

1 week after starting the medication. Sleep outcomes will be measured by polysomnography, daily sleep diary, and the Insomnia Severity Index. RESULTS/ANTICIPATED RESULTS: We hypothesize that (1) within the placebo group data both subjectively and objectively measured outcomes will similarly show improvement in insomnia symptoms, (2) the increase of the placebo medication dose will result in an increased benefit, (3) the trauma-related insomnia placebo group will have the same type and similar rate of side effects reported in previous suvorexant trials. DISCUSSION/SIGNIFICANCE OF IMPACT: Most previous studies examining placebo effects focused on pain and depression. Information obtained from this project will complement our current understanding of placebo effects by characterizing placebo effects on trauma-related insomnia. This study will inform the development of novel strategies to maximize utility of placebos in future clinical trials.

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Feasibility of maternal holding during therapeutic hypothermia for infants with encephalopathy

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OBJECTIVES/SPECIFIC AIMS: Therapeutic hypothermia (TH) is a neuroprotective therapy regularly used in newborn infants following traumatic births. The infant's temperature is maintained at 33.5°C for 72 hours by a cooling blanket upon which the infant is placed. Parents are not permitted to hold their infant while TH is ongoing due to concerns for unintentional rewarming or accidental dislodging of catheters or other monitoring equipment. Our prior qualitative research with nurse and parent interviews described the inability to hold an infant during TH as a significant source of stress. We assessed the feasibility of a 30-minute period of maternal holding for infants being actively treated with TH and assessed both the maternal experience of holding and the nurse experience of supporting holding. METHODS/STUDY POPULATION: This was a feasibility study employing a mixed-methods approach. Inclusion criteria were gestational age at birth of 35 weeks or greater, absence of clinical or electrographic seizures during the first 24 hours of TH, and designation as "clinically stable" by the attending neonatologist with the infant on room air, nasal cannula, or continuous positive airway pressure. Quantitative data were obtained from vital sign monitoring every 2 minutes before, during and after holding and from maternal and nurse research surveys. Qualitative data were obtained from nurse surveys. Infant rewarming was prevented through use of a thin foam insulating barrier placed between mother and infant during holding. Adverse events were defined as a change in infant temperature greater than 0.5°C above or below 33.5°C, accidental dislodging of central lines/disruption of EEG leads or early termination of holding due vital sign instability present for greater than 2 recorded measurements including infant bradycardia defined as heart rate less than 80 beats per minute, hypotension defined as mean arterial pressure less than 40 mmHg or oxygen saturation of less than 93%. RESULTS/ANTICIPATED RESULTS: There were 10 newborn infants undergoing TH for neonatal encephalopathy (median gestational age 39.4 weeks) and their mothers (median age = 31 years) were recruited. Infants remained on the hypothermia blanket during holding and were transferred safely to their mother's arms without medical equipment malfunction/dislodgement. Holding occurred at a median of 47 hours of life. The mean temperature prior to holding was 33.4°C and at completion of holding the mean temperature was 33.5°C ($p = 0.18$). There were no significant bradycardia, hypotension or oxygen desaturation events. In total, 80% of mothers reported difficulty bonding with their baby prior to holding and 90% reported a high level of stress before holding. After holding, all mothers felt their bond was "stronger" or "much stronger" and all felt "less stressed" or "much less stressed." After holding, 75% of nurses reported that they felt a more positive emotional response to the infant. One nurse stated, "being a part of this emotional experience made me feel closer and more connected to this family and gave me a different perspective on just what they had been dealing with and feeling since giving birth to their child." In free text responses, on 5 separate occasions, nurses commented on the relaxed, calmed or less irritable appearance of the infant while being held during TH. DISCUSSION/SIGNIFICANCE OF IMPACT: In this sample of term infants treated with TH, a 30-minute period of maternal holding was not associated with increased temperature or other adverse events. Holding during TH was associated with extremely positive feedback from mothers and nurses. Future larger studies could consider assessing the impact of holding on endocrinological markers of stress and bonding, on infant glycemic control, on breastfeeding

success rates, and the impact of earlier and improved bonding on the developmental outcomes of children held during their treatment with TH. Increasing the duration of holding and allowing both parents to hold on more than one occasion during the 72 hours of TH may increase the proposed benefits of this intervention.

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Influence of alcohol use disorder and comorbid psychopathology on discounting of delayed rewards

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OBJECTIVES/SPECIFIC AIMS: Alcohol use disorder (AUD) has been associated with greater discounting of delayed rewards relative to healthy controls. The relationship, however, has been inconsistent, likely because previous studies had relatively small sample sizes and inadequately controlled for comorbid psychopathology and substance use. In the present study, we analyzed one of the largest clinical research samples to date to assess the influence of alcohol use on delay discounting, and examine the influence of confounding variables including substance use disorder. METHODS/STUDY POPULATION: In total, 801 participants completed a delay discounting task where they chose between smaller, immediately available monetary amounts (\$0–\$90) and \$100 available after a delay of 7–30 days. Delay discounting behavior was summarized as the natural log of k , a constant derived from a hyperbolic discounting equation. Participants also completed Structured Clinical Interviews for DSM-IV disorders, 90-day Timeline Followback interviews, and the Fagerström Test for Nicotine Dependence. Participants were divided into 4 groups: healthy controls ($n = 298$), past AUD ($n = 69$), and current AUD with ($n = 224$) and without ($n = 210$) comorbid psychopathology or substance use disorder. Kruskal-Wallis test was used to examine the effect of group on delay discounting. RESULTS/ANTICIPATED RESULTS: There were significant differences in the distribution of delay discounting scores by group ($H = 80.195$, $p < 0.001$). Healthy controls and past AUD showed lower levels of delay discounting than current AUD and current AUD + comorbidity groups with medium effect sizes (Cohen's $d = -0.635$ and Cohen's $d = -0.614$, respectively). There were nearly no differences between current AUD with and without comorbid psychopathology groups (Cohen's $d = -0.024$). The past AUD group showed almost no difference relative to the healthy control group (Cohen's $d = 0.007$). DISCUSSION/SIGNIFICANCE OF IMPACT: Individuals with current AUD were shown to discount rewards greater than those without current AUD, although comorbid psychopathology did not significantly affect discounting. Surprisingly, individuals with past AUD were more similar to controls than to those with current AUD. Our findings suggest that current problematic alcohol use is related to greater discounting of delayed rewards, but comorbid diagnoses do not significantly impact this relationship. However, once problematic patterns of alcohol use cease, delay discounting appears to return to levels comparable to healthy controls.

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Long-term response to treatment and disease recurrence in a prospective cohort of morphea patients

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OBJECTIVES/SPECIFIC AIMS: Morphea (localized scleroderma) is an autoimmune disease characterized that is widely thought to have a monophasic course, in which an initial period of inflammation (activity) ultimately results in scarring, atrophy, and functional impairment (damage). Understanding the long-term clinical course of morphea is important for the planning of future interventional studies, and as a tool for clinicians in determining risk for poor disease outcomes. METHODS/STUDY POPULATION: We conducted a prospective cohort study of 130 participants enrolled in the Morphea in Children and Adults Cohort over a median follow-up time of 4.3 years, to determine the rates of response to treatment and disease recurrence as measured by the Localized Scleroderma Cutaneous Assessment Tool (LoSCAT). To determine risk factors for recurrence of disease activity, survival analysis using the log-rank test was used to compare subgroups by morphea type, therapy, and age at disease onset. RESULTS/ANTICIPATED RESULTS: Within a 1-year follow-up period, 66% of patients treated with methotrexate and 46% of patients with UVA1 phototherapy had achieved complete response to treatment. In patients who had achieved response to treatment, 29% experienced disease

recurrence at an average of 1.7 years after documented disease inactivity. Patients with generalized morphea experienced higher recurrence rates than those with linear morphea (HR: 3.03, 95% CI: 1.48–6.22), and those treated with UVA1 phototherapy had higher recurrence over those treated with methotrexate (HR: 2.33, 95% CI: 1.03–5.31). In patients with follow-up periods longer than 5 years ($n=50$), disease recurrence was observed in 44% of patients and the majority of recurrence represented new activity in an area of pre-existing morphea (82%). **DISCUSSION/SIGNIFICANCE OF IMPACT:** This study highlights the previously under-studied dynamic long-term course of morphea, and identifies the clinical characteristics that predispose patients to having a relapsing-remitting course. We conclude that patients with morphea should be followed closely over time even in the absence of disease activity due to the potential for disease recurrence.

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Mixed meal effects of neprilysin inhibition

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OBJECTIVES/SPECIFIC AIMS: Test the hypothesis that neprilysin inhibition with sacubitril/valsartan will increase endogenous intact GLP-1 after a mixed meal compared with valsartan. **METHODS/STUDY POPULATION:** Adults 18–80 years with pre-diabetes or type 2 diabetes and elevated blood pressure. **RESULTS/ANTICIPATED RESULTS:** We anticipate higher intact GLP-1 area under the curve after the meal when subjects receive sacubitril/valsartan compared with valsartan. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Neprilysin inhibition may be a target for anti-diabetes therapy by decreasing degradation of GLP-1.

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National dissemination of the accrual to clinical trials (ACT) network across the Clinical and Translational Science Award (CTSA) Consortium*

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OBJECTIVES/SPECIFIC AIMS: The ACT Network was developed by 46 members of the CTSA Program hubs in collaboration with NCATS to help investigators explore and validate feasibility of clinical studies in real-time using linked electronic health record data for cohort discovery. ACT is being disseminated nationally across the CTSA consortium. **METHODS/STUDY POPULATION:** Diffusion of Innovation Theory and Lean Start-Up principles inform dissemination strategies. Core materials were developed nationally and are being tailored to meet local CTSA dissemination norms. An advisory board, with expertise in communications, journalism, customer channel management, pharmaceutical commercialization and health IT entrepreneurship, is providing strategic advice to develop and refine dissemination strategies. Evaluation of dissemination methods will include network usage and web analytics for the ACT Network's interactive digital content and log-in portal, and surveys-interviews of ACT users using the RE-AIM implementation framework. **RESULTS/ANTICIPATED RESULTS:** Formative research identified ACT's primary value proposition for clinical researchers: "Explore patient populations in depth, in real time, from your desktop;" "Confirm study feasibility by iteratively testing and refining inclusion and exclusion criteria;" "Demonstrate feasibility in funding proposals and IRB submissions;" and "Identify collaborating sites for multi-site studies by searching for patients across the CTSA network." Early dissemination metrics, including number-type of registered users, queries performed, and web analytics, will be presented. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Researchers nationwide face common barriers in accruing enough participants for clinical trials. The inability to identify the right number and type of people to participate often makes clinical trials slow and costly. Better cohort discovery at the protocol development phase is a necessary requirement. By end of 2018, the ACT Network will

reach 60% of the CTSA consortium providing a new tool for investigators to improve the design and execution of clinical trials.

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Obstructive sleep apnea as an independent predictor of postoperative delirium and pain: An observational study of a surgical cohort

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OBJECTIVES/SPECIFIC AIMS: To study the role of OSA as an independent predictor of perioperative outcomes. **METHODS/STUDY POPULATION:** For this single-institution cohort study, we included data from patients who were enrolled into 1 of 3 prospective parent studies. All participants underwent inpatient surgeries, excluding neurosurgeries, which required general anesthesia and a postoperative stay of at least 1 day. Patients included in this study were assessed daily for postoperative delirium and pain severity as part of the parent studies. In the current study, determination of delirium diagnosis was based on the 3-minute Diagnostic Confusion Assessment Method (3D-CAM), and the Visual Analogue Pain Scale (VAS) was used for pain severity. Data on OSA diagnosis (determined by sleep study); OSA risk (determined by the STOP-Bang tool; snoring, tiredness, observed apnea, high blood pressure, body mass index > 35 kg/m², age > 50, neck circumference, male gender); and compliance with treatment were obtained from the preoperative assessment record. Participants were grouped into 1 of 3 categories: high risk of OSA (HR-OSA; including patients with a previous positive sleep study or STOP-Bang score ≥5); intermediate risk of OSA (IR-OSA; including patients with a STOP-Bang score of 3 or 4); and low risk of OSA (LR-OSA; including patients with a previous negative sleep study or STOP-Bang score <3). Candidate risk factors for delirium and pain were also extracted from this record. **RESULTS/ANTICIPATED RESULTS:** Logistic regression will be used to test whether OSA independently predicts postoperative delirium and linear regression to assess OSAs relationship to acute pain severity. We hypothesize that patients in the HR-OSA category will experience a higher incidence of postoperative delirium and greater postoperative pain severity. We also predict a step-wise increase in risk of these adverse outcomes when analyzing patients stratified by OSA risk (HR-OSA vs. IR-OSA vs. LR-OSA). For our secondary analyses, we anticipate these outcomes are modified by compliance with CPAP treatment. We believe patients with OSA who do not use prescribed CPAP will experience a higher incidence of postoperative delirium as well as increased pain severity. **DISCUSSION/SIGNIFICANCE OF IMPACT:** OSA is a common and frequently undiagnosed perioperative problem associated with altered pain processing and a high incidence of postoperative delirium. While likely providing stronger evidence of OSA's reported impact on postoperative delirium and pain, our findings might also help discern points of intervention for treatment and prevention. Since OSA's presumed impact poses challenges to clinicians and patients, prospective, randomized trials testing preventative or mitigating interventions are necessary. We hope to use these results to design such trials and clinical plans, with the goal of reducing postoperative delirium and acute postsurgical pain severity for the large number of patients at risk due to OSA.

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Pembrolizumab for patients with leptomeningeal disease from advanced solid tumors

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OBJECTIVES/SPECIFIC AIMS: Pembrolizumab is an anti-PD-1 immune checkpoint antibody that has demonstrated promising anti-tumor activity in patients with solid tumor malignancies, including patients with brain metastases from malignant melanoma and non-small cell lung cancer. Leptomeningeal disease (LMD) is a rare form of malignant spread to the central nervous system (CNS), that occurs in 2%–10% of patients with solid tumors, most commonly in breast cancer and non-small cell lung cancer. We propose an open-label phase II study of pembrolizumab in patients with LMD from advanced solid tumors

*Submitted on behalf of the ACT Network Research Team.