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CATEGORY A - Cardiovascular Biology and Neuroscience

Decreasing Alpha-Synuclein Through Reduction of Pftk1: Implications for PD Therapeutics

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ABSTRACT

Introduction | Parkinson's Disease (PD) is a debilitating neurodegenerative disease characterized by the abnormal accumulation of alpha-Synuclein (a-Syn) in Lewy bodies and neurites. In patients and model organisms, overexpression of a-Syn appears to drive toxicity, and its reduction is neuroprotective. Therefore, reducing a-Syn levels may be a promising therapeutic approach to treating PD. Moreover, achieving this via classical pharmacology is a minimally invasive approach, of particular importance in treating a chronic illness of the ageing population.

Methods | We previously identified druggable modulators of a-Syn levels via a large-scale screen of over 7,500 genes. The screen identified PFTAIRE protein kinase I (PFTK1), a kinase of largely unknown function, as a robust regulator of a-Syn levels. We genetically reduced Eip63E, the Drosophila homologue of PFTK1 in a Drosophila synucleinopathy model and measured locomotive ability. We also created a double mutant mouse line by crossing Pftk1(+/-) mice to a-Syn overexpressing mThy1-Snca(Tg/y) mice. Currently, we are testing this genetic interaction by behavioural, histological and biochemical analyses to determine if the double mutant mice mitigate Parkinson-like symptoms via reduction of transgenic a-Syn levels.

Results | In the Drosophila synucleinopathy model, loss of function of dPFTK1 rescued motor deficits. Preliminary data suggest that the double mutant Pftk1(+/-) ; mThy1-Snca(Tg/y) mice may show improved locomotion, procedural ability and gut motility, through pole, nesting, and fecal count tests.

Conclusion | Further testing will shed light on the potential of PFTK1 as a clinically relevant target for reducing a-Syn toxicity and ultimately treating PD.

Mapping Physiological Post-translational Modifications of Parkin in Human Brain

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ABSTRACT

Introduction| Recessive mutations in PARK2, the gene coding for Parkin, cause early-onset Parkinson's disease (PD). We have found that Parkin can act as a redox-active molecule. Parkin has a high number of cysteine residues (35; 7.5%), and we have demonstrated that through the oxidation of these cysteines, Parkin is able to reduce reactive oxygen species. In a similar manner, Parkin can covalently bind reactive nitrogen and quinone species to mitigate potentially harmful effects. This includes forming covalent adducts with dopamine and its metabolites through Parkin's cysteines. We postulate that the loss of this anti-oxidant function results in the selective degeneration of oxidatively demanding, dopamine-producing neurons in PD.

Methods | Liquid chromatography-based mass spectrometry is used to map cysteine modifications on recombinant and cellular-expressed human Parkin exposed to pro-oxidant conditions as well as Parkin derived from post-mortem human brain. The samples are sequentially incubated with iodoacetamide, dithiothreitol, and n-ethylmaleimide to differentially and irreversibly label oxidized vs. reduced (non-oxidized) cysteine residues.

Results | Our results reveal progressive oxidation of recombinant human Parkin cysteines by hydrogen peroxide. In parallel experiments, adducts of aminochrome, an oxidized metabolite of dopamine, are mapped at eight of the 35 available cysteines. Ongoing work aims to further map the cysteines that are most vulnerable to oxidation and/or dopamine adduct formation, and to compare these findings to Parkin purified from human brain.

Conclusion | By mapping the oxidation patterns of Parkin's cysteine residues we will gain better insight in its physiological role as a redox-active molecule in human brain.

CATEGORY A - Cardiovascular Biology and Neuroscience

Predicting Long Term Outcomes in MS with a Blood Test

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ABSTRACT

Introduction | With more powerful treatments for multiple sclerosis (MS), prognostic biomarkers are badly needed. Levels serum of neurofilament light chain (sNfL) result from the destruction of central nervous system (CNS) axons and correlate with the aggressiveness of the disease. Our objective was to evaluate the prognostic value of sNfL levels obtained close to MS onset in detemining long-term clinical outcomes.

Methods | In this prospective cohort study, we identified patients with serum collected within 5 years of first MS symptom onset with more than 15 years of follow-up. Clinical course, treatments and Expanded Disability Status Scale (EDSS) were recorded longitudinally. Levels of sNfL were quantified in the patients as well as non-inflammatory matched controls using digital immunoassay.

Results |Sixty-seven patients fit the inclusion criteria, median follow-up 17.4 years (range: 15.1-26.1). Median serum NfL levels were 39.8% higher in MS patients compared to the 37 controls (p=0.004). Patients reaching EDSS≥4 had 62.0% higher levels compared to the patients who did not (p=0.0001). The best NfL cutoff for predicting progression was 7.62 pg/mL; patients with NfL >7.62 pg/mL had 8.9-times higher risk of developing progressive MS (p = 0.034, 95% CI:1.2-68.1). Patients with the highest NfL levels (3rd-tertile) progressed most rapidly, EDSS annual rate 0.16 (p=0.004), remaining significant even after adjustment for sex, age, and disease-modifying treatment (p=0.022).

Interpretation |This study demonstrates that higher levels of serum NfL detected early in the disease are associated with poorer long-term clinical outcomes. These patients may benefit from a more aggressive initial approach to initial treatment.

Tranexamic Acid for Off-pump Coronary Artery Bypass Grafting Surgery

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ABSTRACT

Introduction| Tranexamic acid (TXA), an intravenous antifibrinolytic, has been shown to reduce bleeding in on-pump cardiac surgery. It's role in off-pump coronary artery bypass surgery (OPCAB) remains unclear. This study explores the usage, efficacy and safety of TXA in OPCAB surgery at a high volume OPCAB center.

Methods | We conducted a single center retrospective data-base review assessing IV TXA usage patterns, efficacy and safety in adult cardiac surgical patients who underwent primary elective OPCAB surgery. The primary outcome measure was cumulative chest tube drainage (CTD) 12h post-operatively. Secondary outcome measures included CTD at 3, 6, 24h post-operatively, chest tube duration, blood product transfusion, adverse events, ICU and hospital length of stay.

Results | 165 patients were identified. 74 patients received TXA and 91 did not. There were no statically significant differences between groups at baseline. The mean dose of TXA was 2.12 ± 1.7 g. Post-operative CTD was significantly reduced in patients receiving TXA at 12h postoperatively (337.4 ± 169.4 v 428.4 ± 188.4 mL, p < 0.002). No significant differences were observed for blood product transfusions, adverse events or hospital/ICU length of stay.

Conclusion |TXA was associated with decreased postoperative blood loss at all time points in OPCAB surgery, although there was no difference in blood transfusions or adverse events. Preferential administration of TXA to patients at higher risk of bleeding may have underestimated the efficacy of TXA . A prospective randomized controlled trial is needed to further explore the efficacy and safety of TXA in OPCAB surgery.

CATEGORY A - Cardiovascular Biology and Neuroscience

The Role of Irx5 in Establishing Ventricular Transmural Gradients

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ABSTRACT

Introduction | For harmonious contraction and relaxation of the heart, the subendomyocardial (ENDO) and subepimyocardial (EPI) regions of the ventricle are physiologically different, and the loss of this heterogeneity is associated with increased susceptibility to heart diseases, such as arrhythmias. However, the molecular and regulatory mechanisms preserving such regional differences remains elusive. Here, we show that Iroquois Homeobox 5 (Irx5), a transcription factor (TF) expressed in an ENDO-to-EPI gradient, is required for establishing transmural repolarization gradients.

Methods | To investigate transcriptomic heterogeneities within the ventricular wall in an Irx5-dependent and -independent manner, we utilize ENDO and EPI regions of left ventricle (LV) from adult wild-type (WT) and Irx5 knock-out (KO) mice to examine transcriptomic profiles using RNA-sequencing (RNA-seq) and bioinformatics analysis.

Results | RNA-seq data demonstrates distinct transcriptomic profiles in WT-ENDO and WT-EPI mouse hearts. In ENDO, TFs (Irx5, Hoxa4), hypertrophy-markers, contractile-fiber genes and calcium-regulators are enriched. In EPI, potassium channels and sodium/hydrogen transporters are enriched. Loss of Irx5 largely disrupts the transcriptomic ENDO-EPI gradient, demonstrated by the similarity between Irx5KO-ENDO and Irx5KO-EPI profiles. Nevertheless, transmural gradients for some spatiotemporal patterning TFs (Hey2, Etv1 and Bambi) persist even in Irx5KO, implying that Irx5 may cooperate with other signaling pathways during the initial gradient establishment. Moreover, IRX5 gradients are observed in pig and human LVs, suggesting a conserved role for IRX5 in the heart.

Conclusion | Our data demonstrates that the transcriptomic heterogeneities within the ventricular wall are largely regulated by Irx5. Future studies to examine the gene regulatory mechanism of Irx5 will be performed.

CATEGORY B - Innovative Therapeutics & Systems Biology

Characterizing Effects of Nuclear-Localized Endogenous Alpha-Synucein in a Novel Mouse

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ABSTRACT

Introduction | Parkinson's disease (PD) and related synucleinopathies are devastating neurodegenerative disorders characterized by the accumulation of misfolded alpha-synuclein (a-syn) throughout the brain. While a-syn is natively found in the synapse and the nucleus (hence its name), data from our lab and others have shown that the nuclear accumulation of a-syn is toxic and occurs in PD. The toxic mechanism(s) of nuclear a-syn remain(s) elusive.

Methods | We have created a mouse in which endogenous flag-tagged a-syn is localized to the nucleus via a nuclear localization signal (NLS) tag, termed the a-syn-NLS-flag mouse. Characterizing this novel mouse will provide insight into the potentially neurotoxic effects of nuclear-localized endogenous a-syn. We are characterizing this mouse line on behavioural, histological, and biochemical levels to determine whether these mice phenocopy aspects of synucleinopathy, specifically PD, over time (up to 18 months of age).

Results | Behaviour testing up to 10-months of age have currently been analyzed and a significant motor deficit has been observed in multiple motor assays. Histological and biochemical analyses of the young cohort revealed no significant neurodegeneration nor a-syn post-translational modifications at 2-months of age, suggesting that the motor phenotype observed at 10 months is not developmental in origin. Further research is focused on determining the behavioural, histological, and biochemical attributes of the 18-month-old mice to track the progression of pathology and determine whether these animals exhibit neurodegeneration.

Conclusion | Determining the presence and extent of the neurotoxic effects of nuclear-localized a-syn provides a meaningful step forward in elucidating the mechanisms of neurotoxicity that are involved in PD and related synucleinopathies.

Interferon-Induced Cytokines to Detect Interferon Signature in ANA+ Individuals

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ABSTRACT

Introduction | Increased expression of interferon (IFN)-induced genes, known as the IFN signature, is found in Systemic Autoimmune Rheumatic Diseases (SARD). We have previously shown that a subset of asymptomatic Anti-Nuclear Antibody (ANA) positive individuals (NS ANA+) have an elevated IFN signature and that they may be at increased risk for progression. However, the IFN signature is cumbersome to measure, limiting its clinical utility. It has been shown that levels of CXCL-10 and Galectin-9 correlate with the magnitude of IFN signature in SARD patients. Here we sought to determine whether a similar correlation is observed in NS ANA+.

Methods | Healthy controls (HC), NS ANA+, individuals with at least one SARD symptom (Undifferentiated Connective Tissue Disease, UCTD), or meeting SARD classification criteria were recruited. The expression levels of five IFN-induced genes were measured and summed to generate an IFN5 score. The concentrations of CXCL-10, galectin-9, and IFN-α were measured by Enzyme-Linked Immunosorbent Assay.

Results | Preliminary results in a subset of the study population, HC (n=8/49), NS ANA+ (n=22/83), UCTD (n=14/51), and SARD patients (n=30/58), showed higher levels of Galectin-9 and CXCL-10 in NS ANA+, UCTD, and SARD patients compared to HC. We observed weak correlations between IFN5 score with CXCL-10 ($r=0.22$, $p=0.047$), and Galectin-9 ($r=0.23$, $p=0.049$).

Conclusion | Our preliminary results suggest that higher levels of IFN-induced cytokines are observed in a subset of NS ANA+ individuals. If the strength of the correlation increases with inclusion of the entire study population, these cytokines may be useful as surrogate markers of the IFN signature.

CATEGORY B - Innovative Therapeutics & Systems Biology

High-Throughput Identification of Modifiers Effecting TDP-43 Localization to Understand ALS

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ABSTRACT

Introduction | Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease of the motor neurons. Although the majority of ALS cases are sporadic caused by de novo mutations or unknown mechanisms, a pathological hallmark of almost all cases is the nuclear-to-cytoplasmic mislocalization and aggregation of the RNA binding protein, TDP-43. Mislocalization of TDP-43 occurs upstream of aggregation, however the mechanisms driving cytoplasmic accumulation remains unclear. Identifying the forces underlying TDP-43 mislocalization will not only provide insight into the modes of neurotoxicity, but also identify potential avenues of interception.

Methods | Using a CRISPR/Cas9 knock-in approach, we generated cell lines that label endogenous TDP-43 with Green Fluorescent Protein (GFP). We ensured that the TDP-43-GFP fusion does not impact native TDP 43 function by assessing its localization, levels, and downstream targets. Building on this new cell line, we made and characterized a clone bearing the ALS-linked mutation Q331K. As TDP-43 pathology is observed in ALS cases without TDP-43 mutations, we performed a high content imaging screen to identify modifiers of wild type TDP-43 localization.

Results | We show that the ALS-linked mutation, Q331K, confers basal mislocalization and loss-of-function of TDP 43. Furthermore, we identified kinases that affect the localization of TDP-43 and may contribute to ALS pathology.

Conclusion | Our results provide insight into potential mechanisms causing TDP-43 pathology in ALS. Further studies will dissect the mechanisms in the context of ALS to identify avenues of therapeutic interception and better understand the causes of ALS.

CATEGORY C - Medical Educations, Patient Care, and Public Health

Pediatric Stroke Protocols in Canada

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ABSTRACT

Introduction | Pediatric acute ischemic stroke (AIS) occurs in 3/100,000 children annually. Pediatric AIS is diagnosed with a median delay of 23 hours after symptom onset due to a lack of early identification. Due to the diagnostic delay, most children with AIS will not be identified within the window for tissue plasminogen activator (tPA) administration, which is a thrombolytic drug used for AIS treatment. Pediatric stroke protocols have shown to decrease time to diagnosis. This study aims to understand the current landscape for management of pediatric stroke across Canada.

Methods | We contacted pediatric neurologists across 16 pediatric hospitals to inquire about their stroke management.

Results | Our response rate was 100%. Seven centers have an official protocol, and two have a protocol that is under development. Seven centers do not have a protocol – two redirect their patients to adult neurology, and five rely on a collaborative local expert approach to manage AIS. Analysis of the seven protocols revealed differences in: 1) age cut-off for IV-tPA treatment; 2) application of intra-arterial tPA; 3) exclusion criteria for tPA administration and; 4) variation in the time window for mechanical thrombectomy.

Conclusions | The seven protocols differ substantially in their level of detail and content. We aim to understand the basis for discrepancies via a teleconference discussion and a literature search. Our overarching aim is to raise awareness of pediatric stroke and improve the acute management of those critically ill children, with the ultimate goal of minimizing irreversible neurological deficits

Using Placenta Pathology to Identify High Cardiovascular Risk following preeclampsia

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ABSTRACT

Introduction | Preeclampsia (PE), a hypertensive pathology of pregnancy, is independently associated with premature cardiovascular disease (CVD). Therefore the postpartum period offers an opportunity for CVD risk screening and preventative intervention. Considering 50% of women with PE are low-risk, new modalities to identify potentially high-risk women are warranted. We propose placenta pathology as a means of high-risk identification, flagging a PE subclass with a predominant utero-placental vascular disorder whom can be referred to postpartum clinics for CVD risk screening.

Methods | 50 women with singleton pregnancies complicated by PE were followed until six months postpartum at the Maternal Health Clinic. Biochemical and clinical characteristics were used to calculate a lifetime CVD risk score (≥39%=high-risk). Clinical placenta pathology examinations were blindly performed in terms of the presence, absence and severity of 30 microlesions. Logistic regression and receiver operator curve analysis were used to assess the accuracy of placenta pathology findings to predict CVD risk.

Results | 70% of high-risk women had maternal vascular malperfusion lesions (OR:4.10[2.55-7.45]) while 55% of low-risk women had chronic inflammation lesions (OR:2.82[0.60-13.24]). Placenta pathology demonstrated a 68% accuracy for high CVD risk prediction, increasing to 93% (sensitivity:94%, specificity:67%) when basic clinical variables were added.

Conclusions | Poor utero-placental perfusion is more prevalent in high-risk women, whereas chronic inflammation is more prevalent in low-risk women. This demonstrates that CVD risk profiles of PE patients may depend on the type of underlying placental disease providing insight on the potential cost-effective benefits of placental pathology as a means of high-risk identification at delivery.

CATEGORY C - Medical Educations, Patient Care, and Public Health

Early and Late Outcomes After Surgery for pT4 NSCLC Reclassified by AJCC 8th Edition Criteria

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ABSTRACT

Classically, pT4 non-small cell lung cancers (NSCLC) are tumours of any size with features of local extension, often precluding surgical resection or necessitating complex extended pulmonary surgery. However, the new AJCC 8th edition includes tumours greater than 7cm regardless of adjacent organ extension. Our goal is to examine perioperative and long-term outcomes from pT4 resections based on the AJCC 7th edition versus those of the expanded criteria of the 8th edition.

We retrospectively reviewed pT4 surgical resections at the Montreal General Hospital from 2011 to 2018 and identified 158 patients with pT4 tumours based on AJCC-8: 40 by AJCC-7 criteria (Group 1) and 118 with tumors >7cm considered pT4 in AJCC-8 (Group 2). Both cohorts have similar long-term outcomes, as demonstrated by similar overall survival (75% at 1 year, 41% at 3 years and 32% at 5 years), median overall survival (25.8 and 27.4 months for Group 1 and 2, respectively; p=0.7) and recurrence rate (25% vs 27%; p=0.8). Nevertheless, Group 2 has better peri-operative survival than Group 1: 99% vs 92% 90-day mortality (p=0.02) and 95% vs 83% 6-month mortality (p<0.01). Furthermore, Kaplan-Meier curves adjusted for predictors of survival with Cox regression analysis show early mortality in Group 1 with equalization of the curves at 1 year. Finally, 80% of patients in Group 2 were disease-free at last follow-up compared to 58% for Group 1 (p=0.17).

In conclusion, outcomes from pT4 NSCLC resections must be contextualized to the increasingly heterogeneous classification offered by the new AJCC-8 staging system.

Does the World Health Organization Assess Health Equity in Guidelines?

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ABSTRACT

Introduction | The World Health Organization (WHO) uses the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework to develop clinical guidelines. The GRADE group developed the Evidence to Decision (EtD) framework, which promotes the assessment of health equity implications, acceptability and feasibility. This was adopted into the WHO guideline development process in 2014. This study aims to assess health equity considerations in WHO guidelines since the adoption of the EtD framework.

Methods | We developed an extraction form to evaluate health equity considerations in WHO guideline review committee (GRC) approved guidelines published from 2014 to May 2019. We used the PROGRESS (Place, Race, Occupation, Gender, Religion, Education, Socioeconomic Status, Social Capital) Framework to identify disadvantaged populations in guidelines and evaluated how health equity was assessed using the GRADE equity criteria.

Results | We evaluated 110 guidelines published in this period focused on sexual and reproductive health (22.7%), Nutrition (16.4%) and Tuberculosis (13.6%). Most (71.8%) of the guidelines included equity as criteria in the formulation of recommendations. About half (46.4%) described the target audience for the guidelines using PROGRESS with socioeconomic status being the most frequent (56.9%). Most (91%) of the guideline development groups consisted of representatives of disadvantaged populations. Over half (52.7%) of the included guidelines used the EtD framework. All of those guidelines considered health equity in recommendation implementation.

Conclusion | Guidelines using the EtD framework report more equity considerations. Acknowledgment and a priori elaboration of how health inequities will be assessed in guideline development may help resolve issues of social injustice.

Investigating Suicidal Behaviours and Cortical Thickness in Frontal Brain Regions

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ABSTRACT

Introduction | Our knowledge of the neurobiology of suicide has been limited. This study compared cortical thickness measures of the frontal regions in individuals with and without a lifetime history of suicidal behaviours in patients with treatment-resistant major depressive disorder (MDD).

Methods | Structural brain correlates associated with suicidal behaviours (SB) were assessed using magnetic resonance imaging (MRI) in 29 participants with a lifetime history of suicidal ideation and a current diagnosis of treatment-resistant MDD. Suicidal behaviours are defined as any actual, interrupted or attempt history as well as preparatory acts or behaviours. T1-weighted structural images were collected on a 3T Siemens MR-PET system using a multi-echo magnetization-prepared rapid gradient echo (MPRAGE) protocol. Cortical reconstruction and segmentation were performed using FreeSurfer-6.0.0. SB was assessed using the Columbia Suicide Severity Rating Scale and depressive symptoms were assessed using the Montgomery-Asberg Depression Rating Scale.

Results | Controlling for age and depression severity, a univariate analysis revealed a significant difference between individuals with and without suicidal behaviours in the right anterior cingulate cortex ($p=0.026$), the right medial orbital frontal cortex ($p=0.007$) and the right rostral middle frontal cortex ($p=0.007$). No significant associations were found in the left hemisphere of the proposed regions.

Conclusion | Contrary to our hypothesis, individuals with a lifetime history of suicidal behaviours had a thicker anterior cingulate cortex, rostral middle frontal cortex and medial orbitofrontal cortex in the right hemisphere. Further research is required to further investigate the involvement of these regions of interest in the etiology of suicidal behaviours.

Artificial Intelligence in Rheumatology for Improving Models of Care

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ABSTRACT

Medical decision-making is becoming increasingly complex due to rapidly expanding knowledge and increasing burden of chronic comorbidities and medications, which will continue to contribute to worse patient outcomes and increased costs. Several advancements in Rheumatology Models of Care (MOC) have alleviated these challenges with limited success, however innovations in MOC that assist with complex decision making and redefine Rheumatology workflow are needed. Recent advancements in Deep learning Artificial Intelligence (AI) technology have provided a platform with enormous potential that can assist us in completely redefining our concept of healthcare delivery and medical practice. It is also being used to analyze thousands of patient data sets and medical literature to predict disease morbidity and assist physicians in making the best possible treatment decisions for each individual patient. There are several areas within the Rheumatology MOC framework that we can target for inefficiencies, including referral and triage, medical management, and patient self-management. Several Chatbot assistants have been developed that are capable of interacting with patients through natural language text in order to take detailed histories, provide a likely differential diagnosis, as well as answer personal questions. Furthermore, personal home assistant devices have also been developed to improve patient self-management. Although there are many potential benefits of AI, we have yet to thoroughly study its effectiveness on patient outcomes and cost effectiveness to support widespread implementation. Despite its current limitations, AI provides us with a powerful tool that can be used as a platform to redefine medicine and improve quality of care.

Interventions to Prevent Anastomotic Leakage after Esophageal Surgery: A Meta-analysis

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ABSTRACT

Importance| Anastomotic leakage is a common and serious complication among patients following esophagectomy. Many methods designed to minimize anastomotic leak have been proposed and utilized.

Objective| To provide a synthesis of the published literature on the efficacy and safety of existing methods to minimize esophagogastric anastomotic leak.

Evidence Review| We searched MEDLINE and Embase from 1946 to January 2019 for randomized controlled trials investigating any interventional technique to minimize esophagogastric anastomotic leakage. Two reviewers independently reviewed 441 abstracts to identify candidate articles. Random effects meta-analyses were performed to calculate pooled risk ratios and 95% CIs for primary and secondary outcomes.

Findings| Seventeen RCTs (ranging from 40 to 515 participants) met full inclusion criteria and were included in the systematic review, 12 studies were pooled across 3 interventions. Esophagectomy patients that received omentoplasty had an 88% lower risk of leakage [RR: 0.22; 95% CI: 0.10, 0.50; I2 0%] compared to no flap (3 studies, n = 611 patients). Esophagectomy patients with no NG tube or early removal demonstrated a significant 88% reduction in risk of leakage [RR: 0.12; 95% CI: 0.02, 0.65; I2 0%] compared to prolonged (7-10 days) NG tube decompression (2 studies, n = 293 patients). Esophagectomy patients that received stapled anastomosis had an 8% reduction in risk of leakage [RR: 0.92; 95% CI: 0.45, 1.87; I2 40.1%] compared to hand-sewn (6 studies, n = 1454).

Conclusion| Our review demonstrated that there is high quality evidence that omentoplasty significantly reduces the risk of AL. There was low quality evidence that early (or no) NG tube decompression reduces the risk of AL. The risk of AL among patients that received stapled versus hand-sewn techniques was similar. Therefore, there is a need to further clarify the role of interventions to prevent AL.

Early Initiation of Substance Use and Adolescent Distress

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ABSTRACT

Objective | To examine sex differences in the association between substance-use related behaviours (binge drinking, alcohol use disorders, cannabis use, and substance use disorders), age of substance initiation, and psychological distress (as measured by the K6 scale) in high school students.

Methods | Data were obtained from the Ontario Student Drug Use and Health Survey, a cross-sectional questionnaire regarding drug use and demographic and health information administered to students in grade 7 to 12. The sample for analysis included 4,543 high school students (50.3% male). Sex-stratified multivariate regression analysis was performed to assess the association between substance-related behaviours, age of substance initiation, and distress. There was no significant interaction between substance use and age of initiation.

Results | There were no sex-specific associations between substance use behaviours and psychological distress. >2 times past- month cannabis use (Adj-ORMALE = 2.63, 95% CIs = 1.42-4.85; Adj- ORFEMALE = 2.15, 95% CIs = 1.06, 4.37) but not past-month binge drinking or hazardous drinking (AUDIT >8) was associated with severe psychological distress after controlling for grad, education, and subjective social standing. First trying alcohol or cannabis in grade school was also associated with severe distress independent of current substance use (Adj-ORMALE = 4.27, 95% CIs = 1.89-9.97; Adj- ORFEMALE = 3.34, 95% CIs = 2.26, 4.94).

Conclusion | These findings reinforce the potential links between cannabis use and distress among high schoolers and emphasize the need to discourage the initiation of substance use at early ages.

Une Étude Qualitative sur L'Acharnement Thérapeutique dans un Hôpital Universitaire

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ABSTRACT

Introduction | La problématique aborde les admissions de patients de centre soins de longue durée (CSLD) en Centre hospitalier de soins aigus (CHSA). Dans la région d'Ottawa, on constate un nombre important d'admissions évitables, voire futiles, de bénéficiaires provenant de CSLD alors que les soins pourraient être prodigués en milieu d'origine. Ils peuvent aussi demeurer en soins hospitaliers aigus pour un séjour de durée indue avec des investigations et traitements qui ne coincident pas à leur plan de traitement. en CLSD Une hypothèse est que cette problématique est accentuée dans un hôpital universitaire.Cette étude préliminaire vise à de dresser un modèle élucidant les étapes impliquées dans la prise de décision d'admettre un patient de CSLD à l'hôpital.

Méthode | On échantillonne cinq CLSD dans le rayonnement de l'Hôpital Montfort, de jurisdiction municipale, privée et provinciale. Leurs gestionnaires ont été contactés pour établir les personnes-clé, les considérations et les démarches effectuées avant le transfert du patient à un CHSA. La prise en charge hospitalière sera ensuite examinée par un médecin hospitaliste soulevant la problématique. Après cette démarche initiale, un schéma général des étapes décisionnelles est élaboré.

Résultats (escomptés) | Nous comptons identifier les étapes-charnières et les professionnels de la santé impliqués dans la décision de l'admission du patient. En abordant les facteurs généraux et spécifiques influençant cette prise de décision, i.e. cliniques, émotionnels et logistiques, nous pourrons déceler des points d'amélioration pour cibler des admissions plus pertinentes ainsi que réduire la durée de séjour de ces patients spécifiquement.

Conclusion | Créer un modèle décisionnel efficace.

Barriers to Timely Use of Infliximab for Severe Immune Checkpoint Inhibitor-related Colitis: a Single Centre Audit

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ABSTRACT

Immune-checkpoint inhibitors, used as effective cancer therapeutics, have been shown to cause immune-related colitis/diarrhea in up to 45% of patients. To prevent complications, timely management is critical. Guidelines suggest administering infliximab within three days of severe steroid-refractory immune-related colitis/diarrhea. This study audits the management of severe immune-related colitis/diarrhea at a single centre to understand whether suggested targets are being met and to identify barriers to rescue therapy.

In this retrospective chart audit, all instances of infliximab administration at The Ottawa Hospital between 2014 and 2018 were screened through pharmacy records. Patients treated with immune checkpoint inhibitors for cancer were selected. Patient demographics and data of each patient's cancer profile, colitis/diarrhea management and infliximab screening were collected.

Of 197 patients receiving infliximab between 2014 and 2018, 8 received it for the management of severe immune-related colitis/diarrhea. With one patient non-evaluable, 2/7 patients required multiple admissions until either gastroenterology intervention or infliximab. In total, the median time from onset of severe diarrhea to infliximab administration is 12 days (range: 8-54 days). Prior to infliximab administration, 1/8 (12.5%) and 2/8 (25%) patients did not get screened for hepatitis B and tuberculosis, respectively.

To optimize management, gastroenterology intervention should occur prior to the onset of severe symptoms. Further research is required to optimize the characterization of all gastrointestinal toxicities in order to efficiently diagnose immune checkpoint inhibitor-related colitis/diarrhea. Furthermore, screening for tuberculosis and hepatitis B should be more heavily enforced prior to infliximab administration as preventative measures against (re)activation and complications.

Left Atrial Appendage Function at Cardiac Surgery Predicts Post-Operative Events

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ABSTRACT

Background | Post cardiac surgery stroke is a potentially devastating complication that carries a 3-6 fold increase for in-hospital mortality and seen in up to 2-5% of cardiac surgical cases. Atrial fibrillation (AF) is an important risk factor for the development of post operative stroke and occurs in up to 40% of cases following cardiac surgery. Pre-operative paroxysmal-AF (P-AF) may be clinically silent and may predispose to post-operative AF. P-AF may lead to reduced emptying of the left atrial appendage (LAA) with subsequent thrombus formation. We hypothesized that LAA function would predict post cardiac surgery atrial fibrillation and stroke.

Methods | A retrospective analysis of TEEs in consecutive patients in sinus rhythm undergoing cardiac surgery was performed. We identified consecutive cases from the UOHI clinical Peri-operative Cardiac Anesthesia Database. Using optimized TEE windows, LAA function was assess using LAA –EF and LAA-max. Clinical follow up was recorded in the Cardiac Anesthesia Database. Analysis of univarible and multivariable clinical and echocardiographic parameters was performed to determine the influence of LAA function to predict post operative cardiac surgery events. In P-AF the LAA function is reduced during periods of AF and sinus rhythm. LAA function may therefore serve as a predictor of P-AF and potential stroke3. LAA function can be determined at the time of cardiac surgery by measuring the LAA ejection fraction (LAA-EF) or the maximum emptying velocity of blood from the LAA (LAA-max) using intra-operative transesophageal echocardiography (TEE).

Non-Invasive Detection of IDH Mutant Gliomas by Magnetic Resonance Spectroscopy

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ABSTRACT

Background | Genetic mutations to isocitrate dehydrogenase (IDH) are highly prevalent in cerebral gliomas and can serve as prognostic indicators for disease. IDH-positive tumours characteristically produce the oncometabolite 2-hydroxygluarate (2-HG) in abnormally high concentrations. Our objective was to examine the feasibility of using magnetic resonance spectroscopy (MRS) to non-invasively detect levels of 2-HG in gliomas.

Methods | From 2015 to 2019, sixty-eight subjects who underwent surgical resection of glioma at our institution were prospectively included in the study. For all subjects, MRS was performed both during pre-operative planning and immediately (within 24-48 hours) after surgery. Two long-echo MRS protocols ([PRESS, TE 97ms, voxels 1-8 cm3, acquisition time ~5min], [SEMI-LASER, TE 110ms, voxels 1-8cm3, acquisition time ~5-10min]) were used. IDH mutation status specific for the R132H mutation was assessed by immunohistochemistry and/or amplicon DNA sequencing.

Results | Of the included subjects, 61.7% were male and 82.5% were Caucasian. The most common chief complaint, tumor location and affected cerebral hemisphere were seizure (39.7%), frontal lobe (45.5%), and left side (51.4%), respectively. The frequency of WHO grades II, II and IV for all included gliomas were 16.1%, 25.0% and 58.8%, respectively. Post-operative pathologic data showed that 19 out of 68 gliomas (27.9%) were IDH-positive. Using a Cramér–Rao lower bound (CRLB) of <30%, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of MRS for detecting IDH-positive mutants were 50%, 87.7%, 62.5% and 81.1%, respectively.

Conclusion | Our results suggest that MRS can identify in-vivo IDH-positive gliomas through 2-HG detection with high specificity.

ED Visits and Hospitalizations: Does Language Matter?

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ABSTRACT

Introduction | Patients who face language barriers are less likely to follow health prevention guidelines and to adhere to treatments. Consequently, these patients may be more likely to utilize healthcare services for exacerbations of their chronic conditions. The objective of this study was to 1) compare the rate of emergency department (ED) visits and hospitalizations across linguistic groups in Ontario, and 2) determine whether neuropsychiatric comorbidities modify the rate of ED visits and hospitalizations within each linguistic group.

Methods | We conducted a population-based retrospective cohort study in Ontario using administrative databases. We included Ontario residents who completed a home care assessment from April 1, 2015 to March 31, 2017. We identified all ED visits and hospitalizations within 1 year of the first home care assessment. We estimated the rate of ED visits and hospitalizations using a Poisson regression.

Results | At baseline, Allophones (i.e., patients whose primary language is not English or French) had the lowest rates of ED visits and hospitalizations. Compared to Anglophones, Francophones had similar rates of ED visits and hospitalizations but significantly longer hospital stays. After adjusting for potential confounders, both Allophones and Francophones had lower rates of healthcare utilization. The rates of ED visits and hospitalizations was lower for patients with stroke and dementia and higher for patients with other psychiatric comorbidities, and there was no synergistic interaction between patient language and neuropsychiatric comorbidities.

Conclusion | Home care recipients whose primary language is not English are less likely to utilize healthcare services, even after adjusting for potential confounders.

International Relations in pre-OMSAS Admissions and pre-CaRMS Residencies at uOttawa, 1951-1961

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ABSTRACT

Introduction | Today, both the admissions and residency matching processes are significant stressors for Canadian medical students. This historical case study employs the variable of International Relations (IR) to help explain the origins of systems used in Canada to select medical students and eventually match them to residency spots. The Faculty of Medicine at the University of Ottawa opened in 1945. Medical students from across Canada and several foreign countries were admitted to undertake 6 years of training: 2 years of "pre-med" to learn basic sciences; a 4-year medical degree including a 1-year internship in an Ottawa hospital; finally, a residency to pursue specialist training (not required for general practice). Method: For each medical graduate between 1951 -1961, the related demographic, biographic, and institutional information was compiled in a database and analyzed quantitatively and qualitatively. These data were collected from yearbooks (created by students themselves) and cross-referenced with archival documents and student records in the University of Ottawa Archives.

Results | Preliminary findings indicate that IR played a determining role in higher admission rates for students in particular foreign countries, notably the United States and China, and in a sizable number of Canadian graduates who chose to do residencies in the United States. Many never returned to Canada. Discussion: Investigating the role of IR in admissions and in graduates' decisions about where to do a residency illuminates the historical development of complex and sometimes problematic systems such as the Ontario Medical School Application Service (OMSAS) and the Canadian Resident Matching Service (CaRMS).

A Competency-Based Continuing Professional Development for Routine Pessary Care in Primary Care

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ABSTRACT

Introduction | Pelvic organ prolapse affects up to 50% of parous women and causes significant morbidity. Vaginal pessaries are recommended as first-line management for these patients. Routine Pessary Care (RPC) is within the scope of practice of family physicians (FPs), though training opportunities are limited. Evidence suggests that continuing professional developments (CPD) without practice-based reinforcement strategies have little impact on changing physician practice. To address this gap, we developed a simulation-based CPD program to teach RPC and measured the impact of reinforcement strategies on the integration of RPC skills in FPs' practice.

Methods | Eighteen academic FPs participated in a two-hour simulation-based CPD session on RPC. We reinforced their training by incorporating a procedure template within their electronic medical record and transferred the RPC care of their eligible patients from our women's health clinic (WHC) to them. We evaluated: 1) the proportion of RPC visits to the FPs after the intervention, 2) FPs' confidence before, immediately after and 12 months after the intervention, and 3) the quality of RPC before and after the intervention.

Results | We observed: 1) a significant improvement and maintenance of FPs' confidence in providing and teaching RPC after the CPD; 2) an increase in the proportion of visits for RPC care provided by FPs versus the WHC; and 3) no difference in the quality of RPC provided by FPs versus WHC.

Results | Although our participant numbers are small, this study suggests that reinforcement strategies can be successfully incorporated into procedural CPDs and lead to practice change.

Improving Medical Students' Competence in French through Clinical Skills Workshop

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ABSTRACT

Introduction | In Canada, it is much easier to access a physician who speaks English than a physician who speaks French.1,2 This leaves numerous Francophone patients struggling to access appropriate healthcare and leads to some of the health disparities observed between Anglophones and Francophones.1,3 Our goal is to provide medical students with training to enhance the quality of care they deliver to Francophone patients.

Methods | Prior to Clerkship, uOttawa medical students are offered the opportunity to engage in a French Clinical Skills Workshop. During the workshop, students attend a lecture by a Francophone physician followed by a 5-station OSCE-style circuit where they practice their history and physical examination skills in French. Individualized feedback is provided by the physician tutor throughout each encounter. Participants are surveyed at the end of their third year regarding their experiences with Francophone patients to evaluate the effectiveness of the workshop.

Results | In 2018, the first workshop was held with eight MD2020 students. About half used French to communicate with a patient once per rotation (42.9%; n=7), and the same used it a few times per week (42.9% n=7). Most students agreed or strongly agreed that the workshop improved their encounters with Francophone patients (71.4%; n=7).

Conclusion |The French Clinical Skills Workshop improved students' communication with Francophone patients. The next workshop will be held in August 2019 with twelve participants. In the future, this workshop will be scaled up and implemented at other medical schools across Canada with the aim of improving care to Francophone patients.

Publication Bias in the Diagnostic Imaging Literature

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ABSTRACT

Objective | To evaluate whether imaging diagnostic test accuracy conference abstracts with positive conclusions or titles are more likely to reach full-text publication than those with negative (or neutral) conclusions or titles.

Methods | Diagnostic accuracy research abstracts were included if they were presented at the 2011 or 2012 RSNA conference. Full-text publication status at 5 years post conference abstract submission was determined. Conclusion and title positivity of conference abstracts were extracted, as well as potential confounding factors. The associations of conclusion and title positivity with publication status at 5 years post conference abstract submission were assessed using a multivariable logistic regression model. Conditional odds ratios were calculated to express the strength of associations, adjusting for the confounders.

Results | 282/400(71%) of included conference abstracts reached full-text publication. 246/337(74%) conference abstracts with positive conclusions resulted in full-text publications, compared to 26/48(54%) with neutral conclusions, and 5/15(33%) with negative conclusions. In multivariable logistic regression, conclusion positivity was significantly associated with full-text publication (odds ratio 3.6; 95% CI: 1.9-6.7 for conference abstracts with positive conclusions, compared to those with non-positive conclusions); this did not apply to title positivity (odds ratio 1.2; 95% CI: 0.47-3.0).

Conclusion | Imaging conference abstracts with positive conclusions were more likely to be published as full-text articles. Title positivity was not associated with publication. This preferential publication pattern may lead to an over-representation of positive studies in the literature. An over-representation of positive studies may contribute to inflated estimates of test accuracy and has the potential to adversely influence patient care.

A Prioritization Framework for Test-Ordering Feedback Interventions

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ABSTRACT

Introduction | Lab testing is argued to be a precursor for 70% of all medical decisions.[1] Considering that 20-50% of tests may be inappropriately ordered,[2] reduction of inappropriate use is a clear target for improving efficiency and care. Audit and Feedback (A&F), the collection of performance data and presentation of the results to care providers, can be an effective intervention for changing practices like test ordering, on average showing improvement of 4% in desired behaviours, with 25% of studies showing better than a 16% improvement.[3] While many decision makers have large datasets on test-ordering practices that could serve as the basis for an A&F intervention, there is no clear guidance on how to prioritize which tests should be targeted for intervention first.

Methods | Our objective is to develop a prioritization framework that will assist feedback developers in determining which tests should be the targets of feedback intervention. This work will involve two approaches, 1) a scoping review of the factors that guided previous test ordering prioritization decisions, and 2) interviews of experts who will inform and modify the draft framework developed based on the review.

Discussion | Our framework will ensure that feedback providers are able to systematically choose which tests are the best candidates (e.g. most cost effective, highest volume) to target for intervention. The framework will provide decision makers with the factors and considerations relevant to selecting between target tests. In the long term, the impact should be an increased efficiency of resource utilization and improved clinical decision making.

Image-Guided Radiofrequency Ablation of Benign Thyroid Nodules: A Literature Review

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ABSTRACT

Introduction | Thyroid nodules (TN) are common clinical problems traditionally treated with surgery or radioiodine therapy leading to adverse events while being costly and time consuming. More recently, novel nonsurgical techniques of radiofrequency ablation (RFA) are being used to treat TNs. Thus, it is of importance to evaluate the methodology, efficacy, safety and utility of RFA in treating TNs.

Methods | A systematic literature search was performed on four health databases: PubMed, Embase, WEB OF SCIENCE and the Chochrane library.

Results | This search yielded 28 studies from 2006-2017, incorporating 2639 patients with 2870 TNs treated with RFA. Here we review principles, history and techniques of RFA including the moving shot technique and fixed electrode technique. Additionally, we address brand and manufacturer of equipment used in RFA procedure, complications, costs and reoccurrence of nodules after RFA. We also evaluate factors that may influence the efficacy of RFA in treating TNs. These include: initial nodule volume, initial nodule solidity, initial nodule functionality, vascularization, training of RFA operators, energy delivered per nodule volume and number of RFA sessions.

Conclusion | Overall, the findings display the efficacy and safety of RFA in treating TNs. Although some literature favours treating predominantly smaller and cystic nodules with short and powerful sessions of RFA for greater efficacy and safety, there still remains uncertainty around the elements that influence efficacy. RFA shouldn't necessarily replace surgery, despite being a promising candidate. Instead, it can play an effective complementary role in the management of nodules and presents alternatives for practitioners.

Pre-analytical Specimen Labelling and Processing Errors in the ICU

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ABSTRACT

Introduction | Specimen rejections have been associated with increased in-hospital stay and cost. Majority of errors can occur in the pre-analytic phase involving specimens improperly collected, mislabelled or lost. Finally, specimen rejection can lead to high rate of recollection, delay in result availability and high rate of test abandonment. These factors can ultimately affect patient care and safety.

Methods | Retrospective review of Patient Safety Learning System (PSLS) reports and prospective review using interviews, surveys and process mapping.

Results | From 2098 PSLS reports for the ICU at The Ottawa Hospital – General Campus between 2010 to 2018, 52.6% of these reports were related to laboratory specimen collection and processing (pre-analytic phase). Of note, 9.8% of pre-analytical error reports were due to specimen mislabelling with wrong patient identifier and 16.4% were due to non-sufficient quantity (NSQ) of specimen. Examples of NSQ samples were INR specimen with insufficient amount of blood in tubes leading to rejection by machine. Cytology specimens make up 12.2 % of pre-analytical error reports.

Conclusion | Pre-analytical errors are not only costly and resource draining but may place a burden on patients. Areas where potential errors can occur include; 1. Patient labels and requisitions stored in cabinets, 2. Inconsistencies between specimen labels and requisitions, 3. Lab manual not up-to-date, difficult to access and lacking information, 4. Discrepancies between physician orders and requisition tests, 5. Non-sufficient quantity specimen collection. In the future we hope to start new initiatives to tackle these issues in hopes to improve patient safety and hospital efficiencies.

Cardiac Sarcoidosis: Relationship between PVC Burden, Disease Activity and Steroids

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ABSTRACT

Introduction | Ventricular tachycardia (VT) commonly occurs in cardiac sarcoidosis (CS). In these patients, increased immunosuppression (IS) is often used in response to recurrent VT despite minimal data supporting this recommendation. We sought to explore the relationship between PVC burden (from ICD diagnostics), disease activity and corticosteroid use in patients with new onset clinically manifest CS.

Methods |A single center, prospective cohort study was performed on CS patients with ICD devices. Data was collected for each device interrogation visit for all patients in the study. The daily average PVC count was then calculated using the total PVC count since the last visit and the total number of days since the last visit. Each inter-visit period was classified into 1 of 3 subcategories based on the patient's current treatment.

Results | A total of 20 patients with mean age 59.7 ± 7.7 years were recruited (63% of patients were female) and 82 inter-visit periods were analyzed. Summary data is shown in the table. Patients with active untreated CS had an average of 496.4 ±879.1 PVCs per day. After treatment with steroids the average PVC count increased to 2041.3 ± 2641.7 per day. Eighteen patients were not on steroids at time of device implantation and of these 16/18 (89%) had an increase in PVC burden after steroid initiation.

Conclusion| This study demonstrates a four-fold increase in daily PVC count in clinically manifest CS patients actively treated with corticosteroids. 16/18 patients (89%) had an increase in PVC burden after steroid initiation.

The Association between Concurrent Clarithromycin and DOAC Use and Hemorrhage

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ABSTRACT

Background | Direct oral anticoagulants (DOACs) are used in the treatment and prevention of venous thrombosis and the prevention of stroke in atrial fibrillation. Clarithromycin, a commonly prescribed antibiotic, alters DOAC metabolism, resulting in a postulated increased risk of hemorrhage. However, there have been no studies demonstrating increased incidence of hemorrhage with combined use of these medications.

Methods | We conduct a population-based, retrospective cohort study of patients prescribed a DOAC (dabigatran, apixaban, rivaroxaban) in Ontario, between 1995 and 2015. Adjusted cox proportional hazards are performed to determine the association of hemorrhage with clarithromycin use compared to fluroquinolones. An additional self-controlled case study (SCCS) is done to examine periods of use to non-use of clarithromycin compared to fluroquinolones and the relative risk of hemorrhagic events among DOACs users. Our primary outcome is a hemorrhagic event requiring hospitalization or emergency room visit within 30-days of antibiotic initiation.

Results | 21,958 eligible patients were prescribed clarithromycin (n=2,699) or fluroquinolones (n=19,259). The 30-day adjusted relative risk of hemorrhage is similar with clarithromycin use compared to fluroquinolones (n=110 events, HR 1.48 95%CI 0.88-2.50). Using the SCCS design, a total of 982 events occurred (185 with clarithromycin, 797 with fluroquinolones). A higher risk of hemorrhage was observed with exposure to either antibiotic compared to non-exposure with no significant relative increase with clarithromycin compared to fluroquinolones.

Conclusion | Concurrent treatment with clarithromycin and a DOAC resulted in no clinically detectable increase in hemorrhagic risk.

Patterns of Maternity Care Utilization of Women Living With HIV

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ABSTRACT

Introduction | The incidence of new HIV cases in women is increasing in Canada, as is the population of women living with HIV (WLWH). Due to the availability of highly effective antiretroviral therapies and near-elimination of mother-to-child transmission of HIV in Canada, more women are expressing fertility intention and are becoming pregnant. The majority of research on pregnant WLWH focuses on neonatal outcomes and mother-to-child transmission of HIV, limiting our knowledge of maternal health outcomes. A recent Ontario study indicated that WLWH are at a higher risk of postpartum maternal hospitalizations than women living without HIV, however, there is little data on the types of maternal morbidities affecting this vulnerable population. The aim of this study is to assess adverse maternal outcomes of WLWH in Ontario.

Methods | This study is the second phase of a three-part project co-designed by an interdisciplinary team of clinicians, researchers, and community scholars with lived experience. We are conducting a population-based retrospective cohort study using linked health administrative databases at ICES. The cohort includes all pregnant and birthing WLWH delivering at Ontario hospitals from 2003/04 to 2017/18. Data is analyzed using multivariable regression to evaluate associations between adverse maternal outcomes and HIV status, as well as sociodemographic and clinical variables.

Results | We will determine whether maternal HIV status is associated with an increased risk for acute severe maternal morbidity, severe maternal morbidity, and adverse birth events.

Conclusion | Our results will identify potential gaps in obstetrical care for WLWH and provide insights for improving outcomes.

The Frequency and Healthfulness of Child-Targeted Food Advertising in Cinemas

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ABSTRACT

Background | Approximately one third of children in Canada and the US are overweight or obese. Food advertising is a contributor to obesity. The regulation of food advertising in Canada and US is self-imposed by the industry. Self-regulation has been found to be ineffective. Regulations also do not include advertising in movie theatres which are frequented by children.

Methods | N = 7 movie theatres in Ontario and Virginia were visited once monthly for four months. Data was collected on a pre-established template to record information and advertisements from the environment and during pre-screening. Ads were determined to be child-targeted using a pre-established criterion. Food marketing, food categories, food companies, and child-targeted techniques were described using frequencies, medians, and ranges. Nutritional analysis was conducted using the World Health Organization's European Nutrient Profile Model to determine permissibility of advertising to children.

Results | On average Canadians were exposed to 11.3 food ads per film and 4.2 ads per film in Virginia. There were more food ads in Ontario (n =2460) compared to Virginia (n =108) on the screens located in the movie theatre environment and during the pre-screening of children's movies (Ontario n = 316; Virginia n = 147). 96-100% of food products advertised were not permissible for advertising to children.

Conclusions | Food advertising made up a significant portion of ads in movie theatres. However, most food products advertised should not be permitted for viewing by children. Policy makers should have a more active role in regulating the advertisement of unhealthy foods to children.

Palliative Bowel Surgery: Are We Helping Patients?

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ABSTRACT

Introduction | Malignant bowel obstruction (MBO) is a frequent complication in the metastatic cancer population with a reported incidence of 28-51% and is associated with high morbidity and mortality. Selecting appropriate management, either surgical or medical, is crucial in prolonging survival and maximizing quality of life. As a 2015 Cochrane review demonstrated no consensus, a prediction model to identify patients who would most benefit from palliative surgery is needed.

Methods | A retrospective single-center study examined demographic, clinical and surgical variables/outcomes for patients presenting with MBO between 2008-2017. Mann-Whitney-U test was used to compare continuous variables; Fischer's-exact test for dichotomous variables; Log-rank for survival curves. In the surgical group, univariate and multivariate logistic regression analysis identified predictors of death at 3 months following surgery.

Results | Among 402 patients, 144(36%) were surgically managed and 258(64%) were medically managed. Significant differences($p<0.05$) between surgical/medical groups: survival, ascites, lymph nodes/soft tissue metastases, active treatment at acute presentation, discharge location. The surgical group had higher survival at 3 months [68.4%(95%CI:60.6-76.2) vs 34.9%(95%CI:28.8-41.0)], at 24 months [31.8%(95%CI:23.6-40.0) vs 8.7%(95%CI:4.78-12.6)]($p< 0.001$) and longer median survival [8 months(0-70) vs 1 month(0-87)($p<0.001$)]. In the surgical group, low albumin, diversion surgery, ascites and ≥2 metastatic sites were combined to form a multivariate prediction model (R^2:0.532) of death at 3 months.

Conclusions | Predictors of death at 3 months following MBO surgery were combined to form a strong prediction model. From this model, we hope to develop and validate a simple clinical risk score that will guide clinical decision-making when evaluating potential surgical candidates.

Deprescribing Benzodiazepines in the Geriatric Population

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ABSTRACT

Introduction | Benzodiazepine and benzodiazepine-like medication (BZD) use in the elderly has dangerous consequences and adverse events (AE) including falls, fractures, delirium, emergency department (ED) visits, and motor vehicle accidents. There is a push for primary care physicians to deprescribe these medications in our patient populations.

Methods | A retrospective chart review was conducted to determine the number of patients > 65 at the Nation River Health Clinic that were on a BZD for > 6 months. Primary outcomes included: number of falls and ED visits while on therapy. Secondary outcomes included: number who experienced fractures, admission to hospital, delirium, motor vehicle accidents, and cognitive decline.

Results | Approximately 10% of patients > 65 were on benzodiazepine therapy. 60% experienced a fall and 44% presented to ED while on treatment. Furthermore, 48% were placed on overlapping opioid therapy.

Conclusion | Findings support dangers of benzodiazepine medications in elderly. Many patients were started on these medications in the past and continued through their geriatric years. Furthermore, given polypharmacy in the elderly, these patients were on dangerous combinations of medications which could potentiate AE. Choosing wisely Canada and deprescribing.org offer educational material and supports for physicians interested in deprescribing these medications in their practice. These materials are based on patient empowerment and information as this has been found to be the most successful in medication tapering and cessation. However, a true cost-benefit analysis will need to be conducted given the large time constraints a deprescribing model has on a clinic setting.

Reconstitution Of The Sterol Transporter ABCG5/G8 in Nanodiscs

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ABSTRACT

The ATP-binding cassette (ABC) transporter ABCG5/G8 functions as a heterodimeric membrane protein and is involved in regulating cholesterol homeostasis. Mutations on ABCG5/G8 have been shown to cause many cholesterol-related illnesses, such as sitosterolemia, hypercholesterolemia, or premature coronary heart disease. The membrane scaffold proteins (MSP) are a modified form of the apolipoprotein A-I. Their use allows to recreate membrane-memetic environment (nanodiscs) to carry out structure-function studies of membrane proteins. My honours thesis study aims to characterize the enzymatic activities of ABCG5/G8 by reconstituting the transporters into nanodiscs with the most optimal lipid composition and size of the nanodiscs. First, recombinant MSP from E. coli cells and wild-type ABCG5/G8 from Pichia pastoris yeast cells will be purified. I will then assemble ABCG5/G8-nanodiscs using purified proteins and a series of phospholipid contents. The ATP hydrolysis event that takes place in ABCG5/G8 will be evaluated to establish an optimal protocol of nanodisc reconstitution. The ATPase activities of both wild-type and disease-causing mutants will then be analysed. The optimization of the technique will enable us to facilitate structural analysis of ABCG5/G8 using single-particle approaches and to develop in vitro functional assays to further study the interaction between the transporter and sterols. Ultimately, the in vitro studies will pave the way to a better understanding of disease mutations and their impacts on the protein function, creating new lines of approach for the treatment of those illnesses..

10 Year Healthcare Data On Child Maltreatment at CHEO

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ABSTRACT

Introduction | Child maltreatment is common with a reported prevalence of 32.1%. Physical abuse (PA), sexual abuse (SA), and exposure to intimate partner violence (IPV) are reported by 26%, 10%, and 7.9% of Canadian adults, respectively. While many child maltreatment cases require health evaluation, there is little data on the medical assessment of these cases. The Canadian Incidence Study of Reported Child Abuse and Neglect (CIS-2008) reviewed child welfare cases but not data on their medical aspects, despite 5% of substantiated PA cases being sufficiently severe to require need for medical assessment. There is no published data describing the type, breadth, or outcomes of cases seen in the Canadian healthcare system.

Methods | Secondary data was analyzed using descriptive statistics from a preexisting quality improvement database where information was collected from the CHEO Child and Youth Protection Review Committee (CYP RC) over 10 years (April 2009-April 2019).

Results | There were a total of 2652 cases reviewed at the CYP RC. Fifty-nine percent (1580/2652) of child maltreatment cases were substantiated. The most common types of substantiated child maltreatment were caregiver capacity 30% (n=476), PA 19% (n=304), emotional abuse 18% (n=287), neglect 15% (n=230), SA 14% (n=227), sexual assault 2% (n=36), and abandonment 1% (n=20). Forty three percent (1140/2652) of cases were alerted in the medical record for child protection purposes.

Conclusions | Our findings expand our knowledge of the different types of child maltreatment by linking child welfare and medical assessment information. This information may allow for more comprehensive health recommendations.

Identification of Activated Neurons in the Motor Cortex Before and After Stroke

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ABSTRACT

Inducible transgenic mice models that express immediate early gene (IEG) driven fluorophores in response to cellular activation provide high temporal and spatial specificity to identify cells activated when performing a behavioural task. Here we utilized the ARC IEG (ArcCreERT2:RosaYFPf/f) mouse model that allows for the conditional and permanent labeling of specific populations of cells activated when performing motor tasks at two time points in vivo. Naïve ArcCreERT2:RosaYFPf/f mice were trained and tested at two time points in either a gross or a fine motor task, using the rotarod and staircase tests, respectively. The cells that were activated when 1st performing the motor task were identified by their permanently expression of YFP. Reactivated cells were identified by their expression of YFP and protein expression for the endogenous immediate early gene (Arc or c-Fos) at the 2nd time performing the motor task. Quantification of labelled cells in sub-regions of the motor cortex revealed increased density of activated cells at both the 1st (YFP+) and 2nd time point (c-Fos+) in mice performing the rotarod task, but not in the staircase task, compared to non-behaving littermate control mice. These results suggest that the ArcCreERT2 mouse is able to reliably label motor networks used to perform a gross motor task and is being used to identify neural populations used during motor recovery following stroke.

Biophysical Study of Interactions Between Liposome and Cholesterol-Regulating Proteins

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ABSTRACT

ATP-binding cassette (ABC) transporter ABCG5/G8 and proprotein convertase subtilisin/kexin type 9 (PCSK9) are important in regulating cholesterol metabolism. ABCG5/G8 is essential in cholesterol secretion from the liver into bile and from enterocytes into the intestinal lumen[1] [2]. PCSK9 can circulate in the plasma and interacts with both low-density lipoprotein (LDL) and the LDL receptor (LDLR)[3]. Its binding to LDLR promotes the receptor's endocytosis and lysosomal degradation in the liver. Loss-of-function mutations in ABCG5/G8 cause sitosterolemia, a rare genetic disorder characterized by hypercholesterolemia and premature heart disease. Gain-of-function mutations of PCSK9 result in less LDLR on the cell surface and more LDL cholesterol in the bloodstream, causing familial hypercholesterolemia. What is common in both is interaction with some lipid-surface entity in the form of phospholipid-bile acid micelles (ABCG5/G8) or LDL particles (PCSK9). Little is known on how their activities are influenced by the presence of such lipid-surface entities, which is key to understanding how they detect and control cholesterol level in the body. With the elucidation of these potential interactions as a goal, my honours project will employ a biophysical approach, namely isothermal titration calorimetry (ITC), as an in vitro probing method. We will use unilamellar liposomes as model membranes and examine the heat exchange between this model liposome and proteins of interest. We will first test wild-type proteins, and then investigate the impact of disease mutations on protein-liposome interactions. The results of this assay will answer the question of how these proteins interact with lipid particles and to what extent.

Feasibility of a Coaching App to Enhance Post-Concussion Outpatient Care

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ABSTRACT

Background | Patients with persisting mTBI/concussion symptoms can experience significant somatic, social, economic and psychological impacts. Following specialist consultations, patients often exhibit challenges with treatment recommendations, including medication and lifestyle modifications. An internet-based health coaching tool may allow for more timely and consistent patient contact, which could provide the support needed to help patients optimize their health outcomes.

Objectives | To assess the feasibility of a scheduled interactive personal health log with a coaching component, in the management of patients with post-concussion syndrome.

Methods | Seven patients were recruited prospectively to use the App and track 2-4 individual treatment goals derived from their initial consultation, for 5-6 weeks. Patients completed weekly progress questionnaires and the health coach and physician provided scheduled weekly health coaching, through the App. Data collected included patient App activity, patient satisfaction and feedback, physician and coach satisfaction, and pre and post symptom comparison using the Rivermead post-concussion symptom questionnaire.

Results | A majority of satisfaction questions (61.5%) received scores of "Agree" or "Strongly Agree" from all participants. All participants found the App easy to use, and five participants (71.4%) felt that the coaching and App helped them improve their symptoms. All participants believe that this is an effective tool that could be used in patient care.

Discussion | Our results show promising evidence that an online coaching App is a feasible tool to improve the adherence and symptom management of patients with post-concussion symptoms. Further studies should focus on determining the effectiveness of this intervention on a larger scale.

Necroptosis and Neuroinflammation in the Pathogenesis of Spinal Muscular Atrophy

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ABSTRACT

Spinal muscular atrophy (SMA) is a neuromuscular disease characterised by motor neuron loss, leading to muscle weakness and decreased mobility. The disease is caused by mutations in the Survival motor neuron 1 (SMN1) gene, which leads to a depletion of the SMN protein. Neuroinflammation has been established as a contributor in many neurodegenerative disorders and is a key player in the pathogenesis of amyotrophic lateral sclerosis (ALS). Given that ALS and SMA share many clinical features, it is possible that neuroinflammation may be contributory to motor neuron cell death and shortened lifespan. Recent findings in cell death signaling have exposed necroptosis as a major contributor to motor neuron death in different forms of ALS. Necroptosis is mediated by receptor-interacting protein kinase 1 (RIPK1) and RIPK3. When RIPK3 is phosphorylated, inflammasome activation occurs which associates with caspase-1, ultimately causing secretion of pro-inflammatory cytokines. Interestingly, in-vivo Rip3 knockdown increased motor neuron survival in mice exposed to toxic ALS mutant astrocytes. Here, we explore the pathogenic significance of this molecular death pathway in SMA with the hypothesis that necroptosis mediated neuroinflammation is the basis of cell death in the spinal cord. To gain insight into the role of caspase-1 and RIPK3 in SMA, we've generated a triple knockout (TKO) mouse model: Smn2B/-, Caspase1-/-, RIPK3-/-. Our preliminary data shows increased survival and mobility in the TKO mice compared to Smn2B/- mice. Motor neuron counts, neuromuscular junction pathology and myofiber size is currently being investigated in the TKO. Understanding the implications of the necroptosis pathway in SMA pathogenesis may suggest the need to target Caspase-1 and RIPK3 to inhibit multiple cell death pathways and ameliorate neuroinflammation in the disease context.

Chronic Disease Self-management Among Marginalized People Who Use Drugs

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ABSTRACT

Introduction | Despite calls to consider substance use as a chronic health issue,[1-2] chronic disease self-management initiatives have rarely been explicitly applied to people who use drugs (PWUD). Self-management support interventions improve health behaviours, health outcomes, and quality of life across chronic diseases,[3-4] yet there is a gap in understanding whether similar benefits can be achieved among this population. We aim to explore the self-management experiences of socioeconomically marginalized PWUD, as well as implementation considerations and outcomes of delivering a standardized program for this population.

Methods | We propose several studies using community-based participatory research, informed by implementation science principles and an intersectionality lens. First, we will conduct a qualitative exploration of self-management experiences among marginalized PWUD, using interview methods and thematic analysis. Second, we will conduct a mixed methods feasibility study of the evidence-based, peer-led Chronic Disease Self-Management Program (CDSMP)[5] among a subset of this population. The program will be evaluated in two ways: a multi-stakeholder assessment of process factors, and qualitative interviews using Interpretative Phenomenological Analysis to understand participant experiences.

Results | We anticipate PWUD will describe unmet self-management support needs. Further, with careful consideration of implementation concerns, the CDSMP will be feasible and acceptable among this community, providing benefits including improved confidence and social connectedness.

Conclusion | Our findings will inform public health stakeholders currently delivering chronic disease self-management initiatives to expand their reach to PWUD, contributing to meeting their health equity objectives. Moreover, findings will broadly inform the development of new self-management supports for PWUD and other marginalized groups.

Role of perihematomal CT perfusion parameters in predicting hematoma expansion

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ABSTRACT

Hematoma expansion (HE) in intracerebral hemorrhage (ICH) is an adverse prognostic feature that strongly increases the likelihood of death and neurological deficits. Currently reported CTA spot sign predicts HE at an inconsistent positive predictive value (PPV) ranging from 22-77%. Our study aimed to retrospectively investigate CT perfusion (CTP) as a novel method of predicting HE. Methods: contrast-enhanced CTP images of 84 patients were obtained by a 320-row volume CT scanner (Toshiba Aquilion ONETM) within 6 hours of ictus. Vitrea Advanced Visualization software was utilized to establish a processing protocol for analyzing 4D perfusion data. Our protocol included regions of interests (ROIs) in both ipsilateral and contralateral areas of 1. Hematoma zone 2. Perihematomal zone (PHZ) and 3. Area encapsulating the spot sign. For all ROIs, CBV, TTP, CBF, MTT, and Delay were quantified. Data was then divided into spot +/- and HE +/- for multivariate regression analysis. CTP values for each parameter was calculated to investigate differences in CTP intensity of ipsilateral lesion compared to the contralateral side. Results: our preliminary analysis indicates that within spot+ group, HE positive cases had average PHZ CTPs ratio of CBV=0.91, TTP=1.02, CBF=0.78, MTT=1.04, and Delay=1.93. Within the same spot positive group, HE negative cases had average CTPs ratio of CBV=1.04, TTP=0.99, CBF=0.97, MTT=1.03, and Delay=1.16. Although still speculative, our data suggests that using specific parameters such as CBF, CBV, and Delay may be a pivotal addition to spot sign data in predicting hematoma expansion and enhancing management of ICH patients.

A Qualitative Study to Explore the Effectiveness of Narrative Feedback Using a Resident Driven Workplace-Based Assessment Tool to Assess CanMEDS Competencies in Anesthesiology

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ABSTRACT

Introduction | The transition to a competency-based medical education (CBME) curriculum has required novel and valid methods of assessing the CanMEDS competency framework using workplace-based assessment (WBA). Our objective is to understand how residents and faculty in the Department of Anesthesiology and Pain Medicine at the University of Ottawa interact with the CanMEDS 2015 Competency Framework using WBA.

Methods | Anesthesiology residents and faculty (n=20) will be invited to participate in this study. Through semi-structured interviews, participants will reflect on questions pertaining to 1) experiences with WBA using the CCAT 2) documentation of narrative feedback for formative assessment, and 3) knowledge of and interactions with the CanMEDs 2015 Competency Framework. Interviews will be audio-recorded, transcribed and anonymized.

Data Analysis | Qualitative analysis of interviews will be informed by constructivist grounded theory (CGT) and will occur in three analytical stages: initial, focused, and theoretical coding. During initial coding, the first two transcripts from each participant group will be coded using gerunds or participants' words (Nvivo coding). Most frequently occurring initial codes will be consolidated into preliminary themes to do focused coding of the next 3-4 transcripts to test their relevance. The research team will meet frequently to discuss preliminary findings, and finalize a list of consensus-based categories that will be used to theoretically code the entire dataset.

Conclusion | Results of this study will hopefully contribute towards ameliorating WBAs, creating better opportunities for self-reflection and feedback. We also hope to reveal underlying barriers that may limit utilization of the CanMEDS competency framework.

Use of Resident-led Peer Education to Improve Antimicrobial Stewardship

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ABSTRACT

Introduction | The Royal Lancaster Infirmary is a 387-bed teaching hospital in the United Kingdom. An audit in the surgical units (5 units and 151 patients in total) showed that only 62% of patients were on the correct antibiotics per the hospital guideline, 76% of patients had the antibiotic indications documented, and 59% of patients were on the correct duration of antibiotics. We organized two near-peer teaching sessions in our hospital.

Methods | The teaching was led by a second-year resident physician and delivered to the hospital first and second year residents (n = 39), because they tend to prescribe most of the medications in hospitals. Teaching feedback forms were given to the participants. Three months after the teaching, a re-audit was conducted that included all inpatients in the surgical units (5 units and 84 patients in total).

Results | Based on a 5-point Likert scale, the participants felt significantly more confident about prescribing antibiotics after the tutorials (scores 4.00 vs. 4.54). They preferred having resident physicians rather than attending physicians or pharmacists delivering prescribing tutorials (scores 4.39, 3.63 and 3.13, respectively). In the re-audit, 66% of patients were on the correct antibiotics per the hospital guideline, 83% of patients had the antibiotic indications documented, and 66% of patients were on the correct duration of antibiotics.

Conclusion | We observed a trend of improvement in compliance to the guidelines. We encourage clinicians to conduct similar studies on peer teaching and validate whether resident-led education improves prescribing practice.

Admission and Specialization Trends of uOttawa's Medical Alumni, 1945-1967

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ABSTRACT

Introduction | After World War II, Canada faced a shortage of General Practitioners. The University of Ottawa's Faculty of Medicine, opened in 1945, was viewed as part of the solution, especially for underserved Catholic and French-Canadian populations. This research identifies significant and unexpected patterns in medical admissions and specialization decisions at uOttawa between 1945 and 1967. The typical Canadian medical student in this period was a white male from an upper-class background. Yet these data indicate that uOttawa admitted a more diverse group of students. Many new Ottawa M.D.s chose to specialize and/or practice outside of Canada, even after the implementation of Medicare and the possibility of military conscription in the United States.

Methods | A database of demographic, biographical, and professional information was compiled for graduates between 1951 and 1967. From institutional records, archival materials, online databases of professional bodies and journal articles, relevant data were identified, extracted, and entered into the database. Data on gender, geographic origins, post-graduate training, and locations of practice were analyzed quantitatively and qualitatively, and results contextualized historically.

Results | Preliminary analyses show that the University of Ottawa admitted significant numbers of medical students who were not white or male, and that numerous Ottawa graduates chose to specialize and/or practice outside Canada.

Conclusion | Numbers of female and foreign graduates may indicate that the Faculty of Medicine's current commitment to multiculturalism and socio-economic diversity is longstanding. Moreover, even as it helped to address Canada's shortage of General Practitioners, many alumni opted to specialise or practice outside of Canada.

The Role of Glucocorticoid Signaling in Adult Muscle Stem Cells

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ABSTRACT

Duchenne Muscular Dystrophy (DMD) is an X-linked disease caused by mutations in the dystrophin gene occuring in approximately 1:3500 male births. The first-line of treatment is glucocorticoid therapy, powerful anti-inflammatory agents and potent regulators of differentiation processes. Glucocorticoid treatment of DMD patients can improve muscle strength during the first 6 months of treatment, and can delay loss of muscle function by ~3 years. To date, the mechanism by which glucocorticoids (GCs) improve muscle strength in DMD patients in the short-term and the cause of treatment failure in the long term remains elusive. Adult myogenesis is mediated by muscle satellite cells (SCs), which are primarily responsible for the repair and regeneration of damaged muscle. Comprehensive in vivo studies examining the role of GC signalling in postnatal muscle, particularly in SCs, are lacking and have not been explored in the context of DMD. We have developed a conditional null mouse model in which glucocorticoid receptor (GR) expression is knocked out specifically in muscle satellite cells to study the role of glucocorticoid signaling during muscle regeneration. Analysis of this model revealed that loss of GR in satellite cells results in a rapid decrease in average muscle fiber size with a concomitant increase in newly formed fibers, marked by the expression of embryonic MyHC staining, in resting muscle of juvenile and adult mice. However, loss of GR in satellite cells impairs myogenic differentiation in culture and muscle regeneration after acute injury. GR expression is this necessary for muscle homeostasis.

Development of a Rural Medicine Training Module for Medical Students

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ABSTRACT

Introduction | There is a known discrepancy between the number of Canadians living in rural communities versus the number of medical personnel available to meet their health needs (Stat Can, 2018; CIHI, 2013). Various attempts have been made to improve this discrepancy, including selective admission policies, mandatory rural rotations in undergraduate training, and establishing residency positions in rural communities. Careful attention to the preparation for and process of a rural experience may improve students' enjoyment of their experience and opinions about rural practice. In addition to increasing the number of graduates who choose rural practice, the University of Ottawa's social accountability mandate emphasizes cultural safety teaching within the Faculty of Medicine. We have developed a rural medicine pre-departure training module to prepare medical students for clinical interactions with people from rural communities.

Objectives | 1. Create an online training module, with an emphasis on cultural safety, for pre-clerkship medical students undergoing rural clinical placements or interacting with peoples from rural areas. 2. Help pre-clerkship students to feel better prepared in clinical practices in rural or remote areas or with people from these communities. 3. Support a more favourable view of rural medicine.

Methods | We developed a new Self-Learning Module (SLM) for pre-departure training directed at medical students pursuing clinical opportunities in rural locations. A literature search was performed to see if there were any medical student pre-departure training modules. Comprehensive, semi-structured, interviews were conducted with experts in rural medicine including physicians, the Director of DME, the Director of SA, and a medical student to create a comprehensive SLM framework for medical learners. We will pilot this new SLM for medical students and evaluate whether it helps to prepare them to work in rural areas and if they view rural medicine more favourably.

Results | There is a lack of Canadian pre-clerkship training modules centered around rural clinical placements. From our in-depth interviews, we created an SLM framework that consists of 3 sections to aid the learner: pre-departure, placement experiences, and debriefing and reflections (Thomas, ST et al., 2018). At its center is cultural safety, which we emphasize by including clinical scenarios, interactive activities, and quizzes for students to better understand the demographics, available transportation, and accessible and available health resources in their rural community placement.

Next Steps | 1. Have the SLM implemented as a part of the University of Ottawa Medical School undergraduate pre-clerkship curriculum. 2. Students will complete a pre and post rural clinical experience online survey. 3. The survey will assess their opinions about whether the SLM aided them in their rural clinical practice and if they have an increased preference for rural medicine.

Conclusion | We anticipate the proposed SLM will be implemented into the University of Ottawa Medical School Curriculum. We hope this SLM aids in preparing students for rural medicine experiences, so that they may consider rural practice more favorably.

Impact of Physical Activity on Sleep in Children with Epilepsy

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ABSTRACT

Introduction | Children with epilepsy (CWE) have impaired sleep (1). Inadequate sleep is a trigger for seizures, and poor sleep leads to lower quality of life in CWE. Physical activity (PA) may improve sleep in healthy children, but the effect of PA on sleep in CWE is unknown. We hypothesize that an increase in PA will improve the sleep of CWE.

Methods | Twenty-two CWE aged 8-14 years were individually motivated to increase their PA weekly by an exercise counsellor for 12 weeks. Participants continuously wore a wrist pedometer (Fitbit Flex®) to capture daily PA (number of steps) and sleep quality (sleep efficiency, SE; total sleep time, TST). Baseline PA and sleep for each participant was established for four weeks prior to the intervention. Subjective quality of sleep was assessed pre- and post-intervention with the Children's Sleep Habits Questionnaire (CSHQ).

Results | PA, SE, and TST did not change with the intervention. Our cohort was relatively active (11,271 +/- 3189 mean steps per day). Mean SE and TST were 87.4% ± 3.08 and 521 min ± 30.4 respectively. Subjective sleep quality score improved with the intervention (mean total CSHQ was 44.5 ± 5.8 at baseline and 41.6 ± 7.2 at the end of study, P=0.05).

Conclusion | This study provides the first longitudinal measurement of both PA and objective and subjective sleep in CWE. Our results show that our group of active CWE have good subjective and objective sleep. Future analysis will characterize the interplay between daily variations in PA and sleep.

Effective Physical Literacy Screening among Children with Medical Conditions/Disabilities

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ABSTRACT

Introduction | Children with medical conditions and disabilities (MC&D) are less likely to participate in recreation programs/activities1. Research suggests that they often have limited physical literacy (PL), and that understanding these limitations facilitates their inclusion by recreation leaders. The purpose of this study is to determine whether efficient PL screening tasks could accurately identify the PL deficits of children with MC&D.

Methods | Children, ages 6-14, who were identified by the treating physician as ambulatory and able to follow simple directions, were recruited through neurology, cardiology, oncology, haematology, rheumatology, rehabilitation, concussion, respirology, mental health, and thrombosis clinics at three paediatric hospitals. Screening tasks consist of: a wall sit, balancing on one leg, forwards and backwards run, body mass index, and questions relating to screen time, perceived adequacy, as well as barriers and support for physical activity. Associations between screening task results and outcomes from a detailed PL assessment are evaluated.

Results | A total of 748 children with MC&D (341 female), 10.0 2.7 years of age, attempted the screening tasks. Successful performance was 92% for wall sit, 82% for running, and 79% for one-leg balance. For any screening task, a maximum of 15 participants were unable to complete the task due to their MC&D. Analyses of a subset of participants who did both the screening tasks and the detailed PL assessment1 are ongoing.

Conclusion | Screening tasks are feasible for most participants. Recreation professionals can easily include these screening tasks into warm-up activities, with the children's performance providing information about the expected level of PL.

CANHEART-CODE: Patients and Family Physicians CO-DEsign Patient Reported Cardiovascular Disease Outcomes – A Nominal Group Study

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ABSTRACT

Background | With cardiovascular disease (CVD) posing a significant disease burden in Canada, preventative efforts must continue to take place; primary care providers (PCPs) play a pivotal role in this effort. We determined the patient-reported outcomes related to CVD prevention and lipid management deemed most important by patients and providers for use in practice improvement efforts.

Methods | 4 patient partners and PCPs selected to represent diverse perspectives were led by an expert moderator in nominal group methods, a well established consensus technique. Each participant wrote down items/questions they believed important in measuring performance of CVD prevention and lipid management. Following discussions about each, all items underwent anonymous ranking as "definitely include", "definite exclude" or "unsure". Items were included or excluded based on 75% agreement. Remaining items were similarly categorized based on further rounds of ranking.

Results | The panel produced 10 items from a total of 26 following three rounds of ranking. The top three items were: "Is your treatment plan tailored to you?", "Was your physician good at giving information about your risk factors?" and "Did your physician involve you in decision-making?"

Conclusion | A questionnaire consisting of prioritized patient-reported items on CVD prevention and lipid management is valuable in quality improvement and continuing professional development needs assessment initiatives. Further evaluation of these questions will be done through their deployment in a direct patient feedback system (CPIN) across 4 Ottawa sites. The questionnaire will also be used for evaluation in CANHEART CHOICES, a community-based trial aimed at improving cholesterol management among PCPs.

The Impact of Serious Illness Communication Training on Clinician Skill and Confidence

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ABSTRACT

Introduction | Advance care planning and serious illness conversations require effective communication from clinicians in order to ensure patients' decision making is supported overtime. Gaps in such communication skills can be addressed through training (1). The Serious Illness Conversation Guide (SICG) has been developed as a guide for initiating these conversations using language which has been patient-tested (1,2). The SICG was adapted to paediatrics (SICG-Peds) to incorporate issues which are unique to children. A serious illness communication training program, using the SICG, has been implemented at the Children's Hospital of Eastern Ontario and Roger Neilson House to improve clinician communication practices.

Objective | To assess the impact of Serious Illness Communication training on clinicians' skills and confidence in conducting difficult conversations with parents of seriously ill children.

Methods | We conducted surveys of clinician self-reported skills and confidence as well as attitudes towards serious illness conversation before and after participating in the training workshops. We also conducted interviews with the same participants to explore their themes.

Results | Clinician confidence levels in leading serious illness conversations increased by 2.32 (23.2%). Eighty-four percent of participants' skills and effectivity in identifying individuals needing SIC were increased post workshop. Ninety-six percent agreed that the clinical guide would enhance their clinical care for patients. Ninety-nine percent plan on integrating the SICG-Peds guide in their clinical practice.

Conclusion | Serious illness Communication training may improve clinician skills and confidence levels in communicating with parents about their goals and values in the setting of serious illness.

Implementing a Family Caregiver Needs Assessment in a Pediatric Hospice

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ABSTRACT

Introduction | Family caregivers of children with serious illness provide the most significant role in daily care, and caregiver well-being is crucial to achieving optimal health outcomes for children.[1,2] However, assessing the needs and supports of family caregivers is not routine practice. The interRAI Family Carer Needs Assessment Form is part of an internationally validated suite of instruments developed for assessing vulnerable persons.[3] This study is the first to utilize this tool in caregivers of children, seeking to evaluate and improve its ability to capture their needs.

Methods | This is a prospective pilot study of a convenience sample of family caregivers of children with serious illness receiving care at the Roger Neilson House pediatric hospice in Ottawa, Ontario. 20 caregivers have completed the self-assessment form. Additional feedback was sought inquiring about missing information and the appropriateness of questions. Responses were analyzed using a mixed methods approach.

Results |All participants report the assessment identifies important information across multiple domains. Questions flagged as unsuitable are related to age and ability of care recipients rather than children as a group. Additional questions surrounding financial health, school supports, inclusion of longer recall time periods and use of scales rather than dichotomous answers are identified as important adaptations.

Conclusion | A comprehensive needs assessment form is feasible, and several key modifications can improve its use in family caregivers of children. Future research administering a newly adapted pediatric version will determine its utility as a clinical tool in evidence-based care planning that can address unmet needs.

The Therapeutic Effects of MicroRNAs in Preclinical Studies of Acute Kidney Injury: A Systematic Review

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ABSTRACT

Introduction | Acute kidney injury (AKI) causes significant morbidity and mortality, and there are currently no effective treatments to enhance renal recovery. MicroRNAs (miRNAs) are short chain nucleotides that regulate protein expression, and have been implicated in the pathogenesis of AKI. Recently, preclinical studies in vivo have uncovered a therapeutic role for administration of specific miRNAs in AKI. However, this strategy has not been reviewed systematically, and its potential for clinical application in humans is unclear.

Aims | The primary aim is to conduct a systematic review of the therapeutic properties of miRNAs in preclinical studies of AKI. The secondary aim is to determine adverse effects of miRNA administration in these studies.

Methods | A comprehensive search strategy identified relevant studies in AKI in vivo models published up to the end of 2018, using the MEDLINE, EMBASE, OVID, PUBMED and Web of Science databases. The initial search strategy identified 1566 titles/abstracts. Two independent investigators will initially screen abstracts, and selected articles that meet eligibility criteria will be reviewed for data abstraction and analysis. The SYRCLE RoB tool for animal studies will determine risk of bias, and meta-analysis will be performed as appropriate. The GRADE methodology will assess the quality of evidence.

Conclusions | The administration of selective miRNA mimics or antagonists exerts beneficial effects in mammalian models of AKI, although multiple obstacles must be addressed prior to translation to human clinical trials. The proposed systematic review will document key miRNA candidates and identify gaps in knowledge which could guide future directions in AKI research.

Glucose Affects Thymic Stromal Lymphopoietin in Thyrotropin-induced Adipocyte Dysfunction

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ABSTRACT

Introduction | Thyrotropin (TSH) is elevated in subclinical hypothyroidism to preserve thyroid function but may cause adipocyte dysfunction. Our laboratory has found TSH-stimulated human adipocytes express thymic stromal lymphopoietin (TSLP), a proinflammatory cytokine implicated in atherosclerosis (3). The study aim was to investigate whether different glucose concentrations alter TSH receptor regulation of TSLP using human primary differentiated adipocytes.

Methods | Subcutaneous abdominal adipose tissue was obtained during elective surgery. Stromal preadipocytes were isolated by collagenase digestion and then differentiated for 14 days into adipocytes (2) in low (2.0 mmol/L; LG), normal (5.0 mmol/L; NG), or high (25 mmol/L; HG) glucose media. Stimulation studies were conducted on differentiated adipocytes using TSH and other proinflammatory cytokines, tumour necrosis factor alpha (TNFα) and interleukin-1 beta (IL-1β), at low, normal, or high glucose concentrations. TSLP released into the medium after 24-hours of stimulation was measured by enzyme-linked immunosorbent assay (ELISA).

Results | Adipocytes stimulated by TSH, TNFα or IL-1β produced the highest TSLP concentration under LG conditions. There was no cell death of LG-exposed cells. There was no effect of LG on unstimulated TSLP levels. HG had no effect.

Conclusion | The findings suggest that LG may be an enabler of pro-inflammatory adipocyte responses. Further research is needed to understand the mechanism by which low glucose accentuates the TSLP response, and whether other pro-inflammatory cytokines are affected.

In-Hospital Mortality and Morbidity Among Patients Presenting with Intracranial Hemorrhage: A Single Center's Experience with Vitamin K Antagonists and the Direct Oral Anticoagulants

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ABSTRACT

Introduction | The treatment of venous thromboembolism and prevention of stroke in patients with atrial fibrillation traditionally consists of vitamin K oral antagonists. Intracranial hemorrhage (ICH) is the most feared complication as this form of bleeding has the highest mortality and morbidity. However, clinical trials using direct oral anticoagulants (DOAC) suggest a lower incidence of ICH and a better safety profile. The aim of this study was to evaluate anticoagulation use, in-hospital mortality rates and functional outcome among patients presenting with ICH to a large tertiary care centre in Canada.

Method | A retrospective chart review was conducted of patients who presented to The Ottawa Hospital with ICH between January 2016 and December 2017. Data collected included patient demographics, indication for anticoagulation, and type of anti-platelet/anticoagulation. The primary outcome of interest was in-hospital mortality and the secondary outcome of interest was functional disability.

Results | Manual chart review confirmed 429 patients diagnosed with ICH. In-hospital mortality was 45.8% in DOAC-related ICH, 29.4% in warfarin-related ICH and 15.5% in patients not on an anticoagulant or antiplatelet. Average modified Rankin Scale at the time of discharge was 4.52 in DOAC-related ICH, 4.23 in warfarin-related ICH and 3.2 in patients not on an anticoagulant or antiplatelet.

Conclusion | DOAC-related ICH tended to lead to higher in-hospital mortality and worse functional outcomes among survivors on discharge. Although DOACs are reported in the literature to have an overall lower incidence of ICH, further information is still needed to understand the clinical impact when a bleeding event occurs.

Retrospective Analysis of Invasive and Non-Invasive Assessments of Coronary Physiology in Patients With Diabetes Mellitus

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ABSTRACT

Introduction | Ischemic heart disease is the leading cause of cardiac mortality in patients with diabetes. An understanding of each patient's coronary physiology and anatomic complexity is required to determine whether treating with medical therapy, coronary artery bypass grafting, or percutaneous coronary intervention will result in the best outcome. Myocardial flow reserve (MFR) obtained through non-invasive positron emission tomography (PET) and fractional flow reserve (FFR) obtained through invasive angiography are measurements used to make clinical decisions about revascularization. Our objective was to investigate the association between the MFR and FFR measurements in patients with diabetes.

Methods | We conducted a retrospective chart review of 174 patients who underwent MFR and FFR measurements between 2012-2018. Data collected included patient demographics, cardiovascular risk factors and outcomes at 1 and 3 years were collected.

Results | Of 174 patients, 68 had diabetes (DM+) and 106 did not (DM-). The average MFR for DM+ patients of 2.08 was significantly lower than the average MFR for DM- of 2.41 (p=0.0143), while there was no difference between the average FFR for DM+ of 0.80 and for DM- of 0.82 (p=0.1908). The nature of the relationship between the FFR and MFR differed in a statistically significant manner for patients with diabetes compared to those without (p=0.0233).

Conclusion | Our study found that while FFR values did not seem to differ in patients depending on diabetes status, MFR measurements did. This provides further evidence to suggest that DM+ are more likely to have more diffuse, multi-vessel disease compared to DM-. In the future, we aim to explore whether FFR and MFR values are more likely to be discordant in DM+ compared to DM-, which will aid in the development of more robust treatment guidelines for patients with diabetes.

Pseudotyping MG1 to Enhance Its Ability to Selectively Kill HIV Infected Cells

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ABSTRACT

Human immunodeficiency virus (HIV), the cause of acquired immunodeficiency syndrome (AIDS), is a lentivirus that mainly targets CD4+ T-cells (1). Although antiretroviral therapy (ART) can reduce the amount of virus in the blood to undetectable levels, it is still not able to cure the infection due to the latent reservoir established in memory CD4+ T-cells(2). While there are no markers to distinguish latently HIV infected cells from their uninfected counterparts, we have recently shown that latently infected cells have defects in their interferon signaling pathway. By taking advantage of this defect, the oncolytic virus MG1 can kill the cells latently infected by HIV(3). However, it will be necessary to increase the specificity of MG1 if it is to be developed into a viable therapeutic option. This project aims to pseudotype MG1 with HIV envelope protein gp160 in order to target only CD4+ T-cells, and to limit any possible off-target effects. 3 types of pseudotyped MG1 clones with full length gp160 insert, and two truncated versions of gp160 insert will be created. These MG1 clones will be tested on CD4+ cell line models of latency, primary CD4+ T-cell models of latent infection and memory CD4+ T-cells from ART treated patients, and the infection rate and cytotoxicity of recombinant MG1 to MG1 virus will be compared. This project will provide a novel therapeutic approach to eliminating the latent reservoir in HIV+ patients.

Cardiac-specific *Ankrd11* knockout mice present with Patent Ductus Arteriosus

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ABSTRACT

Introduction | KBG syndrome is a rare disease characterized by the presentation of skeletal deformities, distinct facial features, intellectual delay and occasionally cardiac symptoms. Although these symptoms are mild and common, for this very reason, patients are often underdiagnosed or misdiagnosed. Mutations associated with Ankyrin repeat domain-containing 11 (ANKRD11), a transcription factor, account for the symptoms in KBG patients. However, the cellular and molecular role of ANKRD11 in the pathogenesis of KBG syndrome, especially in regard to the cardiac symptoms, is currently not well understood.

Methods | Through the creation of a cardiac-specific knockout (KO) mouse model using an Nkx2.5-Cre driver in cardiac progenitor cells, we hope to better understand in particular the cardiovascular symptoms of KBG syndrome.

Results | From our initial observation of an extremely low survival outcome of the Ankrd11-KO mice at 3 weeks of age, we further examine the embryological and postnatal developmental stages for the pathological cause. Through phenotypic and histological analysis, our findings indicate the development of patent ductus arteriosus (PDA), a common congenital heart defect (CHD), in postnatal Nkx2.5-Ankrd11 KO mice. Cell-lineage tracing further confirms that Nkx2.5+-derived cells contribute to the closing of the ductus arteriosus.

Conclusion | This novel finding implicates a plausible role of Ankrd11 in cardiac development, and more specifically in PDA. Thus, this cardiac-specific mouse model can be used to further our understanding of the extremely prevalent yet somewhat unfamiliar CHD in order to develop early diagnostic and treatment measures, beyond just KBG patients.

Canadian Environmental Scan of Perioperative Geriatric Models of Care: Pilot

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ABSTRACT

Introduction | The rate of aging worldwide is much greater than it has been in the past. Accordingly, the average surgical patient is becoming older and more frail. Older patients undergoing surgery are at increased risk of adverse post-operative outcomes compared to younger patients. Increasing evidence shows that structured perioperative geriatric care programs have positive effects on the outcomes of elderly patients. Despite this, there is little published data regarding what models of perioperative geriatric care are delivered in Canada. It will be important to survey and evaluate whether structured perioperative geriatric programs exist in hospitals across Canada, and the components of these programs.

Methods | We developed a web-based survey to evaluate the existence of perioperative geriatric care models and how these services are delivered. To evaluate comprehensiveness, reliability and validity of the survey, it will be sent for review by a group of physicians in surgery, anesthesiology and geriatric medicine. The survey will be finalized based on revisions made by these group of respondents. Pilot testing will also assess test-retest reliability. Final participants of the survey will be identified through departmental leads at each university hospital for surgery, anesthesiology, and geriatric medicine.

Expected Results | We expect the data collected from this survey to demonstrate a variety of different models of perioperative geriatric care. This will serve as a foundation for future development of standard best practices and contribute to the development of a national strategy on improving clinical outcomes of geriatric surgical patients.

Students' Perception of a Peer Support Program in Medical School

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ABSTRACT

Medical school provides the opportunity to address high levels of stress, depression and anxiety early in medical training. Studies show that students and trainees prefer seeking support from peers rather than reaching out to health professionals or faculty members for help. To assess help-seeking behaviours in medical students at the University of Ottawa and to receive their input on the implementation of a peer support program, a 24-question survey was conducted. The Survey Monkey link was sent via email and posted on Facebook pages. 137 medical students from years 1-3 (29% response rate) completed the survey between January and February 2019. Only 17.5% (n=24) of participants reported rapidly seeking help when experiencing mental health distress. The most common barriers to current faculty services are 1) not thinking one is stressed enough for help, 2) fearing impact on career progression and 3) being unable to identify personal distress. Participants ranked Peer Supporter ahead of Faculty Services as a preferred source of support. 85.4% of participants would feel relieved (n=62) or neutral (n=55) if a Peer Supporter checked-in on them based on behavioural changes. Students favoured a program that offers variable hours (n=96), at a location chosen between peers (n=69) and with their Peer Supporter of choice (n=80). Students support the implementation of a peer support program at the Faculty of Medicine. Designed to meet students' needs, the pilot project Side by Side could be a valuable addition to existing programs and services offered at the faculty.

Neuropsychological Impact of Childhood Acute Lymphoblastic Leukemia Treatment

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ABSTRACT

In children diagnosed with ALL, 5% will develop CNS involvement. However, this number rises to 50- 75% without adequate prophylaxis therapy such as cranial radiation therapy (CRT) and chemotherapy. However, there is clear evidence that with this therapeutic success, late neuropsychological deficits develop in some survivors. By looking at early markers in children diagnosed with ALL, it is hypothesized that developmental neuropsychological trajectories following CNS therapies can be predicted. Children diagnosed with ALL were asked to complete a continuous performance task during various time points in their treatment plan (early at diagnosis, before and after cranial irradiation, and annually for 4 years). We investigated the three parameters (mu, sigma, tau) of ex-Gaussian distribution which is known to provide a very good fit to empirical reaction time data. Mu and sigma control the mean and the variance of the normal component and lambda the rate of exponential component (the right-skew of the distribution). These longitudinal data will be analyzed using a multivariate latent variable approach, where the parameters of the individual growth curves are modeled as latent variables. We will determine how early trajectories (over the first 15 weeks of treatment) can predict long-term trajectories (over the first 4 years since diagnosis). This approach would allow defining early predictors of long-term deficits.

Deciphering the functional redundancy of USP4 and USP15

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ABSTRACT

Ubiquitin-specific proteases (USPs) are a class of deubiquitinating enzymes that catalyze the removal of ubiquitin, a polypeptide post-translational modification that is essential in many cellular processes, from various proteins. Previous work established the USP paralogs USP4 and USP15 emerged from an ancestral USP about 500 million years ago from a whole genome duplication, and the majority of known vertebrate genomes contain a functional copy of both. High expression of USP4 is correlated with decreased overall survival in lung adenocarcinoma, whereas high expression of USP15 is correlated with increased survival. Both USPs are known to be involved in some of the same signalling pathways such as Wnt/β-catenin, however subfunctionalization has occurred such that they each regulate the stability of distinct substrates. Although USP4 and USP15 have diverged over evolutionary time, we hypothesize that there are mechanisms in place that allow one to perform the other's functions to a certain extent when deficient in one USP. To study the extent of this functional redundancy, we are analyzing the progeny of genetic crosses of mice in which one or both genes have been inactivated. Embryos null for both genes die at midgestation and are physically smaller than embryos heterozygous for both genes. They have underdeveloped livers, indicating a possible defect in hematopoiesis. Proper fetal hematopoiesis requires signalling through Wnt/ β-catenin pathway, and a systematic analysis of the components of this pathway has been undertaken to correlate deficiencies with the genotypes of our knockout mice. These findings will have implications for potential targeted therapies.

Creating partnership in the NICU; Parent's perspective

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ABSTRACT

Introduction | The neonatal intensive care unit (NICU) is a stressful environment for parents. Their involvement in their child care could reduce their stress and increase their satisfaction. It is crucial for parents to stay involved in the care of their newborn to facilitate parent-child attachment, transition to home, and future development of the child. Other NICU family-centered care and Neonatal Intensive Parenting Unit (NIPU) models have been proposed but need to be adapted to our NICU environment.

Aims | This study was conducted to identify facilitators and challenges from the parents' perspective that would encourage their involvement in their newborn's care.

Methods | Focus groups were recorded and transcribed. From content analysis of the verbatims we identified key elements and classified them under different themes that illustrate "facilitators" and "challenges" to parents' involvement.

Results | Between August and October 2018, we conducted three focus groups in which ten parents participated. We identified nine themes; Parent-Staff interactions, Consistency in care and caring staff, Newborn care, Nurse support, Family, Resources for parents, NICU environment, Resting moment and connection, and Academic and research.

Conclusions | The themes and examples identified will allow the NICU team to prioritize working strategies to implement in the NICU a workflow to create partnership with parents in the care of their newborn. More than implementing facilitators, we need to address the challenges to improve parents' satisfaction related to their participation in their newborn's care.

Stratégies pour Impliquer Les Patients Partenaires dans L'Éducation Médicale

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ABSTRACT

Contexte | L'enseignement de la médecine s'est développé à travers les années, favorisant aujourd'hui le concept de soins centrés sur le patient. Pour arriver à cette fin, l'Université d'Ottawa a créé le programme de patients impliqués dans l'éducation des professionnels de la santé (PIEPS) regroupant les patients standardisés, simulés et partenaires. Les patients partenaires (PP) sont des individus vivant avec une maladie chronique qui participent activement à l'enseignement médical. En partageant leur vécu avec la maladie aux étudiants, les PP contribuent au développement d'un partenariat entre médecins et patients. Dans le programme de médecine de l'Université d'Ottawa, les PP sont généralement recrutés par bouche à oreille et n'ont pas toujours accès à une formation adéquate. Pour assurer un enseignement de qualité, il y a nécessité de développer le volet PP du programme PIEPS.

Méthode | Nous avons complété une revue de la littérature sur l'implication des PP dans l'éducation médicale. De plus, nous avons organisé un groupe de discussion de 75 minutes regroupant 3 PP déjà impliqués auprès de la Faculté.

Résultats | Nous avons établi des stratégies de partenariat selon 4 axes : le recrutement, la sélection et la formation des PP, ainsi que la collaboration avec les enseignants. Nous avons aussi soulevé des stratégies visant à optimiser l'expérience des PP impliqués dans notre programme. Le programme de formation des PIEPS/PP mis en place par les Affaires francophones permettra aux enseignants d'avoir accès à des PP bilingues, fiables et engagés pour participer à leurs cours.

Conclusion | Notre recherche démontre que l'implémentation d'un réseau de recrutement centralisé ainsi qu'un meilleur encadrement des

How Language Impacts the Use of Outpatient Psychiatric Care for Homecare Patients With a Chronic Psychotic Disorder

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ABSTRACT

Introduction | People with chronic psychotic disorders have high healthcare needs to manage their illnesses. Language barriers may negatively impact their access to and quality of healthcare. The objective of this project was to evaluate how language status impacts use of psychiatric services for patients with chronic psychotic disorders.

Methods | A population-based retrospective cohort of Ontario home care recipients with pre-existing psychotic disorder was created using data from ICES. Home care data was used to identify patients' primary language. We captured three elements of mental healthcare utilization: outpatient psychiatric care, and mental health related hospitalizations and emergency department (ED) visits. Descriptive statistics were used to describe patient characteristics, and multivariable regression to evaluate the association between use of mental health care and primary language.

Results | The cohort consisted of 9,436 patients (8,097 Anglophones, 313 Francophones, 1,036 Allophones). Across all linguistic groups, use of psychiatric care was low with 53.4% of the cohort having no psychiatrist visits during the study period and 83.3% of the cohort having no mental health related hospital admissions or ED visits. Patient language did not impact use of outpatient psychiatric services or mental health related ED visits. Francophones had a higher rate of mental health related hospital admissions compared to Anglophones (RR= 1.36, 95% CI 1.02-1.80).

Conclusion | The use of psychiatric services and acute care among all homecare patients with chronic psychotic disorders was low but not associated with patient language. Further research is needed in order to understand the barriers to service these patients are experiencing.

Identifying Targets for Therapeutic Brain Stimulation in a Mouse Model

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ABSTRACT

Background | Evidence suggests that non-invasive brain stimulation, such as optogenetic stimulation and somatosensory electrical stimulation (SES), may enhance functional recovery following a stroke. This project aimed to develop a stimulation protocol using these techniques in mice. Optogenetic stimulation involves the activation or inhibition of neurons using light-activated channels inserted into the membranes of target cells. In SES, a low-level electrical current is used to stimulate peripheral nerves. Finally, these two methods were combined in a paradigm called paired associative stimulation (PAS), where a peripheral nerve and the motor cortex are conjointly stimulated.

Methods | Stimulation was applied in lightly anesthetized mice (Ketamine/Xylazine). Baseline motor-evoked potentials were measured by targeting a 5ms blue light pulse to motor cortex (M1). For the optogenetic and SES trials, cerebral blood flow measures were acquired continually using laser Doppler flowmetry over M1. Mice received either 100 pulses of optogenetic stimulation (10 Hz), 10 minutes of SES (0.5 mA), or 90 pairs of optogenetic stimulation and SES (0.5 Hz PAS). The motor-evoked potential was remeasured following stimulation.

Results | Optogenetic stimulation of M1 resulted in a significant increase in cortical blood flow over the stimulated area (18.4% change; p=0.011), while SES applied to the forepaw produced a significant decrease in blood flow in the contralateral M1 (11.8% change; p=0.030). Both stimulation techniques and PAS produced a non-significant increase in the amplitude of motor-evoked potentials.

Conclusions | Optogenetic stimulation and SES can modulate M1 hemodynamic responses, however these paradigms did not alter the resting motor threshold in our anesthetized preparation.

Maternal Health Outcomes of Women Living with HIV in Ontario

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ABSTRACT

Introduction | The incidence of new HIV cases in women is increasing in Canada, as is the population of women living with HIV (WLWH). Due to the availability of highly effective antiretroviral therapies and near-elimination of mother-to-child transmission of HIV in Canada, more women are expressing fertility intention and are becoming pregnant. The majority of research on pregnant WLWH focuses on neonatal outcomes and mother-to-child transmission of HIV, limiting our knowledge of maternal health outcomes. A recent Ontario study indicated that WLWH are at a higher risk of postpartum maternal hospitalizations than women living without HIV, however, there is little data on the types of maternal morbidities affecting this vulnerable population. The aim of this study is to assess adverse maternal outcomes of WLWH in Ontario.

Methods | This study is the second phase of a three-part project co-designed by an interdisciplinary team of clinicians, researchers, and community scholars with lived experience. We are conducting a population-based retrospective cohort study using linked health administrative databases at ICES. The cohort includes all pregnant and birthing WLWH delivering at Ontario hospitals from 2006/07 to 2017/18. Data is analyzed using multivariable regression to evaluate associations between adverse maternal outcomes and HIV status, as well as sociodemographic and clinical variables.

Results | We will determine whether maternal HIV status is associated with an increased risk for acute severe maternal morbidity, severe maternal morbidity, and adverse birth events.

Conclusion | Our results will identify potential gaps in obstetrical care for WLWH and provide insights for improving outcomes.

Upfront Esophagectomy: an Analysis of Staging Accuracy and Adjuvant Therapy

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ABSTRACT

Background | Esophageal cancer is the eighth most common form of cancer worldwide. The course of treatments for esophageal cancer depend on its etiology and severity. Most esophageal cancers are divided into two subtypes, squamous cell carcinoma (ESCC) and adenocarcinoma (EAC). For locally advanced ESCCs, the current preferred treatment is either neoadjuvant chemoradiation followed by surgery, or in the case of inoperability, definitive chemoradiotherapy. Similarly, locally advanced EACs are often treated with neoadjuvant chemoradiotherapy or perioperative chemotherapy. On the other hand, adjuvant chemotherapy or chemoradiation have shown limited effects and are associated with enhanced toxicities. Although the use of perioperative or neoadjuvant approaches have been reported to improve long-term survival, a single report presented data to suggest surgery upfront for earlier-stage EACs is superior. Results on the optimal treatment regimen are thus scattered, and the best tests to identify patients remain to be determined. Based on the available data, we propose to examine the Ottawa Hospital's experience with upfront surgery as a treatment for ESCC and EAC.

Objectives | What post-operative treatment is provided? What is the overall patient outcome with regards to morbidity and mortality? Do our preoperative staging tests accurately predict the final pathological stage?

Methods | Extracting data from prospectively-collected database of foregut cancer patients, within which we identified all patients that have not received induction therapy as part of their treatment for esophageal cancer. Data has been depersonalized, anonymized and encrypted. Missing information will be obtained from the hospital electronic health record as per the ethics protocol numbered 2011366-01H. From the data, we have extracted the specific details of staging tests, the final operative pathology, any complications and details of post-operative treatment.

Results | Our study population is composed of most males, 50 to 80 years old, suffering from cases of EACs, mainly in the lower-third involving the gastro-esophageal junction (GEJ). Almost half of patients undergo pre-operative treatment, while only a quarter undergo post-operative treatment. Both pre-operative and post-operative treatments almost always include chemotherapy or chemoradiation. Patients outcome in terms of mortality, grouped by associated stage of cancer, will be determined by analysis. Pre-operative staging tests remain to be evaluated using initial diagnosis and final pathological stage.

Conclusion| Further confirmation on the reality surrounding treatment for esophageal cancer at the Ottawa Hospital will allow physicians to make the best decisions in terms of upfront esophagectomy as treatment for esophageal cancer.

Utility of In-Patient Cardiac Telemetry for Sub-Clinical Arrhythmia

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ABSTRACT

Objective | The benefit of continuous ECG telemetry monitoring (CCT) in patients at high risk for developing life-threatening arrhythmia is well established. However, the utility of CCT in unselected General Cardiology in-patients is unclear.

Methods | We prospectively linked our CCT to the EMR of every patient admitted to the Cardiology service in June 2018. Telemetric events were prospectively defined as any arrhythmia that could alter clinical outcomes. CCT reports were read by two cardiac EPs blinded to patient information. We performed retrospective chart review in patients with telemetric events.

Results | 385 consecutive patients (mean age 69 ±14 years, 64% male) underwent 1043 days of CCT. 175 patients (46%) had ≥ 1 telemetric event, with 55 (14%) having ≥ 2 different events. Univariate predictors of events were increasing age, prior arrhythmia or admitting diagnosis of heart failure. The most common arrhythmia detected by CCT was AF/ Flutter (AF) in 82 patients (21%). AF was de novo in 33 patients (40%) with GDMT administered in 30 (91%) prior to chart review. Sustained VT was observed in 6 patients and all received appropriate therapy pre-discharge. Non sustained VT (> 3 beats but < 30 seconds) was observed in 80 patients (20%) but was not clinically significant in any patient.

Conclusion | These results suggest 21% of patients admitted to General Cardiology will have a novel clinically significant arrhythmia detected. The utility of linking CCT reports to electronic medical records appears a promising new avenue to improve quality and patient outcomes in Cardiology.

Protecting Our Hearts... Dyslipidemia Screening for Cardiovascular Disease Prevention

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ABSTRACT

Introduction | Dyslipidemia is an important risk factor for cardiovascular disease, with evidence showing that younger patients (especially those with elevated LDL-C levels) can benefit significantly from long-term therapy, even if they are at low risk over the short-term. The current Canadian Cardiovascular Society (CCS) guidelines recommend dyslipidemia screening for males and females aged 40-75y.o.

Methods | The main goal of this Quality Improvement project is to assess if patients at the Civic Family Health Team (FHT) are being adequately screened for dyslipidemia, and then to undertake a root cause analysis to determine factors that are leading to a potential practice gap using the Model for Improvement from the Institute of Healthcare Improvement.

After developing the inclusion criteria (males and females within the Civic FHT, currently aged 40-45y.o.), nineteen patients were randomly selected for further chart review. Once the results of this review were completed, relevant clinic stakeholders were consulted to develop a holistic plan to address the identified practise gaps.

Results | Overall 74% of reviewed patients underwent dyslipidemia screening. This figure decreased to 47% if patients who were screened before age 40y.o. without any follow-up testing were separated from the results. 26% of patients between 40-45y.o. were not screened; 16% were female and 11% were male.

Conclusion | A practise gap in dyslipidemia screening was identified during the chart review. A root cause analysis identified a combination of patient, healthcare provider, clinic and policy factors. Using an Impact/Feasibility approach, different change ideas were developed to address this practise gap.

Towards Structural Basis of Sitosterolemia Mutations in ABCG5/G8

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ABSTRACT

Introduction | Cholesterol is a major component of cell membranes where it influences its biophysical properties, promotes domain formation, and participates in signaling pathways. While it plays a critical role in maintaining biological functions and cell survival, abnormal elevation of plasma cholesterol causes hyperlipidemia, a key biomarker to many cardio-metabolic disorders, including atherosclerosis and fatty liver disease. The cholesterol-efflux ABC transporters are essential in maintaining cholesterol homeostasis. Among these transporters, ABCG5/G8 is responsible for direct secretion of excess cholesterol (and dietary sterols) into the gut lumen and the bile. Mutations that inactivate ABCG5/G8 can cause sitosterolemia, a rare autosomal recessive disease characterized by the accumulation of plant sterols in plasma, hypercholesterolemia and development of premature coronary heart disease. The molecular events underlying the disease manifestation remain elusive. Functional and structural characterization of these mutants is required for understanding how these genetic defects impact ABCG5/G8 mediated sterol transport.

Methods | We have optimized an improved purification protocol for ABCG5/G8 and established robust and high-throughput in-vitro functional assays in order to characterize the structural-function relationship of naturally occurring sitosterolemia mutations.

Results: I am investigating the missense mutants R419H/P, E146Q (ABCG5), and R543S, G574R (ABCG8), which have been shown to be properly folded and exit the ER. here, I am presenting the expression, purification and the catalytic activity of these disease mutants.

Conclusion | The results will further reveal mechanistic details of ABCG5/G8-mediated sterol transport, ultimately enabling pharmacological manipulation and drug designs to therapeutically modulate the cholesterol efflux function as implicated in cardiovascular diseases.

CT Utilization in the Emergency Department for Symptomatic IBD patients

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ABSTRACT

Background | Computed tomography (CT) imaging of the abdomen is commonly performed in the Emergency Department (ED) to evaluate Inflammatory Bowel Disease (IBD) patients. However, there are concerns over its repeated use due to excessive radiation exposure.

Purpose | To determine the proportion of IBD patients with gastrointestinal symptoms who undergo abdominal CT imaging of the abdomen in the ED, and the proportion of scans with clinically relevant findings.

Methods | We performed a retrospective cohort study between 01/01/2009 and 31/12/2018. ED encounters involving adults (age ≥17 years) with a pre-existing diagnosis of IBD were identified form our institution data warehouse using ICD-10 codes. A chart review determined: study eligibility, CT utilization and CT findings. Encounters were excluded if they did not involve gastrointestinal symptoms, or to evaluate patients within 1-month of surgery. Clinically relevant CT scans were defined as those with penetrating complications (abscess, phlegmon, or internal fistulas).

Results | Thus far 1793 ED encounters have been reviewed. Of these encounters 839 met our study criteria and 954 were excluded. These encounters correspond to 118 Crohn's Disease (CD) patients and 59 Ulcerative Colitis (UC) patients. The primary presenting symptoms, the proportion of encounters that underwent abdominal CT imaging, and the findings from the CT imaging are currently being evaluated.

Conclusion | Understanding the proportion of IBD patients who undergo abdominal CT imaging in the ED and the proportion of scans with clinically relevant findings are important first steps to determine the appropriateness of CT utilization in this setting.

Role of Cdx-mediated Epigenomic Changes in Colon Cancer Progression

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ABSTRACT

Transcription factor Cdx2 is considered as a diagnostic marker for colon cancer. A subset of high-risk stage II colon cancer patients lacked Cdx2 expression were benefitted from adjuvant chemotherapy. In our experience APCMin/+-Cdx2 mouse model recapitulate several aspects of invasive colorectal cancer phenotype. Tumour load in the distal colon increased with the combinatorial loss of Cdx1 along with Cdx2 in these mice. These findings establish a novel role for Cdx family transcription factor in mediating colon tumorigenesis. Co-expression of the Cdx family of homeodomain transcription factors (Cdx1, Cdx2, and Cdx4) in all three germ layers of the mouse embryo are involved in crucial developmental processes. The life-long expression of CDX1 and 2 in intestinal epithelial cells contributes to the regulation of intestinal homeostasis and intestinal patterning. Addressing previously challenging issues of determining the functions of CDX family proteins, Dr. D. Lohnes lab has developed a Cdx1-Cdx2 double-null mutant mice as described in Savory 2009, which eliminates the expression and functions of all Cdx proteins including Cdx4 in the post-implantation embryo and negates the need of a triple Cdx null mice. Synergistic functions of CDX proteins were shown to at least partly regulate transcription of developmentally important genes such as Cyp26a1 through recruitment of the of the switch-sucrose non-fermentable (SWI/SNF) chromatin remodeling complex that contains ATPase subunit Brg17 to the target gene promoters and adopt an open chromatic structure. In the current study relevance of this finding in the context of epigenetic regulation of gene expression and chromatin remodelling during colon cancer tumorigenesis is further explored. In combination with ChIP-seq and expression analyses Cdx2 target genes were identified. Further investigation will explore Cdx2 mediated novel epigenomic mechanism responsible for Colorectal cancer phenotype in our mouse model. This basic, fundamental knowledge is required to understand Cdx2 mediated epigenetic changes that regulate the target gene expression during mouse intestine development, to better understand Cdx2 mediated a subtype of colon cancer progression and possible improved therapeutic strategy for future.

A Living Guideline for Diagnosing and Managing Pediatric Concussion

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ABSTRACT

Autism Spectrum Disorders (ASD) are clusters of serious neurodevelopmental disabilities characterized by social impairments, repetitive stereotyped behaviors, and communication deficits. Additionally, there are studies that also report some ASD patients exhibiting motor deficits and coordination symptoms. The 16p11.2 chromosomal copy number deletion is a strong genetic risk factor associated with autism, and contributes to 1% case prevalence. Previous work from the Dr. Chen laboratory has shown that the 16p11.2+/- mice have significant motor learning delays in a running-disc task, as well as a noradrenergic innervation deficit specific to L2/3 layer of the motor cortex (M1). We then employed an in vivo two photon imaging technique to chronically monitor dendritic spine reorganization of L2/3 pyramidal neurons throughout training process. These experiments show that 16p11.2+/- mice have the same learning-induced spine formation as wild-type mice, but have a delayed spine pruning process, which is highly consistent with their motor learning delay. Since previous literature has shown that the NA system is an important neuromodulator in synaptic plasticity and memory formation, we hypothesized that activating the M1-projecting specific NA neurons during the motor learning will restore normal spine reorganization and improve learning acquisition. Using a designer receptors exclusively activated by designer drugs strategy (DREADDs), we show that noradrenaline stimulation improves spine reorganization and motor learning in 16p11.2+/- mice. Our results demonstrate that the impaired NA neuromodulation contribute to the delayed motor learning phenotype in 16p11.2+/- mice, and targeting this circuit could guide development of therapeutics improving motor developmental learning in ASD patients.

An Exploratory Qualitative Study Examining Markers of Physical Activity and Attitudes towards Exercise in Adolescents with Anorexia Nervosa

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ABSTRACT

Compulsive exercise is a significant feature of anorexia nervosa and is associated with increased inpatient treatment requirements and poorer treatment outcomes (Strober, Freeman, and Morrell, 1997). This qualitative study sought to understand the exercise perspectives of adolescents with anorexia nervosa, specifically (1) healthy versus unhealthy exercise, (2) the perceived effects of exercise, and (3) the role of exercise in treatment. Seventeen adolescents (15 female) with anorexia nervosa, 12-18 years old, were recruited from the Children's Hospital of Eastern Ontario. Six current inpatients, five current day program patients, and six outpatients treated by one of these programs in the past two years, completed semi-structured interviews which were audio-recorded, transcribed verbatim and analyzed in accordance with Braun, Clarke, Hayfield, & Terry's (2019) six-phase thematic analysis guidelines. Emerging themes included: exercise has both benefits and risks, the importance of exercise education, and the five perceived components of an ideal exercise program such as focusing on fun and adapting the program to each individual. Given the discrepancy amongst treatment plans for individuals with anorexia nervosa (Gümmer et al., 2015), understanding patients' perspectives about compulsive exercise and the role of exercise at various stages of recovery is an important first step towards improving treatment.

Characterizing Novel BiSyn Transgenic Mice: Bifluorescent Visualization of Alpha-Synuclein Aggregates

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ABSTRACT

Introduction | Parkinson's disease (PD) is an incurable, neurodegenerative disease with an extensive prodromal phase. The Braak hypothesis suggests a pathological spread of alpha-synuclein aggregates from the enteric nervous system (ENS) to the midbrain in a prion-like fashion occurring over a five- to twenty-year prodromal period. Transmission of a-syn aggregates through the vagus nerve is supported by both human and mouse vagotomy data, however the initiation site of a-syn aggregation and the mechanism of cell-to-cell propagation have yet to be elucidated. Our novel BiSyn (i.e., bimolecular fluorescence complementation of a-syn aggregates) system was developed to address these gaps.

Methods | We packaged an adeno-associated virus (AAV) with our BiSyn construct and infected the striatum of wildtype mice to assess the efficacy of our system. We are currently awaiting results from glutathione-deficient and -null mice to assess whether reactive oxygen species accumulation contributes to an accelerated pathological phenotype.

Results | AAV-BiSyn infection in wildtype mice led to BiSyn fluorescence in neurons at the striatal injection site. A-syn aggregates were also detected in axon terminals in the ipsilateral substantia nigra at 28 days post-infection, supporting retrograde propagation into the nigra.

Conclusion | Our preliminary AAV/BiSyn data demonstrates our system's potential as a critical tool for answering question about the PD prodromal phase, which could lead to novel therapeutic interventions that delay or preclude nigral dopaminergic degeneration. In future experiments, we will assess the potential propagation of a-syn via exosomal transmission by injecting AAV-BiSyn at various sites throughout the ENS.

Restructuring the uOttawa Clinical Research Mentoring Program

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ABSTRACT

Lack of training in clinical research is an unfortunate feature of Canadian medical schools, including The University of Ottawa. In response, a program was launched in 2017 involving 30 students and 30 mentors. The goals of the program included: sufficient exposure to clinical research so that students could determine if they enjoy it, as well as increased cognizance of the steps involved in the research process.

This year, we set out to evaluate the existing program and determine what aspects of it must change in order to achieve the aforementioned goals. Every student and mentor involved in the original program were contacted via email to set up phone interviews. We interviewed 17 mentors and 24 students using 18-item and 19-item surveys, respectively.

We were able to gauge the most valuable aspects of the program, the most lacking components, and the feasibility of its goals. Those that were involved most valued individualized mentorship and student involvement in the mentor's research. The most lacking aspects were identified as a palpable lack of structure and expectations. However, the goals were described to be reasonable, which has led us to restructure the program such that the positive components remain intact under a much more solid framework with multiple interim check-ins and endpoints.

With this revised program structure, we hope to not only effectively combat the lack of familiarity with clinical research experienced by University of Ottawa medical students, but also encourage students to pursue clinical research within their own practices in the future.

Tobacco and Cannabis Use Before and After Living Kidney Donation

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ABSTRACT

Background | End stage kidney disease (ESKD) is an increasingly common cause of morbidity and mortality worldwide. Living kidney donation (LKD) offers superior outcomes as compared to both deceased kidney transplantation and dialysis, necessitating ongoing research into LKD outcomes to ensure donor safety. While potential donors undergo extensive evaluation for surgical and long-term medical risks, there is little known about donor tobacco and cannabis use and their impact on donor kidney function.

Objective | To characterize tobacco and cannabis use in living kidney donors and to establish if use is associated with a decline in kidney function following donation.

Methods | We conducted a retrospective cohort study of living kidney donors at The Ottawa Hospital between January 1st, 2009 and December 31st, 2018 to quantify tobacco and cannabis use prior to donation. Prospectively, we conducted a standardized telephone survey of all donors to establish current use.

Results | A total of 263 donors were contacted, of which 179 completed the survey, 20 declined to participate, and 64 were either unreachable or unsuccessful call backs. Of the 179 donors, 23 reported current tobacco use, 63 reported former use, and 93 had never used. Prior to donation, 30 donors reported tobacco use and 58 reported previous use. Of the 179 donors, 26 reported cannabis use within the past 12 months.

Conclusion |Our preliminary results suggest that tobacco and cannabis use is common within the kidney donor population. Further analysis is required to determine the impact of tobacco and cannabis use on kidney function.

Quantification of I-131 NaI Thyroid Remnant Uptake in Thyroid Cancer

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ABSTRACT

Introduction | Management of patients with thyroid cancer usually involves a total thyroidectomy, followed by radioiodine ablation therapy (RIAT) with I-131 NaI to eradicate thyroid remnant (residual tissue) and metastases. Typically, thyroid remnants are assessed visually. This is the first study that quantifies thyroid remnant uptake on thyroid scan and enables the direct comparison with Thyroglobulin (Tg), a serum biomarker that indicates presence of thyroid tissue.

Methods | Patients referred for RIAT at The Ottawa Hospital from 2015-2017 are reviewed. Post-RIAT images are reconstructed with attenuation corrections for quantification. Total thyroid remnant activity (TTRA) is calculated. Clinical history, lab-work, and imaging are obtained from medical records. Patients with metastases, positive anti-Tg antibodies, and incomplete data are excluded. Cases are divided into subgroups using the median Tg and median TTRA during treatment. Correlations are analyzed using Pearson correlation coefficient.

Results | For 170 patients (mean age: 50.7±16.1 years, 64% female), the median Tg and median TTRA during RIAT (mean dose: 3.3±1.7 GBq) are 6.8 pmol/L (range: 0.15-531.2) and 194.5 g/mL (range: 0.0-25217.5) respectively. There is no statistically significant ($p>0.05$) correlation between Tg and TTRA ($r=0.011$, $p=0.88$). Furthermore, a subgroup (n=37) has Tg lower than the median but TTRA higher. There are patients (n=10, 6%) with significant TTRA and undetectable Tg, indicating probable false negative Tg measurements.

Conclusion | Quantification of I-131 NaI uptake on thyroid scan is feasible. While Tg may indicate presence of thyroid tissue, false negatives can occur, and thus patient follow-ups should also include diagnostic thyroid scans to reliably determine disease recurrence.

Module d'Auto-Apprentissage en Éducation Médicale: Fondements, Principes et Conception

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ABSTRACT

L'apprentissage en ligne est un pré-requis pour l'agrément des programmes de doctorat en médecine au Canada. Ce projet s'est intéressé aux fondements pédagogiques qui sous-tiennent les modules d'auto-apprentissage en-ligne. La question de recherche retenue est : quels sont les fondements pédagogiques de modules d'auto-apprentissage présentés dans les écrits scientifiques ?

Cette recherche s'est déroulée en effectuant une recension critique des écrits sur les fondements pédagogiques des modules d'auto-apprentissage. Nous avons cherché dans les bases de données suivantes : ERIC, MedLine, PubMed, World of Science, Google Scholar. Nous avons retenu les critères d'inclusion suivants : articles publiés dans les derniers 10 ans, disponibles en anglais ou en français et revue par les pairs, et les critères d'exclusion qui suivent : articles portant sur l'acquisition ou mise-en-pratique de compétences cliniques. Nos recherches nous ont conduit à analyser 100 articles. Les articles ont été classés et analysés et l'accord interjugés a été calculé.

Les écrits scientifiques nous indiquent que les modules d'autoapprentissage sont peu ou mal définis. Les principes pédagogiques qui les sous-tendent sont généralement peu explicites quand ils ne sont carrément pas absents. Nous avons également constaté qu'il existait peu de ressources reconnues pour bâtir ces modules ou les évaluer. Il faut généralement s'en remettre à des propositions générales issues du milieu de l'éducation. En nous inspirant de la littérature et des six étapes de développement d'un curriculum proposées par Kern, nous avons élaboré 10 conseils pour élaborer des MAA en ligne : évaluer le besoin, définir les apprentissages, assurer la validité, choisir un design pédagogique, s'appuyer sur une théorie didactique, contrat didactique, intégrer l'évaluation, assurer l'alignement pédagogique, recourir à une stratégie d'implantation, et efficacité.

Sexually Simorphic Anxiety-Like Behaviors in Prenatally Stressed Prepubescent Mice

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ABSTRACT

Introduction | Experiences that occur early during development may increase risk of developing later life physical and mental illnesses in a sex-specific way. Adult rodents exposed to early-life stressors show depressive- and anxiety-life behaviors that differ between males and females, but the age of onset of these sexually dimorphic impairments remains unclear. Our objective was to investigate the effects of a prenatal stressor on physical and behavioral outcomes in pre-pubertal male and female offspring. We hypothesized that prenatally stressed offspring would show abnormal body weight changes across development and exaggerated anxiety-like behaviors at the pre-pubertal stage and that these outcomes would be sex-specific.

Methods | C57BL/6 mice in the first or second trimester of pregnancy experienced a physical restraint stressor (30 minutes, 3 times/day) or were left undisturbed (non-stressed controls). From postnatal day (PND) 1 to PND21, pups were weighed daily. On PNDs 19 and 20, anxiety-like behaviors were tested in the open-field and elevated-plus maze tests, respectively.

Results | Male pups stressed during the second trimester of pregnancy had exaggerated weight gains during development, whereas weight changes did not differ between groups in females. In contrast, prenatally stressed females, but not males, showed anxiety-like behaviors in the elevated-plus maze test, while no differences were observed between groups in the open-field test, in either males or females.

Conclusion | Prenatal stress affects physical growth and promotes anxiety-like behaviors in pre-pubertal offspring and these effects are trimester- and sex-specific.

MRI Texture Analysis To Differentiate Recurrent Brain Tumour from Radionecrosis

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ABSTRACT

Background | Treatment of intracranial metastases and primary malignant brain tumours often involves radiation therapy, whereby treatment progress is monitored by periodic magnetic resonance imaging (MRI). When newly enhancing and enlarging lesions are seen on serial imaging, it is often difficult to discern if it is a result of recurrent brain tumour (RBT) or radiation-induced necrosis (RN). Computer-aided diagnosis using texture analysis (TA) may address this diagnostic challenge by identifying patterns of pixel grey-levels on contrast-enhanced T1-weighted imaging (T1WI) which differentiate RBT from RN (2). The aim of this study was to evaluate TA in accurately differentiating RBT from RN.

Methods | This is a single-centre experience of 53 patients that received radiation for high grade or metastatic brain tumours (55 total lesions) with subsequent RBT suspected on followup MRI. Contrast-enhanced T1WI images for each patient were segmented using ImageJ and analyzed using MaZda TA software. Final diagnosis was determined from histopathology for patients who underwent resection or from serial MRIs/clinical exam for patients who did not undergo resection. TA results of RBT and RN groups were compared using the Mann-Whitney U test.

Results | 3D texture features revealed no significant difference between RBT and RN groups. 2D texture features revealed a significant difference between RBT and RN in coronal variance ($U = 222.00$, $P = 0.0456$) only.

Conclusions | TA was able to discriminate between RN and RBT using the coronal variance 2D texture feature, but no other 2D or 3D texture features.

Network-basis Seizures Induced By Deep Brain Stimulation: Literature Review and Connectivity Analysis

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ABSTRACT

Background | Deep brain stimulation (DBS) implantation surgery has shown efficacy in treating treatment-resistant Parkinson's disease and some psychiatric illnesses. While transient, self-limiting seizures are an infrequent but known complication of brain surgery, electrical stimulation itself has occasionally been reported to cause seizure activity at delayed timepoints. The neural circuitry involved in stimulation-induced seizures is unknown. We report a case of seizure in a 47-year-old female with chronic subcallosal cingulate (SCC) DBS for treatment of refractory anorexia nervosa (AN) occurring with electrical stimulation onset. Voltage greater than that needed for therapeutic effect caused a generalized seizure, with subsequent full recovery.

Methods | We reviewed the literature for other cases of delayed postoperative DBS seizures associated with stimulation. We also investigated whether the higher voltage may have recruited networks involved in epilepsy.

Results | The voltage at which the seizure occurred stimulated a larger area and engaged vulnerable networks including the bilateral hippocampi, cingulate gyrus and temporal lobes. Literature review identified 20 studies reporting delayed seizure after DBS surgery, 13 of which demonstrated a robust association with – mostly non-motor – DBS stimulation.

Conclusions | Non-motor DBS targets, particularly in epilepsy patients, may be more vulnerable to stimulation-induced seizures; as such extra caution should be used when programming stimulation parameters at these DBS targets.

Establishing Uroflow Nomogram for Female Population with Urinary Incontinence

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ABSTRACT

Introduction | Urinary incontinence is a prevalent and often embarrassing problem amongst the female population, estimated to impact 50-75% of women at one point in their lifetime. A thorough assessment of patients with incontinence requires a detailed medical history and physical exam. Additional investigations, such as uroflowmetry, are sometimes warranted in order to gain a better understanding of the patient's symptoms or to confirm the diagnosis. There are very few studies establishing uroflowmetry parameters in the female population. A recent systematic review recommends further research for uroflowmetry measurements (1). Currently, the Liverpool nomograms being used were established 30 years ago and include only 249 females, which potentially biases generalizability.

Methods | This retrospective chart review study included female patients presenting to the Ottawa Hospital's urogynecology clinic between January 2016 and January 2018 (n=2000). uroflowmetry parameters including max flow, average flow, voiding time, flow time, time to max flow, voided volume and post void residual will be recorded. We aim to create a nomogram for maximal urinary flow, average urinary flow and postvoid residual.

Results | Our study included 463 patients. Average age was 54.4 (±13.6 sd), average gravidity was 2.5 (±1.9 sd) and average parity 2.1 (±1.6 sd). 398 patients had previous vaginal deliveries and 44 patients had at least one ceserean section. Voided volume mean was 358ml (± 229 sd) and Maximum flow rate median was 23 (±14.65 sd).

Conclusion | In summary, our study established percentile uroflowmetry nomograms for female patients presenting to a urogynecology clinic with the main complaint of urinary incontinence. These nomograms will help clinicians evaluate different uroflow parameters for patients presenting with urinary incontinence, enabling effective screening for voiding dysfunction, while also evaluating the response to medical or surgical management

Does Clinically Isolated Aortitis Impact Patient Outcome?

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ABSTRACT

Introduction | Clinically isolated aortitis (CIA) is an insufficiently studied entity commonly diagnosed incidentally on pathological specimens following ascending aortic aneurysm repair, and accounts for up to 81% (n = 64) of aortitis operative cases1,2,3. We sought to characterize the clinical and surgical course of patients with CIA compared to matched controls to determine the impact of CIA on outcome.

Methods | From 2004 to 2018, 51 patients who underwent aortic surgery with a pathological diagnosis of CIA were propensity matched 2:1 to 102 control patients without aortitis. Preoperative and postoperative clinical, echocardiographic, and imaging data were evaluated, and the rate of aortic reoperation, aortic events, and mortality were calculated. The median follow-up is 3.0 years and range of 0.0 to 14.3 years.

Results | The rate of mortality was higher in patients with CIA (25.5%) compared to patients without aortitis (18.6%). Of patients with CIA, 56.9% underwent concomitant aortic valve repair and 5.9% underwent concomitant mitral valve repair/replacement procedures, compared to 26.4% and 3.9% respectively in patients without aortitis. At follow-up, a greater proportion of patients with CIA (43.1%) had aneurysms greater than 50 mm in their thoracic aorta compared to patients without CIA (13.7%). Only 25.5% of patients were on systemic corticosteroids at follow-up.

Conclusion | CIA appears to be associated with a higher rate of mortality and post-operative aortic aneurysm. The results of this study will help address a knowledge gap in operative outcomes of patients with CIA, and aide in developing guidelines in its management.

Improving Documentation and Physician Experience Through New EPIC EMR Tools

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ABSTRACT

Introduction | The CHEO Orthopaedic ambulatory clinic went live with EPIC three years ago and has continuously sought to improve both documentation and physician experience with the EMR system. Previous research by our group demonstrated both improvements in documentation, as well as some new deficiencies, in using the EPIC system over paper-based charts. The goal of the current project was to further improve the quality, completeness, usability, and speed of documentation for physicians through the creation and revision of standardized note templates and SmartSets for a series of commonly seen diagnoses in the high-volume ambulatory clinic.

Methods | A total of 8 common diagnoses were selected for SmartSet development and revision, and following their implementation in the clinic, staff, residents and fellows were educated on their use and feedback collected. One month later, a retrospective chart analysis was performed on 20 randomly selected patients for each diagnosis both pre-EMR, post-EMR, and post-SmartSet development. An additional evaluation study to quantify the effect on efficiency of standardized template implementation was also performed with a representative group of clinicians.

Results | Early provisional results show that previously noted deficiencies in EMR documentation were improved through SmartSet use. Standardized note templates appear to decrease the time required for a physician to complete clinical documentation for a common pediatric orthopaedic diagnosis.

Conclusions | Further feedback will be sought from all clinicians to continue to improve the newly created SmartSets, as well as collaboratively developing new templates for additional commonly encountered diagnoses within the Pediatric Orthopaedic division.

Examining the Association between Patients' Sociodemographic Factors and Access to Community Resources?

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ABSTRACT

Introduction | Patients are routinely referred to community resources (CR; e.g., diabetes education, mental health) but often require navigation services to access these resources. The Access to Resources in the Community (ARC) program introduces a lay, bilingual Patient Navigator in primary care practices to help patients overcome access-related barriers (e.g., finances, transportation) and reach the appropriate CR. A randomized controlled trial is evaluating the ARC program vs. telephone-based navigation services (i.e. Ontario 211). This study seeks to identify sociodemographic factors (e.g., age, gender, financial status) that influence patients' ability to access CR.

Methods | This is a retrospective analytical study based on the RCT. Patient data is collected via telephone surveys conducted at baseline and 3 months post-intervention. Bivariate analyses and logistic regressions were performed to investigate the relationship between patient sociodemographic characteristics and access to CR.

Results | The multivariate regression yielded the following predictor variables: higher # of needs, higher # of barriers, cost as a barrier, and low level of social support. This suggests that factors associated with adversity result in higher access. The ARC navigator leads to higher access ($p<0.05$) but does not influence the predictor variables from the regression. Our results suggest that navigation services help patients overcome sociodemographic barriers to access CR.

Conclusion | Patients with certain social complexities may benefit more from navigation services to access CR.

Distributed Network Meta-Analysis of Multi-Regional Data Approximates Individual-Level Multivariable Regression Analysis

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ABSTRACT

Background | When individual-level routinely collected health and demographic data cannot be pooled, international epidemiology studies have used distributed networks and meta-analysis to obtain overall estimates from multi-jurisdictional data. We aimed to validate this methodology using various multivariable regression models and under varying conditions (heterogeneity, sample size, model type, and event rate) using Canadian population-based health administrative data.

Methods | We used Ontario health administrative data to analyze trends in pediatric inflammatory bowel disease health services use in each Local Health Integration Network (LHIN) to simulate multiple jurisdictions. Effect estimates were obtained from Cox proportional hazards, logistic, and negative binomial regression models. LHIN estimates were then meta-analyzed using fixed and random effects models to compute provincial estimates. Beta coefficients from the distributed network and meta-analysis were compared to those from individual-level analyses using the z statistic at 5% significance. The summary effect estimates and 95% confidence intervals (CI) were visually assessed. I2 and Cochran's Q were used to evaluate heterogeneity.

Results | The beta coefficients from the distributed network and meta-analysis were not different than the beta coefficients generated using individual-level data ($p>0.05$ in all cases). Summary effect estimates and 95% CIs were also comparable to those from individual-level data. Fixed and random effects models performed equally well across all conditions used in our study, though random effects models resulted in wider confidence intervals in the presence of significant heterogeneity.

Conclusions | Distributed network analysis, with meta-analysis combining aggregate data, is a useful method of estimating individual-level effect estimates in observational studies where individual-level data cannot be shared. This study has important implications for multi-jurisdictional epidemiology and health services research, particularly in Canada where individual-level data cannot be shared across provinces.

Identification and Characterization of Stem Cells in Skeletal Tissues

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ABSTRACT

IMore than half of the Canadian population suffers from pathologies in bones, cartilage or joints throughout their life. Athletes who endured repeated injuries, as well as aging populations have a much higher risk of being affected by bone complications. While bone tissue has a high regenerative capability, tendons, cartilages and ligaments tend to have a slower and blunted healing process, notably in the elder generation. It is known that stem cells play a role in skeletal tissue regeneration, but it is debated what type of stem cells (skeletal stem cells, mesenchymal stem/stromal cells, pericytes, etc.) has the highest contribution, and why skeletal tissues lose this regenerative capacity with age. Here, we combined classical lineage tracing approaches (using various inducible Cre-driver mouse lines) with whole-organ, 3D multicolor imaging cytometry to identify and localize stem cells in skeletal tissues and monitor their contribution to various tissues during homeostasis and tissue repair. We also used standard cellular and molecular assays, including single cell RNAseq, to characterize these cell populations. So far, our data suggests that Sox9+ cells are bona fide skeletal stem cells giving rise to all bone and cartilage tissues in postnatal animals. These cells are not derived from marrow stroma or pericytes and do not contribute to these lineages in homeostasis. Taken together, our results will help design more effective regenerative therapies for patients by providing a better fundamental understanding of the stem cells in skeletal tissues.

Élaboration d'un Modèle d'offres 'activités sur la Collaboration Interprofessionnelle

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ABSTRACT

Introduction | Pour prodiguer aux patients des soins de santé primaires axés sur eux, le développement de la pratique interprofessionnelle est essentiel. Le niveau de collaboration nécessaire dans une équipe interprofessionnelle en vue d'offrir les meilleurs soins possible n'est atteignable que par la formation d'un programme d'éducation interprofessionnelle au niveau du premier cycle. Par ailleurs, l'évaluation du programme de médecine de l'Université d'Ottawa par le Comité d'agrément a soulevé le besoin de revoir les activités pédagogiques dudit programme. Ce projet vise à élaborer un programme éducatif qui puisse favoriser le développement d'activités interprofessionnelles grâce à l'élaboration de grandes orientations pédagogiques et la présentation schématique du futur programme.

Méthodologie | Révision des objectifs d'apprentissage interprofessionnels des divers programmes proposant des stages cliniques à l'Hôpital Montfort. Révision, proposition et conception d'activités pédagogiques inspirées des programmes interprofessionnels développés par des institutions académiques canadiennes, qui favorisent l'apprentissage collaboratif entre divers programmes et facultés. Une approche de recherche participative et collaborative est privilégiée.

Résultats | Cette recherche permettra la conception d'un programme pan-universitaire qui répondra aux besoins pédagogiques suivants des étudiants : mises-en-situation auxquelles ils auront à faire face comme futurs professionnels ; clarification des rôles/responsabilités cliniques associés à chaque profession ; meilleure communication interprofessionnelle ; interventions interprofessionnelles afin d'apprendre avec, à partir et à propos des autres en milieu clinique.

Conclsusions | Ce projet vise à réaligner les activités interprofessionnelles de l'Université d'Ottawa avec les exigences de l'agrément, les besoins des programmes d'études, les meilleures pratiques dans les domaines et les intérêts des étudiants.

AMPK Promotes Xenophagy through Priming of Autophagic Kinases upon Detection of Bacterial Outer Membrane Vesicles

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ABSTRACT

Introduction | The autophagy pathway is an essential component of the innate immune response, capable of rapidly targeting intracellular bacteria, which are subsequently degraded by lysosomal enzymes. Recent work has begun to elucidate the regulatory signalling for autophagy induction in response to pathogenic bacteria. However, the initial signalling regulating autophagy induction in response to the detection of pathogens remains largely unclear.

Methods | We used a variety of molecular biology techniques such as genomic editing with CRISPR/Cas 9, Western blotting, confocal microscopic, and infection assays to conduct this study.

Results | Here we report that AMPK, an important upstream activator of the autophagy pathway, is rapidly stimulated upon detection of pathogenic bacteria, prior to bacterial invasion. Bacterial recognition is initially achieved through detection of outer membrane vesicles (OMVs). Additionally, we show that AMPK signalling relieves mTORC1-mediated repression of the autophagy pathway in response to Salmonella infection, positioning the cell for a rapid induction of autophagy. Surprisingly, we found that the activation of AMPK and inhibition of mTORC1 in response to extracellular Salmonella are not accompanied by an induction of bulk autophagy. However, upon Salmonella invasion AMPK signalling is required for efficient and selective targeting of bacteria-containing vesicles by the autophagy pathway through activation of pro-autophagic kinase complexes.

Conclusion |Collectively, these results demonstrate a key role for AMPK signalling in coordinating the rapid autophagic response prior to invasion of pathogenic bacteria.

Understanding the Consequence of CaMKIIa SUMOylation on Neuronal Function

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ABSTRACT

Introduction | Calcium-calmodulin dependent kinase II alpha (CaMKIIa) is highly expressed in dendritic spines of glutamatergic neurons in the adult brain and is critically involved in learning and memory. During long-term potentiation (LTP) of glutamatergic synapses, CaMKIIa binds Ca2+/CaM to become active, and phosphorylates AMPA receptors to promote their trafficking to the post-synaptic density; thus, strengthening synaptic transmis-sion. Recently, we have identified all four CaMKII isoforms as targets of a post-translational modification called SUMOylation. As a result, we propose that SUMOy-lation is an important regulator of CaMKIIa and therefore is involved in learning and memory formation. Moreover, mutations within the CaMKII SUMOylation site have re-cently been linked to Autism Spectrum Disorder, further supporting the importance of SUMOylation on proper neurodevelopment.

Methods | We are investigating the mechanisms by which SUMOylation effects CaMKIIa stability, cellular localization, and activity to understand the role of SUMOylation in the context of neuronal function. To do this, we generated a GFP-tagged CaMKIIa fusion protein that allows us to monitor the stability and localization of CaMKIIa through quantitative western blot analysis and fluorescent microscopy, respectively.

Results | We have confirmed that SUMOylation occurs in cells and an HA-SUMO2 tagged mouse model.

Additionally, we have optimized a biolistic transfection approach to study the effect of SUMOylation on the dynamics of the subcellular trafficking of CaMKIIa in individual neurons during plasticity.

Efficacy of Thromboprophylaxis in Reducing Rate of Peripherally-Inserted Central Catheter (PICC)-Associated Thrombosis at CHEO

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ABSTRACT

Background | Central venous catheters (CVCs) are commonly used for medication administration, intensive fluid management and hemodynamic monitoring. However, CVCs are identified as the most prevalent cause of the development of deep vein thrombosis (DVT) in children. Evidence supporting the use of routine thromboprophylaxis for CVCs is limited. As there are currently no evidence-based guidelines, the use of thromboprophylaxis varies widely in children. At the Children's Hospital of Eastern Ontario (CHEO), thromboprophylaxis is administered to patients with peripherally inserted central catheters (PICC) based on the presence of elevated inflammatory markers (including leukocytes, fibrinogen, erythrocyte sedimentation rate and C-reactive protein). Anecdotally, the implementation of thromboprophylaxis at CHEO has decreased the frequency of PICC-associated venous thromboembolism (VTE). However, the impact of this policy has not been formally studied.

Methods | Using a case-control study of CHEO patients, we measured the difference in the rates of PICC-associated VTEs with and without thromboprophylaxis. CHEO patients who underwent PICC insertion and developed a VTE were matched to controls who also underwent PICC insertion and did not develop a VTE. Patients with a pre-existing VTE and/or therapeutic anticoagulation prior to PICC insertion were excluded.

Results| The incidence of PICC-associated VTEs are highest at < 3 months (n=57) and 15 (n=8). Elevated inflammatory markers were present for 47 cases and 50 controls. Thromboprophylaxis was used for 17 cases and 13 controls. The mean number of days from PICC insertion to VTE diagnosis was 8.5.

Conclusion | Thromboprophylaxis may decrease the incidence of PICC-associated VTEs in children, and length of hospitalization.

A Pre-Clerkship Procedural Skills Training Program for Canadian Undergraduate Medical Education

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ABSTRACT

Introduction| There is currently no standardized pre-clerkship procedural skills program available to medical students across Canada, often leaving them unfamiliar with common clerkship procedural skills. With the advent of Entrustable Professional Activities (EPAs) in Canadian Undergraduate Medical Education (UGME), which are requiring medical students to demonstrate competency in procedural skills, standardized pre-clerkship training is becoming considerably more necessary. Early exposure to procedural skills would render students more prepared for their clinical rotations and encourages participation in procedures.

Our research group developed a formal procedural skills program using a neer-peer model of education in hopes to implement similar programs across Canada. This study investigated the effects of such a training program on medical student anxiety and confidence.

Methods | Thirty six second year medical students participated in the study. Participants completed a State Trait Anxiety Inventory Questionnaire (STAI) and a validated confidence questionnaire prior to training. The STAI questionnaire assessed anxiety in regard to performance of procedures, while the confidence questionnaire assessed confidence of each individual skill. Over the academic year, students participated in eight skill training sessions taught by expert physicians. The skills taught include suturing, airway management, IV insertion, local anesthetic, casting, NG insertion, foley catheterization, and phlebotomy. At each session, students learned a new skill and had the opportunity to practice previously learned skills. Anxiety and confidence questionnaires were repeated at the end of the program for both program and control groups.

Results | The procedural skills program group showed a statistically significant ($p<0.05$) decrease in anxiety for performing procedures, whereas the control group anxiety increased. The program group also demonstrated a statistically significant improvement in confidence across all skills ($p<0.05$), whereas the control group did not show a statistically significant change in majority of skills.

Conclusion | Integration of a pre-clerkship procedural skills training program within Canadian medical school curricula would provide students with a technical foundation for further learning in clerkship, thus easing student anxiety and improving confidence for an easier transition into clerkship. Future iterations of this project will assess the program's ability to improve medical student competency in the skills taught.

Change in Functional Cup Orientation at Minimum 10 Years after Primary Total Hip Arthroplasty

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ABSTRACT

Reducing the number of post-operative complications that occur following Total Hip Arthroplasty (THA) could have a large impact on the number of revision surgeries performed, as they accounted for roughly 9% of all hip replacement surgeries in Canada from 2014-20151. Implant orientation is one variable that has been shown to cause post-operative complications2 and is believed to change over time due to naturally occurring changes in pelvic tilt that occur with ageing3. The purpose of this study was to determine if there is a significant change in acetabular cup inclination and anteversion in the ten-years following THA that should be accounted for during surgery. A retrospective, radiographic cohort study was conducted analysing 46 patients initial post-operative radiographic and an additional radiograph taken a minimum of 10 years post-operation. Using measurements taken from both radiographs, a change in cup anteversion and inclination angle was calculated. No significant difference was detected between measurements taken from the initial post-operative radiograph and the measurements taken a minimum of ten years later ($p>0.45$), with the median (inter quartile range) change in anteversion and inclination being 0° (-1° to 3°) and 1° (-3° to 1°) respectively. Therefore, the risk of post-operative complications during the 10-year period following THA did not increase due to a change in cup orientation that occurred naturally with time.

Détection des crises épileptiques par des interpréteurs non-experts en EEG

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ABSTRACT

Introduction| Les crises épileptiques à l'unité de soins intensifs pédiatriques (USIP) sont souvent subcliniques et nécessitent une surveillance électroencéphalographique (EEG) pour leur détection.1 Sans traitement, elles sont associées à un mauvais pronostic.2 Dans le cadre d'un projet d'amélioration de la qualité, nous avons évalué les retards dans la surveillance et l'interprétation de l'EEG à l'USIP de CHEO. Dans le but de détecter et de traiter plus rapidement les crises épileptiques, nous croyons que les non-experts en EEG peuvent apprendre les principes d'interprétation de l'EEG pour identifier les crises épileptiques.

Méthodes | 1. Les patients de l'USIP à CHEO sont suivis prospectivement pendant 8 mois afin d'évaluer les retards dans la surveillance EEG.
2. Les apprenants en médecine assistent à une séance d'enseignement sur l'EEG, y compris un test sur l'interprétation des EEGs.

Résultats | 19% des patients nécessitaient la surveillance par EEG. Le délai médian de surveillance était de 22 heures, avec un délai d'interprétation dépassant 24 heures. Un projet pilote d'enseignement a démontré que des fellows USIP étaient capables de détecter l'activités épileptiques d'EEG après notre cours didactique. Notre étude principale recrutera 50 étudiants en médecine, résidents et fellows.

Conclusion | Les ressources limitées entraînent des retards dans la surveillance de l'EEG à l'USIP. Si nous réussissons à enseigner les non-experts à interpréter l'EEG pour détecter des crises épileptiques, cela permettra d'orienter les soins en attendant qu'un interpréteur EEG plus qualifié devienne disponible. Cette stratégie facilitera la détection et la prise en charge rapides des crises épileptiques, améliorant le pronostic des patients.

Association Between C-Reactive Protein, Suicidal Ideation and Adverse Childhood Experiences

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ABSTRACT

Introduction | Suicide remains a leading cause of mortality worldwide, with over 4,000 deaths in Canada each year. Recent investigations have associated suicide-related events with pro-inflammatory states, using acute phase inflammatory markers such as C-reactive protein (CRP). Measures of adverse childhood experiences (ACE) are consistently associated with depression and suicide, however, results regarding the relationship between ACE severity and inflammation remain inconsistent in the literature. Furthermore, no known studies have explored the potential associations between these four constructs concurrently.

Methods | The present study included 28 outpatients with major depressive disorder (MDD) being treated in a tertiary-care hospital (n=8M, n=20F; mean age 53+/-20), with 24% having a suicide attempt history. The associations between high-sensitivity CRP levels and clinical measures of depression, suicide and ACE were explored using Pearson bivariate correlations in IBM SPSS Statistics (v23).

Results | Statistical analysis revealed significant correlations between CRP levels and past 6-month SI severity ($p=0.04$), as well as childhood neglect and past 6-month SI severity ($p< 0.001$), and depression severity ($p= 0.03$).

Conclusion | These results are consistent with other investigations regarding the relationship between inflammation and SI, as well as childhood neglect, SI and depression severity. Further analysis with a larger sample size and other inflammatory markers would be expected to achieve more robust correlations among these four variables.

Translational & Molecular Medicine

Student Projects

Fusion to Prevent Confusion: How Stearic Acid Can Enhance Neurogenesis	Abdi A
Fated for Death: Mitochondrial Dysfunction and Adult Neurogenesis in Alzheimer's	Cuthbert J
Construction and Characterization of a *NdvB* Clinical Isolate Deletion Mutant	Farkas E
Cancer on the Move: PI4P in Focal Adhesion Dynamics and Cell Migration	Jacobsen D
The Effect of the Hedgehog Signalling Pathway on CD8+ T cell Dysfunction in HCV patients with high Liver Fibrosis	Read D
Investigating the Role of Metformin in Abrogating Ovarian Fibrosis	Vaishnav H


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