of our bup precision dosing approach in terms of clinical utility and attitudes by OUD patients and providers in clinics in PR, We will conduct focus groups and surveys to document patients and providers perceptions, beliefs, attitudes and reception of our bup evidence-based dosing approach. RESULTS/ANTICIPATED RESULTS: We seek to answer the following questions: How do OUD providers and patients in PR view, and how will they engage with our buprenorphine precision dosing approach? Will our intervention based in science be accepted be these individuals? What are their attitudes towards this? How they perceive the efficacy of this intervention to be? What are the barriers and facilitators of this evidence based intervention? This knowledge is crucial before clinical implementation is pursued, we expect to comprehend the unique attitudes and perceptions of these population that supports the successful implementation in the nearby future and enhance the innovation uptake of our bup dosing model for OUD in PR. DISCUSSION/SIGNIFICANCE: It is important that adequate assessments that assess acceptability and feasibility prior to implementation and while still in developmental phases are conducted to plan ahead for the implementation of interventions since innovation uptake depends largely on contextual factors, not just innovation effectiveness.

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Translation of novel multidisciplinary health technologies in the Ontario healthcare system: A case study of pharmacogenomic testing

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OBJECTIVES/GOALS: There is a need for high-quality and efficient translation of health technologies in the Ontario healthcare system. The goal of this project is to understand the decision-making processes of government expert groups developing recommendations for the system-level implementation of pharmacogenomic testing. METHODS/STUDY POPULATION: This prospective observational case study includes the Ontario Health Pharmacogenomics (PGx) Working Group focused on developing recommendations for a PGx testing implementation strategy in the province. Ontario Health is the government agency that oversees provincial healthcare planning and service delivery. Using qualitative ethnographic methods, we will observe and document the working group's activities over a 10-month period. Data collection involves meeting recordings, correspondences, researcher field notes, decision-making processes, and group characteristics. Using descriptive statistics and inductive qualitative analyses, the data will be examined to build theory and frameworks for knowledge translation. RESULTS/ANTICIPATED RESULTS: The results will be presented through a case report, process maps, decision milestones, visualizations, and procedural recommendations for future expert groups. This study will contribute to the body of foundational knowledge about translational sciences and support the National Center for Advancing Translational Sciences'guiding principles. To enhance translational processes and train the future translational workforce, this research can be used for educational initiatives. In addition, the observed processes will inform a theory about how expert recommendations are developed in public healthcare systems. DISCUSSION/SIGNIFICANCE: This research addresses a current gap in understanding around translational processes, government decision-making, and the development of recommendations for the adoption, implementation, and dissemination of the novel health technologies transforming public healthcare in Canada.

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Trends Between Periodontitis and Medial Arterial Calcification in Undiagnosed Type II Diabetes Mellitus.

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OBJECTIVES/GOALS: The overall objective of this study is to determine if medial arterial calcification (MAC) is an independent predictor of diabetes and to evaluate the relationship between MAC, periodontitis and Type II diabetes mellitus. METHODS/STUDY POPULATION: A retrospective case-control model analyzing radiographs for periodontitis and MAC to identify potential biomarkers for underlying systemic conditions, such as diabetes. Charts of patients attending UPENN School of Dental Medicine clinics between 2015 and 2022 were reviewed. Demographics, medical and dental history, diabetic status (identified by POC blood glucose level, fasting blood glucose and/or A1C), and medication history were documented amongst other variables. Patients aged 18 years or older with diabetes and having full mouth intraoral radiographs (FMX), panoramic radiographs and CBCTs were included. Patients with radiographs of poor quality were excluded. Multivariate analysis was used to determine possible associations between diabetes and periodontitis among persons with or without MAC. RESULTS/ANTICIPATED RESULTS: In our pilot study involving 28 participants, 53% of the population with moderate or severe periodontitis had MAC. By the Fisher's Exact Test, there was an association, meaning those with more periodontal disease are more likely to have MAC ($p=0.014$). Sixty-three percent of patients with diabetes had MAC, while 19% of patients without evidence of diabetes also had MAC, ($p=0.067$). There was not enough evidence of association between diabetes and presence of MAC at this time, due to a small sample size, however there was a high prevalence of MAC among the diabetics. We hypothesized that periodontitis, a condition that shares many risk factors with diabetes would also be associated with incident MAC. Findings from this study will be key for the implementation of preventive screening protocols and referral systems. DISCUSSION/SIGNIFICANCE: Diabetes is on the rise and about half of diabetics are undiagnosed. CBCT imaging frequently used in dentistry can detect incidental findings such as MAC. This study has the potential of detecting statistically significant links between MAC, periodontitis and diabetes, hence serving as a sensitive radiographic biomarker for diabetes.

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Unitary neural correlates of executive control in pediatric transdiagnostic psychopathology

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OBJECTIVES/GOALS: Childhood psychiatric symptoms are highly comorbid. Their co-occurrence and association with negative life

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outcomes is partially explained by deficits in executive control, or processes enabling self-regulation. Here, we test a novel executive neural target in three fMRI tasks and its relevance to shared psychopathology. METHODS/STUDY POPULATION: We studied 60 children [15 F/45 M; mean age (SD)=11.6 years (1.62)] with diverse diagnoses including attention deficit disorder (n=26) and autism spectrum disorder (n=22). We extracted a latent general factor of psychopathology using principal component analyses applied to parent-report Child Behavior Checklist syndrome scores. Subjects completed 3 executive control fMRI probes, tapping adaptive control, working memory, and inhibition. Correlational psychophysiological interaction (cPPI) analysis measured correlations between executive control-related modulations of activity in 414 network-affiliated parcels. We selected parcels exhibiting control-related cross-network correlations as well as control-related activity across all tasks and tested them for association with psychopathology. RESULTS/ANTICIPATED RESULTS: cPPI connectivity matrices were thresholded and graphs were identified using the Network-Based Statistic toolbox (p90th percentile PC) as well as control-related activation (>10% activated voxels; p DISCUSSION/SIGNIFICANCE: Our results examine cross-network interactions between brain regions during 3 fMRI tasks and their role in explaining individual variation in psychopathology. As executive control links to both comorbidity and life outcomes, identifying the clinically-relevant neural correlates of controlled behavior may lead to transdiagnostic treatments.

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Unraveling and targeting the innate immune response in Multisystem Inflammatory Syndrome in Children (MIS-C)

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OBJECTIVES/GOALS: The innate immune responses to Multisystem Inflammatory Syndrome in Children (MIS-C) are not fully known. Using samples from MIS-C, we will assess the cellular responses and develop a novel Tri-Specific Killer Engager (TRiKE) that engages innate immune cells to improve those responses. METHODS/STUDY POPULATION: We collected blood samples from 60 pediatric patients from which we isolated plasma and peripheral blood mononuclear cells. We received blood samples from 13 MIS-C, 32 severe acute COVID, 5 COVID-19 asymptomatic, and 15 COVID-19 negative patients. Using plasma, we then performed ELISAs to determine IgG antibody levels against SARS-CoV-2 and plaque reduction neutralization tests to determine neutralizing antibody functions. We isolated DNA to look at Fc receptor genetics. We also utilized utilize flow cytometry assays determine the phagocytosis and killing abilities of the innate cells from these patients. This data will be correlated with clinical outcomes. Additionally, we have developed a novel SARS-CoV-2 TRiKE which directs natural killer (NK) cell killing specifically to of COVID-19 infected cells. RESULTS/ANTICIPATED RESULTS: MIS-C patients had higher IgG antibody titers against SARS-CoV-2 compared to children with symptomatic or asymptomatic COVID. MIS-C patients also neutralized SARS-CoV-2 more effectively than children with acute symptomatic or asymptomatic COVID-19. We found natural killer cells and monocytes are dysfunctional in MIS-C patients and do not kill SARS-CoV-2 infected cells as well. Specifically, NK cells do not kill COVID-19 infected cells as well. To combat this, we have successfully generated and are now testing a Tri-Specific Killer engager (TRiKE) which binds one ends to NK cells, one end to the Spike protein on COVID-19 infected cells and contains IL-15 to improve NK cell function. We anticipate that we can improve NK cell killing of COVID-19 infected cells with this TRiKE. DISCUSSION/SIGNIFICANCE: We found that MIS-C patients have antibodies that can neutralize SARS-CoV-2 but that that innate immune cells that engage antibodies are dysfunctional. We are have successfully developed and are targeting this response with a TRiKE to improve innate immune cell functional; this may serve as an adjunctive therapeutic if proven successful.

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Upregulated Genes in Age-Related Lobular Involution Stagnation Represent Potential Biomarkers That Link To Increased Breast Cancer Risk*

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OBJECTIVES/GOALS: Age-related lobular involution (LI) is a physiological process of breast epithelial regression that occurs primarily during perimenopause (ages 45-55); women in this age range for which the process of LI is delayed, defined as LI stagnation, show significantly increased risk of breast cancer as compared to LI progression patients. METHODS/STUDY POPULATION: The Mayo Clinic Benign Breast Disease (BBD) cohort includes ~1000 women who had multiple sequential benign biopsies. 103 patients were found to have sequential biopsies during the perimenopausal period, of which 10 eventually progressed to breast cancer. These patients were assessed for LI stagnation vs LI progression by quantifying 10 lobules per slide and comparing median acini number and median lobule size between initial and subsequent biopsies from the same patients. RNA was derived from whole tissue sections from the initial biopsies, and profiled using NanoString IO360 and BC360, which were normalized using RUVg methods. Differentially expressed genes associated with LI stagnation were defined as having two-tailed, unpaired p-values less than 0.05. RESULTS/ANTICIPATED RESULTS: Analysis showed subsetting patient sets by time between biopsies improves classification of stagnant vs. progression. Differential gene analysis identified 37 genes associated with LI stagnation and LI progression, and 20 of these genes were found to overlap a set of 128 gnese that were differentially expressed between women who subsequently developed breast cancer vs remained cancer-free. These genes represent potential biomarkers of processes that link LI stagnation and increased breast cancer risk. DISCUSSION/SIGNIFICANCE: In future studies, we intend to study these genes that were shown to be upregulated in LI stagnation for their association with subsequent development of breast cancer in independent cohorts of women with BBD. We will use this knowledge to improve individualized risk assessment, which will help focus surveillance and prevention strategies.

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Using Assessments to Create a Translational Pipeline at a Science-Based Inpatient Addiction Treatment Facility

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OBJECTIVES/GOALS: Effective translation of data to inform real-time patient care is lacking in addiction inpatient settings. The

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