

## Biostatistics, Epidemiology, and Research Design

### Sex Differences in Middle Cerebral Artery Velocity in Patients with Persistent Post-Concussion Convergence Insufficiency (PPCS-CI)<sup>†</sup>

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**OBJECTIVES/GOALS:** The objective of this study is to investigate the neurophysiological mechanism of vision therapy in male and female adolescents with persistent post-concussion convergence insufficiency (PPCS-CI). This study may improve diagnostics and inform more effective personalized point of care treatment strategies to remediate symptoms. **METHODS/STUDY POPULATION:** Participants (ages 11-25) were diagnosed with PPCS by a physician, CI was diagnosed by an optometrist and OBVAT was performed by certified therapists. Patients with PPCS-CI were randomly assigned to a therapy type (immediate therapy or natural recovery). Hemodynamic measures were examined in patients with PPCS-CI at baseline (1-3 months post-concussion), and post OBVAT to evaluate recovery outcomes. Non-invasive techniques were used to measure middle cerebral artery velocity (MCAv), blood pressure, heart rate, and end-tidal CO<sub>2</sub> at rest and during objective symmetrical convergence step eye movements. Functional magnetic resonance imaging (fMRI) was acquired during convergence step eye movement experiments contrasted to sustained fixation and resting state data collection. **RESULTS/ANTICIPATED RESULTS:** To investigate the neural mechanism of OBVAT, eye movements, fMRI and physiological measures were collected in 8 patients with PPCS-CI (4 men and 4 women). Results show a 10% decrease in the MCA during 4-degree symmetrical convergent eye movement responses in males post-OBVAT and a 19% increase in MCA during convergent eye movement responses in females. Furthermore, there was a group level activation of the frontal eye fields, which improves post-OBVAT. The beta weights in the left frontal eye fields show a trending decrease in male patients post-OBVAT and trending increase in females. Males had a decrease in MCAv post OBVAT (baseline  $83.6 \pm 7.5$  cm/sec &  $75.7 \pm 12.5$  cm/sec post-OBVAT), while females show a significant increase post-OBVAT (baseline  $53.77 \pm 5.2$  cm/sec & post-OBVAT  $65.13$  cm/sec  $\pm 12.5$ ). **DISCUSSION/SIGNIFICANCE:** This initial pilot demonstrates there may be different underlying pathophysiological outcomes associated with a concussion dependent on sex. This work may have direct implications on treatment strategies for male and female adolescent patients with PPCS-CI.

\*Blue Ribbon Awardee; <sup>†</sup>Gold Ribbon Awardee

1

### A mobile health-supported bundle to improve routine childhood vaccine completion rate in Nigeria

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**OBJECTIVES/GOALS:** Barriers to childhood vaccine completion include forgetting vaccine appointments, lack of clinic access (distance and funds), and vaccine hesitancy. We tested the impact of automated and real-time appointment reminders, vaccine hesitancy counseling, and targeted vaccine drives on receiving the third dose of the diphtheria vaccine. **METHODS/STUDY POPULATION:** An implementation study to determine the feasibility and impact of implementing a mobile health-supported intervention bundle. A digital vaccine registry was developed to manage vaccine uptake data. The intervention bundle was applied sequentially: each registered parent received an automated appointment phone reminder (text and voice). If they delayed for >5 days, they received a real time reminder phone call. If during the real time call vaccine hesitancy was deemed to be a barrier, counseling was provided. If access - lack of funds or long distance - to the clinic was the barrier, vaccination was performed at patient's home on the monthly vaccine drives. We compared vaccine completion (all childhood vaccines before 18 months) during the implementation to the preceding three years. **RESULTS/ANTICIPATED RESULTS:** We anticipate the implementation will be feasible as >90% of all eligible children will be registered. We expect providers will be accepting and would recommend the intervention to other providers. We anticipate the intervention will result in a >10% increase in childhood vaccine completion compared to the average of the past three years. **DISCUSSION/SIGNIFICANCE:** We anticipate applying a multifaceted intervention will be acceptable to providers, feasible to implement, and significantly improve childhood vaccine completion rates moving Nigeria closer to achieving the global target of >95% childhood vaccine completion rate.

3

### Janus Kinase 1/2 inhibition Effect on Cytokine Levels in Tears of Patients with Ocular Graft Versus Host Disease

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**OBJECTIVES/GOALS:** The goal of this study is to identify if ocular graft versus host disease (oGVHD) patients treated with a systemic JAK inhibitor have a change in their tear cytokine profile (a possible bio-marker) and oGVHD score. oGVHD is a severe inflammatory dry eye disease and major cause of morbidity after a hematopoietic stem cell transplant. **METHODS/STUDY POPULATION:** Janus Kinase (JAK) is an upstream regulator of cytokine production. A JAK 1/2 inhibitor, Ruxolitinib, was recently FDA approved for the treatment of chronic GVHD. We propose that JAK inhibition results in cytokine changes in tears and improvement of oGVHD. To study

5

this, we will quantify tear cytokines in patients with oGVHD, with and without systemic JAK inhibition treatment. Patients with 'definite' oGVHD based on the international chronic oGVHD diagnostic criteria (ICOGVHD) whom we have collected tears will be grouped based on JAK inhibition treatment. Tear cytokines are analyzed using Iso spark Meteor bulk quantitative proteomic analysis. RESULTS/ANTICIPATED RESULTS: Seven patients were identified from our patient cohort who met inclusion criteria (oGVHD; tears collected while on Ruxolitinib), five patients were identified whom we have collected tears with oGVHD who have not taken ruxolitinib. The following 10 cytokines will be analyzed in the tears by the Iso spark Meteor bulk quantitative proteomic analysis: GM-CSF, IFN- $\gamma$ , IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-17A, TNF- $\alpha$ . The change in cytokine levels will be compared with the ICOGVHD score, corneal fluorescein staining, schirmers test (measurement of tear production), conjunctival injection score, ocular surface disease index score (validated symptomatic score of dry eye disease). DISCUSSION/SIGNIFICANCE: OGVHD is a major cause of morbidity for patients who undergo a hematopoietic stem cell transplant and is the result of a highly complex immune process including dysregulation of pro-inflammatory cytokines. It is critical to understand the effect of cytokine changes on the eyes to potentially identify a biomarker and possible treatment targets.

## 6 General Psychopathology Factor as a Mediator Between Polysubstance Use and Lower-Order Psychopathology Constructs<sup>†</sup>

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OBJECTIVES/GOALS: We aim to develop an understanding of how polysubstance use (PSU) relates to the general psychopathology factor (p-factor), as well as to individual components of the Hierarchical Taxonomy of Psychopathology (HiTOP) model (e.g., fear, distress). This insight can help identify treatment targets related to substance use and psychopathology. METHODS/STUDY POPULATION: Psychopathology and substance use data, collected at a Baltimore treatment center over several years, will be analyzed. The center aids about 6000 underserved clients per year, and the population is primarily African American clients of all genders. Structural equation modeling (using Mplus software) will be used to develop the latent models and identify relationships between psychopathology and PSU (i.e., direct and indirect pathways). The current latent HiTOP model was developed from symptom checklists completed upon entry at the treatment center. The PSU latent factor will be developed from a biopsychosocial assessment where clients list their drug of choice. Due to the varying organizations of the datasets, smaller-scale preliminary models will be developed to ensure an accurate large-scale final model. RESULTS/ANTICIPATED RESULTS: Current models being tested are derived from January to September 2023 data (i.e., completed months' data), with an N of 1,564. From symptom checklist data collected at the treatment center, a preliminary HiTOP model was derived with reasonable

fit ( $\chi^2 = 4532.35$  (df = 321,  $p < .001$ ), CFI = .77, SRMR = .07, RMSEA = .09 (.089, .094)). Data analysis is being conducted to derive the PSU factor before relating PSU to the HiTOP model. Given previous work at a local treatment center (Pavuluri et al., 2022) and with the National Comorbidity Survey-Replication data, we expect all positive direct relationships, negative indirect relationships between internalizing factors (fear and distress) and PSU when accounting for p-factor, and a positive indirect relationship between antagonism and PSU when accounting for p-factor. DISCUSSION/SIGNIFICANCE: Given our previous work to develop such models, we want to establish proof of concept in larger treatment center population. This confirmation will help provide a path towards conducting therapeutic trials to target psychopathology when treating substance use given the shared relations, some of which are less understood (e.g., fear and PSU).

## 7 Flexible probabilistic methods to unlock the clinical potential of liquid biopsy sampling<sup>†</sup>

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OBJECTIVES/GOALS: Decoding the origins of cell-free DNA (cfDNA) released from dying cells in a liquid biopsy sample (e.g. blood) offers the potential to provide insight into the dynamic, organism-wide changes reflective of health and disease. Thus, making cfDNA an ideal target for serial, minimally invasive monitoring of disease-related changes. METHODS/STUDY POPULATION: We develop a probabilistic method that leverages the co-regulation of neighboring CpG sites on individual methylome-wide sequencing (WGBS) reads to more flexibly model cell-specific methylation compared to prior methods that focus on the methylation rate of a single CpG site. We then extend our cross-sectional model to account for sequential sampling within the same subject. The increased sampling frequency is critical to identifying the evolutionary dynamics of disease progression influencing treatment response and resistance, and disease recurrence. We utilize Bayesian inference techniques to model patient-specific longitudinal profiles of cell-type turnover in simulated serial samples. RESULTS/ANTICIPATED RESULTS: We found our model more effective at capturing a range of methylation patterns on cfDNA fragments with lower Root Mean Square Error across simulations compared to a single CpG model. We apply our model to detect significant ( $p < 0.05$ , Friedman's test) increases in cellular contributions from lung and cardiac tissue in breast cancer patients (n=15) undergoing radiation therapy compared to baseline. We also identify signals of radiation induced toxicity to the liver in right-sided breast cancer patients (n=8) receiving radiation treatment compared to left-sided breast cancer patients (n=7). Finally, we show our extended model results in more efficient estimates of simulated cell-type turnover profiles compared to analyzing serial samples cross-sectionally, ignoring the longitudinal nature of the data. DISCUSSION/SIGNIFICANCE: Here we address an unmet need in developing novel statistical methodologies to decode the origins of methylated cfDNA obtained from liquid biopsy samples. We demonstrate the far-ranging clinical utility of serial liquid biopsy sampling to complement and advance the standards of clinical care in oncology and other pathologies.