CD patients, however such therapy has been associated with considerable risks (such as addiction), side effects (e.g. constipation) and has unestablished efficacy. The objectives of this study are: to compare clinical and demographic characteristics of chronic opioid users and non-chronic users with CD, attempt to determine what baseline characteristics could be predictive of future chronic use in this patient population and lastly, to examine if chronic opioid users had increased healthcare utilization such as ER visits or surgeries. Methods This study utilized a nationally representative dataset of administrative healthcare claims from the years 2007 – 2013. Data for individuals over age 18 with private insurance were obtained for the two years following an initial CD diagnosis. Chronic opioid users were compared to non-chronic users on demographic and clinical characteristics using chi-square and t tests. A logistic regression model was developed to determine which baseline characteristics of CD patients predict chronic use in the two years following the diagnosis. Results Out of 59,673 newly diagnosed Crohn's patients, 2,017 (3.4%) proceeded to use opioids chronically in the two years following their initial diagnosis. Statistically significant differences between chronic users and non-chronic users were observed for baseline demographic and clinical characteristics as well as post-diagnosis healthcare utilization. Significant predictors of chronic opioid use included age, previous opioid exposure, and prior chronic pain disorders. Discussion Clinicians could use the results of this study to identify newly diagnosed Crohn's patients who may be at increased risk of future chronic opioid use. Early identification of these patients may prompt implementation of various strategies to avoid chronic opioid use, the associated risks and increased healthcare utilization.

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CCTS Scholar Presentation Abstracts

Abstract Title:	**Variability of the Finnegan Scoring System in Monitoring Infants with Neonatal Abstinence Syndrome**
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Abstract: The purpose of this study was to determine factors associated with the variability of Finnegan scores in infants diagnosed with Neonatal Abstinence Syndrome (NAS). We reviewed our experience of using Finnegan scores for babies with NAS admitted to the neonatal intensive care unit (NICU). From electronic medical records, we derived all Finnegan scores for each baby with NAS from July 1st to December 31st 2014. The following factors were analyzed for their effect on the variability of Finnegan scores: daily patient census, time of day (7 AM to 7 PM, 7 PM to 7 AM), day of the week (weekday versus weekend), and nurses assigning scores. Statistical methods include descriptive statistics and multivariate linear regression models accounting for within-baby correlation of scores. A total of 9,198 Finnegan scores from 166 babies and 336 nurses were analyzed. Regression results showed that daily census, time of day, and day of week were not significant predictors of Finnegan scores. However, adjusting for these three factors, the mean Finnegan scores significantly differed across nurses ($p<0.0001$). Nursing explained 5.3% of the variability of the Finnegan Scores. The results call for more structure in training healthcare personnel and regular assessments of reliability in scoring of babies with NAS. We have recently accomplished training of personnel in Finnegan scoring with a future plan to analyze changes in variability of scoring post training.

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Abstract Title:	**Abuse Liability of Oral Cannabidiol in Comparison to Smoked Marijuana in Frequent Marijuana Smokers**
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Abstract: Objectives: Cannabidiol (CBD), a naturally occurring phytocannabinoid, is being explored as a pharmacotherapy for several disease conditions (e.g., marijuana dependence, seizure disorder). However, there is little information available regarding the abuse liability of CBD and it remains a Schedule I drug under the United States Controlled Substances Act (e.g., highest risk for abuse, no accepted medical use). The aim of this laboratory study was to examine the abuse liability of a dose range of CBD, under controlled conditions in comparison to smoked marijuana, a cannabinoid agent with known abuse liability. Methods: Healthy marijuana smokers (n=31) were enrolled in this multi-site, within-subject, double blind, placebo-controlled, randomized outpatient study. Eight 7.5 hr weekly sessions were completed during which oral cannabidiol (0, 200, 400, 800 mg) was administered 1.5 hrs prior to smoked marijuana (0, 5.6% THC). An array of participant-rated, performance and physiological measures was collected. Results: Active marijuana reliably produced abuse-related subjective effects (high, good drug effect) compared to placebo marijuana ($p<.05$). In contrast, all CBD doses were placebo-like and did not produce signals of abuse liability ($p>.05$). Further, CBD did not produce any measureable behavioral or performance effects. When combined with marijuana, CBD did not modulate any of the subjective effects of marijuana effects ($p>.05$). Discussion: Oral CBD in doses up to 800 mg (the highest acute dose tested in healthy volunteers to date) were safely tolerated in a population of frequent marijuana smokers. None of the CBD doses tested produced any abuse related subjective effects relative to placebo. Overall, CBD appears to have limited abuse liability, does not modulate the abuse-related effects of marijuana and produces overall placebo-like effects in a cannabinoid-tolerant population. These data have the potential to have an impact on the regulatory decision-making regarding the status of CBD as a Schedule I agent.

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