Schulich School of Medicine & Dentistry

Western University

# Department of Medicine
# RESEARCH DAY

## Friday, May 19, 2023

Best Western Lamplighter Inn

591 Wellington Road South

London, Ontario

This program has no commercial support.

# CME INFORMATION

This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada, and approved by Continuing Professional Development, Schulich School of Medicine & Dentistry, Western University. You may claim a maximum of 3.75 hours (credits are automatically calculated).

Each participant should claim only those hours of credit that he/she actually spent participating in the educational program.

25% of this program is dedicated to participant interaction.

Scan the QR code to complete the **Participant Evaluation** form online.

Or go to: https://uwo.eu.qualtrics.com/jfe/form/SV_eh9KZ9bNmjfSjBA.

# Learning Objectives

**By the end of this research day, participants will be able to:**

- describe new research findings of relevance to Internal Medicine and related subspecialties.
- recognize clinical research conducted by the trainees in the Department of Medicine.
- identify basic research conducted by trainees in the Department of Medicine.

**Dr. Ian Roberts Learning Objectives:**

1. To identify why evidence from large randomised trials is important for patient care.
2. To assess which patients should be treated with tranexamic acid, when and where.

**Dr. Dervla Connaughton Learning Objectives:**

1. To review the utility of genetic testing for patients with chronic kidney disease.
2. To apply emerging research to develop standardized protocols for genetic testing in patients with chronic kidney disease.
3. To identify clinical opportunities to apply a genomics first approach in patients with suspected genetic kidney disease.

**Dr. Jaspreet Bhangu Learning Objectives:**

1. To define the vascular changes which can influence cognition, and their relationship with other forms of dementia such as Alzheimer's disease.
2. To evaluate emerging diagnostic Methods for assessing cerebral blood flow and discuss the future therapeutic potential.

# Brief Biosketches for Keynote and Faulty Speakers

## Keynote Speaker:

### Dr. Ian Roberts

Ian Roberts is Professor of Epidemiology at the London School of Hygiene & Tropical Medicine. He trained as a paediatrician in the UK and then in epidemiology at the University of Auckland, New Zealand and McGill University, Canada. He is a clinical academic who works collaboratively with health professionals world-wide to conduct large multi-centre clinical trials aimed at improving patient outcomes in life threatening emergencies. He works with others to build global research partnerships to answer questions together that could not be answered by anyone working alone. He has played lead roles in several large trials including the CRASH trials and the Woman trials.

## Faculty Speakers:

### Dr. Dervla M. Connaughton MD, MSc, PhD

Dr. Connaughton is a clinician-researcher and nephrologist with extensive expertise and leadership in renal genetics in both pediatric and adult patients. She is the clinical lead of the Ontario Health Renal Genetics Expert Group and clinical lead of the Renal Genetics Program in Southwestern Ontario.

She is an Assistant Professor of Medicine at Western University with a cross appointment in the Department of Pediatrics and Department of Biochemistry at Western University. As the for Eugen Drewlo Chair for Kidney Research and Innovation at the Schulich School of Medicine & Dentistry, her research focus is on understanding the genetic basis and epidemiology of all forms of chronic kidney disease in both adult and pediatric populations. Specifically, her focus is to establish and characterize the molecular etiology of kidney disease using high throughput sequencing techniques including gene panel sequencing, whole exome and genome sequencing.

She received her medical degree from the Royal College of Surgeons in Ireland and her specialist training in nephrology and internal medicine was awarded by the Royal College of Physicians of Ireland. Dr. Connaughton completed a transplant fellowship at the National Centre for Nephrology and Transplantation at Beaumont Hospital in Ireland. She was awarded her PhD degree from Trinity College Dublin Ireland in renal genetics and has a MSc in Epidemiology from the London School of Hygiene and Tropical Medicine. She went on to do a research fellowship in renal genetics at Harvard Medical School.

She is the lead of the renal genetics service of Southwestern Ontario and run a renal genetics clinic for both adult and pediatric patients. She has extensive experience and training in the assessment of patients with rare and inherited kidney diseases as well as the application and interpretation of all genetic and genomic analysis techniques. In this link her team provide comprehensive genetic and genomic evaluation for patients with suspected rare and inherited kidney disease.

The other area of interest for Dr. Connaughton is kidney transplantation. As the Director of Living Kidney Donation at London Health Sciences Centre, she evaluation individual who wish to donate a kidney through the living kidney donation program. She also cares for patients that require hemodialysis and patients undergoing kidney transplant as well as patient wishing to donate a kidney through the live donation process.

## Jaspreet Bhangu, MB, BCh, BAO, MRCPI, MSc, PhD

Dr. Bhangu is an early career investigator with the Dept. of Medicine in the division of Geriatric Medicine. He graduated from the Royal College of Surgeons, Dublin in 2004. He completed his specialist training in Internal and Geriatric Medicine in Ireland in 2016. He completed a PhD. in Medical Gerontology with Trinity College Dublin in 2017 studying falls and cardiovascular disease in older adults. His research at Western involves the associations between cardiovascular disease and aging; principally its effects on cognition and mobility. He is currently a member of the cognitive clinical trials group at Parkwood Hospital and involved in a number of clinical trials aimed at discovering new compounds for the treatment of dementia as well as investigating novel mechanisms for the progression of the disease.

# AGENDA

## DoM Resident Research Day 2023
## Friday, May 19, 2023

Best Western Lamplighter Inn

| Schedule of Events | | | |
|---|---|---|---|
| **Start** | **End** | | |
| 8:00 | 8:30 | **Breakfast** | **Poster Setup**<br>(Crystal Ballroom South) |
| 8:30 | 8:40 | **Welcome & Opening Remarks by Dr. Vipul Jairath**<br>(Crystal Ballroom North) | |
| 8:40 | 9:40 | **Trainee Oral Presentations – (4)**<br>(Crystal Ballroom North)<br>*10 min presentations, 5 min Q&A* | |
| 9:40 | 10:00 | **Faculty Presentation - Dr. Dervla Connaughton**<br>**"Renal Genetics: Is now the time for a genomics first approach?"**<br>(Crystal Ballroom North)<br>*15 min presentation, 5 min Q&A* | |
| 10:00 | 11:00 | **BREAK** | **Poster Presentation and Judging**<br>(Crystal Ballroom South) |
| 11:00 | 11:45 | **Keynote - Dr. Ian Roberts** (virtual)<br>**"Bad bleeding and big trials: why evidence from large randomised trials is important for patient care."**<br>(Crystal Ballroom North)<br>*35 min presentation, 10 min Q&A* | |
| 11:45 | 13:45 | **LUNCH** | **Poster Presentation and Judging**<br>(Crystal Ballroom South) |
| 13:45 | 14:05 | **Faculty Presentation - Dr. Jaspreet Bhangu**<br>**"Vascular influences on cognitive decline: Evolving targets for therapeutic interventions."**<br>(Crystal Ballroom North)<br>*15 min presentation, 5 min Q&A* | |
| 14:05 | 15:20 | **Trainee Oral Presentations – (5)**<br>(Crystal Ballroom North)<br>*10 min presentations, 5 min Q&A* | |
| 15:20 | 15:30 | **Presentation of Awards & Final Remarks**<br>(Crystal Ballroom North) | |

# Trainee Oral Presentations

## Morning

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| **08:55** | Chen, RuoYan | MSc Student | Dr. Lillian Barra | Structural Cerebrovascular Sequelae and Cognitive Impairment in Anti-Neutrophilic Cytoplasmic Antibody-Associated Vasculitis | 21 |
| **09:10** | Chiu, Jodi | PGY-2 | Dr. Alejandro Lazo-Langner | Venous Thromboembolisms Following Haematopoietic Stem Cell Transplantation | 23 |
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# List of All Submitted Abstracts (in alpha order)

## Rami Abazid

### Utility of Downstream Stress Test Imaging For Risk Stratification of Patients Presenting to Emergency Department With Chest Pain and Low HEART Score

Rami Abazid, Nilkanth Pati, Maged Elrayes, Sameh Awadallah, Yves Bureau, Rodrigo Bagur, Nikolaos Tzemos

**Introduction**: HEART score is widely used for risk stratification of chest pain in the emergency department (ED). Current guidelines recommend discharging patients with low-risk heart score (LRHS) as the expected future cardiac events are low. However, there is controversy in the management plan with the increasing evidence of non-negligible cardiac events among LRHS patients. In this study we aim to investigate the value of downstream non-invasive stress imaging test (NISI) in predicting cardiac events in patients with LRHS. **Methods**: We prospectively included 1384 patients with LRHS between 2019 to 2021. All patients underwent NISI (myocardial perfusion imaging or stress echocardiography). Primary endpoints were: Cardiac deaths, nonfatal myocardial infarctions, and significant coronary stenosis. Secondary endpoints define as cardiovascular-related admission or ED visit. **Results**: The mean age was 64±14 years, 670 (48.4%) were women. During the follow-up period of 634±104 days, 58/1384 (4.2%) patients developed 62 primary endpoints and 60 (4.3%) patients developed secondary endpoints. Multivariable cox models adjusted to clinical and imaging variables which showed that diabetes (Hazard ratio (HR): 2.38; 95% CI: 1.25-4.49, P=0.008), prior history of CAD (HR: 2.75; 95% CI: 1.40-5.41; P=0.003), ECG changes (HR: 5.11; 95% CI: 2.61-10.01; P<0.0001), and abnormal NISI (HR:16.4; 95% CI: 9.56-28.03; P<0.0001) in predicting primary endpoints, In contrast, abnormal NISI was the sole predictor of secondary endpoints with (HR:3.05; 95% CI: 1.31-7.14; P<0.0001). **Conclusion**:NISI significantly predict primary cardiac events and cardiovascular-related readmission/ED visits in patients with LRHS.

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## Jahaan Ali

### Evaluating errors in N-acetylcysteine dosing for acetaminophen overdose

Jahaan Ali, Constance Mackenzie, Margaret Thompson, Emily Austin

Acetaminophen overdose is a leading cause of acute liver failure in developing countries. N-acetylcysteine (NAC) is a highly effective antidote for acetaminophen hepatotoxicity. The complexity of the traditional 3-bag IV NAC protocols was associated with medication errors. Since 2019, the Ontario Poison Center (OPC) changed to a modified one-bag protocol. There is little data regarding the rate of errors using a one-bag protocol and recently the Institute for Safe Medication Practices Canada released a report regarding two cases of severe NAC overdoses resulting in patient deaths in another province. This study was undertaken to determine the frequency and types of errors associated with the use of IV NAC with the OPC one-bag protocol. Data were gathered via retrospective chart review of 188 OPC cases identified as receiving IV NAC for acetaminophen overdose between August and September 2022. The error rate was 25%, consisting of dosing errors found in 11.7% of charts, stopping errors 9.0%, initiation errors 3.7%, and interruptions in therapy in 3.2%. Dosing errors were the most common type of error (44.4%), with overdoses occurring three-times more than underdoses. While clinical outcomes were similar in charts with and without errors, this study demonstrates a high rate of error pertaining to the use

of IV NAC in acetaminophen overdose. Although severe outcomes are rare, IV NAC overdose can be fatal, and dosing errors are occurring despite a modified administration protocol. Further evaluation into the factors contributing to error and enhanced education for medical providers is needed to minimize administration errors.

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## Ala Almanaseer

### An Approach to the Investigation of Thrombocytosis: Differentiating Between Essential Thrombocytosis and Secondary Thrombocytosis

Ala Almanaseer, Benjamin Chin-Yee, Ian H. Chin-Yee, Alejandro Lazo-Langner, Jenny Ho, Bekim Sadikovic, Cyrus C. Hsia, Department of Medicine, London Health Sciences Centre, London, Ontario

**Background**: Thrombocytosis is a common reason for referral to internal medicine and hematology clinics. Differentiating between secondary causes of thrombocytosis and essential thrombocytosis (ET) is often clinically challenging. There is a need for a practical diagnostic approach to help physicians identify patients more likely to have secondary thrombocytosis, thus avoiding over-investigation of this common referral population. This project aims to characterize a cohort of patients referred for elevated platelet counts to develop a practical diagnostic approach to thrombocytosis. **Methods**: A retrospective cohort of all adult patients with persistently elevated platelet counts (≥ 450 x 109cells /L) at a single tertiary care centre who underwent molecular testing for mutations associated with ET were evaluated. Clinical and laboratory variables were compared between secondary thrombocytosis, probable and confirmed ET (based on WHO 2016 ET criteria) groups. **Results**: 441 patients were assessed, and the overall yield of molecular testing was 55% with 84.7% of the patients harbouring mutations in JAK2, CALR and MPL. Statistically significant differences were identified in the CBC and white cell differential parameters. Clinical factors predictive of probable ET included previous history of arterial thrombosis, whilst chronic inflammatory disease, post splenectomy and iron deficiency were instead associated with secondary thrombocytosis ($p < 0.05$). Further investigations are underway to assess differences between probable and confirmed ET. **Conclusion**: A practical approach to the investigation of patients with persistent elevated platelet counts would assist in accurately identifying patients more likely to have secondary causes of thrombocytosis and reduce over-investigation, particularly costly molecular diagnostic testing.

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## Lotus Alphonsus

### Medical therapies for the treatment and prevention of pouchitis: A systematic review and meta-analysis

Lotus Alphonsus, Theshani A De Silva, Christopher Ma, John K. MacDonald, Jurij Hanzel, Melanie Beaton, Talat Bessissow, Maia Kaya, Rocio Sedano, Siddharth Singh, Vipul Jairath

**Background**: We conducted a systematic review to assess medical therapy for treatment and prevention of pouchitis. **Methods**: Randomized controlled trials (RCTs) of medical therapy in adults with pouchitis were searched to March 2022. Primary outcomes included clinical remission/response, maintenance of remission and prevention of pouchitis. **Results**: Twenty RCTs (830 participants) were included. Acute pouchitis: One study compared ciprofloxacin with metronidazole. At 2 weeks, 100% (7/7) of ciprofloxacin participants achieved remission, compared with 67% (6/9) of metronidazole participants (RR 1.44, 95% CI 0.88 to 2.35, low

certainty evidence). One study compared budesonide enemas with oral metronidazole. Fifty percent (6/12) of budesonide participants achieved remission compared with 43% (6/14) of metronidazole participants (RR 1.17, 95% CI 0.51 to 2.67, moderate certainty evidence). Chronic pouchitis: Two studies (n=76 participants) assessed De Simone Formulation. Eighty-five percent (34/40) of De Simone Formulation participants maintained remission at 9-12 months compared with 3% (1/36) placebo participants (RR 18.50, 95% CI 3.86 to 88.56, moderate certainty evidence). One study assessed vedolizumab. Thirty-one percent (16/51) of vedolizumab participants achieved clinical remission at 14 weeks compared with 10% (5/51) of placebo participants (RR 3.20, 95% CI 1.27 to 8.08, moderate certainty evidence). Prophylaxis: Two studies assessed the De Simone Formulation. Ninety percent (18/20) of De Simone Formulation participants did not develop pouchitis compared with 60% (12/20) of placebo participants (RR 1.50, 95% CI 1.02 to 2.21, moderate certainty evidence). **Conclusions**: Apart from vedolizumab and the De Simone formulation, the effects of medical interventions for treating and preventing pouchitis are uncertain.

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## Ahmed Alshaer

**Impact of denosumab on vascular calcification in ESKD**

Ahmed Alshaer, Rachel Holden, Andrea Cowan, Kristin Clemens

Vascular calcification (VC) is associated with increased risk of cardiovascular events and mortality in patients with end-staged kidney disease (ESKD). Denosumab is a monoclonal antibody that is used to treat osteoporosis and bone metastases. There is evidence suggesting that denosumab may have a role in preventing vascular calcification in ESKD. We aimed to examine the medical literature on the impact of denosumab on vascular calcification in those with ESKD. **METHOD**: We conducted narrative librarian-guided review of the literature across databases. We included observational studies, randomized controlled trials (RCTs), and evidence-based reviews. **RESULT**: We identified 26 relevant citations and are actively screening abstracts and full-text articles. Upon preliminary review, we note that the efficacy of denosumab in preventing vascular calcification has been investigated in several studies, including (RCTs) and observational cohort studies. Studies which used coronary artery calcium score (CACS) as a measure of vascular calcification, have not noted a benefit with denosumab compared with control. Observational studies that used aortic arch calcification (AoAC) as a measure of vascular calcification, have noted a beneficial effect of denosumab although further research is needed to confirm these findings and to explore the underlying mechanisms.
**CONCLUSION**: The evidence regarding the efficacy of denosumab in preventing vascular calcification remains inconclusive, with some studies suggesting a potential benefit in reducing AoAC, but others noting no impact upon CACS. Further studies are needed to determine the potential benefit of denosumab treatment for preventing vascular calcification, and to identify patients who may benefit most from this therapy.

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Alonso Alvarado-Bolanos

**Takotsubo Cardiomyopathy (TCM) And Subsequent Risk Of Major Adverse Cardiovascular Events: A Cluster Analysis**

Alonso Alvarado-Bolanos, Sebastian Fridman; Diana Ayan; Luciano A. Sposato

**Introduction**: TCM is a form of transient regional ventricular dysfunction. The risk of MACE after TCM is poorly understood. **Methods**: Retrospective study of patients admitted to LHSC hospitals with TCM between 2014 and 2021. MACE during follow-up included stroke, acute coronary syndrome, admission for heart failure or CV death. A two-step cluster analysis was used to stratify patients. Variables for clustering included: aetiology, age, sex, hypertension, dyslipidemia, smoking, previous stroke, diabetes, chronic kidney disease, ejection fraction, AF, and antithrombotics. A Cox proportional-hazards model was used to determine the association between clusters and MACE. **Results**: We included 152 patients. Median age was 72.5 years. Median CHA2DS2VASc was 2.0. Overall, 80% received antithrombotic drugs. At a median follow-up of 22.0 months, 11.8% experienced a MACE. Cluster 1 included more males (31.7%), and the highest rate of hypertension (100%), dyslipidemia (92.7%), smoking (31.7%), previous stroke (14.6%), and antiplatelet use (82.9%). Cluster 2 included older patients (78 [73.5-84.5] years) with the highest prevalence of diabetes (23.8%), AF (95.2%) and anticoagulation (71.4%). Cluster 3 included younger patients (69 [62.7-84.0] years) with the lowest burden of CV risk factors and antithrombotic therapy (68.9%). Cluster 1 had an increased risk of MACE (HR 2.9; 95%CI 1.1-7.3; p=0.02) and stroke (HR 4.9; 95%CI 1.1-20.6; p=0.02). **Conclusion**: CV events are relatively frequent after TCM. We identified a phenotype, characterized by male sex, a higher burden of CV comorbidities, and low anticoagulation rates, which was associated with an increased risk of MACE and stroke.

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Alonso Alvarado-Bolanos

**Atrial Fibrillation Detected on 14-day Cardiac Monitoring has a Lower Stroke Recurrence Risk than EKG-diagnosed AF**

Alonso Alvarado-Bolanos, Diana Ayan, Sebastian Fridman, Luciano Sposato

**BACKGROUND**: Recent meta-analyses suggest that atrial fibrillation (AF) detected after stroke (AFDAS) is heterogeneous with a lower risk of stroke than AF known before stroke occurrence (KAF). We hypothesized that AFDAS found on 14-day cardiac monitoring (AFDAS-CM) entails a lower risk of recurrent ischemic stroke (IS) than AFDAS identified on admission EKG (AFDAS-EKG). **METHODS**: We included IS or transient ischemic attack (TIA) patients with AFDAS-CM (>30s) and AFDAS-EKG from the London Ontario Stroke Registry. Patients who died in the first 14 days of the ischemic event were excluded. The primary endpoint was recurrent IS. All-cause mortality was explored as a secondary outcome. We applied marginal cause-specific Cox proportional hazards models adjusted for qualifying event type, $CHA_2DS_2$-VASc score, anticoagulation, left ventricular ejection fraction, left atrial volume index , and high-sensitivity troponin T to estimate adjusted hazard ratios (aHR). **RESULTS**: We evaluated 366 patients (IS 291, AFDAS-CM 148). Median age was 79.2 [71.5-85.5] years. Net monitoring time was 12 [8.8-14.0] days. AFDAS duration was 5.2 [0.3-33.0] hours. Follow-up duration was 17 [5.0-34.0] months. AFDAS-EKG was independently associated with a higher recurrent IS risk (aHR 5.06, 95%CI 1.13- 22.7; p=0.034) and higher all-cause mortality (aHR 2.50, 95%CI 1.20 to 5.19; p=0.015). **CONCLUSIONS**: Recurrent IS risk and all-cause death were higher in AFDAS-EKG than AFDAS-CM, suggesting that AFDAS identified on cardiac monitoring is a more benign type

of arrhythmia than EKG-diagnosed AF. We hypothesize that AFDAS-EKG is a high burden AF, with similar risk profile to KAF.

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## Monica Arnaldi

**Impact of Sodium-Glucose Cotransporter-2 Inhibitor (SGLT2i) Use in Kidney Transplant Recipients**

Monica Arnaldi, G. K. Alzaneen, A. House

The SGLT2i have been robustly demonstrated in the CKD population, and are increasingly used in the non-transplant population to improve renal and cardiovascular outcomes. The efficacy and safety of SGLT2i in Kidney Transplant recipients have not been well characterized. All kidney transplant recipients prescribed SGLT2i were retrospectively reviewed. Changes in BP, weight, eGFR, albuminuria, and glycated hemoglobin (A1C) were analyzed using IBM SPSS (v. 28.0.1.1), and adverse events including ketoacidosis and urinary tract infections were collected. Paired T-tests after a minimum of 6 months are presented.Over a study period of 1 year, 42 patients were prescribed SGLT2i, 78% were male, and 78% were diabetic. The median age and eGFR at the time of initiation of therapy were 63 years and 61.8 mL/min per 1.73m2, respectively. The eGFR declined 4.69% at 6 months (p=0.031). After 6 months, the mean ACR decreased from 74.4 to 41.5 mg/mmol (p=0.037); the mean systolic BP reduced from 133.4 to 127.9 mmHg (p=0.008). Mean weight also fell by 3.1 kg (p=0.006). UTI occurred in 6 patients (14%) while on SGLT2i, 3 of the patients had at least 1 UTI prior to starting the medication, and none of the UTI episodes required hospitalization. There were no cases of ketoacidosis.Among kidney transplant recipients, regardless of the presence or absence of diabetes, SGLT2i led to better control of albuminuria, systolic BP reduction, and weight loss. UTI, while infrequent and not serious in this small study, did emerge early in some male patients and bears further scrutiny.

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## Kaan Y. Balta

**Resuscitative transesophageal echocardiography during the acute resuscitation of trauma: a retrospective observational study**

Kaan Y. Balta, Ross Prager, Eric Walser, Anton Nikouline, William R. Leeper, Neil Parry, Robert Arntfield

The use of point-of-care ultrasound (POCUS) may be limited by body habitus and ongoing procedures. Resuscitative transesophageal echocardiography (TEE) is an emerging POCUS modality that produces high quality views regardless of positioning or body habitus, and can remain in-situ. We describe using TEE in trauma and identifying cases in which TEE altered management.Trauma patients who underwent TEE within 24 hours of arrival to a Level I trauma center- with an established resuscitative TEE program-from Jan 2013 to Dec 2022 were identified using a prospectively maintained POCUS database. TEE images, electronic medical record, and paper charts were reviewed in duplicate.TEE was performed for 54 patients. 28 (52%) died in hospital; 33 (61%) required operative intervention within 24h. Median Injury Severity Score was 29 [IQR 22-43], and median transfusions within 24h was 6 [2-20]. Most common indications for TEE were hemodynamic instability (34, 63%), inadequate POCUS windows (14, 26%) and cardiac arrest (11, 20%). Most common TEE diagnoses were hypovolemia (20, 37%), pericardial effusion (11, 20%), and right ventricular dysfunction (11, 20%). New diagnoses were made by TEE in 31 (57%) cases and ruled out major cardiac injury in 83% of cases. Use of TEE led to a

change in resuscitative strategy (17, 32%), diagnostic imaging approach (6, 11%), operative approach (5, 9%), and disposition (4, 7%). Resuscitative TEE during acute trauma resuscitation provides additional information to existing trauma diagnostic pathways. TEE resulted in a change in resuscitative, diagnostic, procedural, or disposition plans for a clinically important number of patients.

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## Kaan Y. Balta

**Near 5-year survival in metastatic pancreatic cancer patient with ROS1 rearrangement, HER2 amplification, and KRAS G12C mutation. Case Report**

Kaan Y. Balta, Stephan Welch; Mark Vincent; Daniel Breadner

Pancreatic cancer is a significant cause of cancer-related deaths in Canada. Although it is less common than other cancers, the mortality rate has remained high and stable since 1984. Limited options for detection and treatment contribute to the high mortality. A developing area of treatment is tumour site agnostic targeted therapy. A 52-year-old man with no prior medical history presented with anemia and 8-10 lbs of unintentional weight loss over a 1-year period. A CT scan of the abdomen revealed pancreatic ductal adenocarcinoma and diffuse liver metastasis. He received multiple local and non-targeted systemic therapies. Serial genomic analyses sequentially revealed ROS1 rearrangement, HER2 amplification, and KRAS G12C mutation throughout his journey, none of which were present at diagnosis. Each new genomic alteration prompted treatment change. Concurrent with systemic therapy, the patient also received numerous local treatments, including hepatic transarterial chemoembolization, Yttrium 90, Whipple procedure, stereotactic body radiation therapy, and CyberKnife. Over the course of the disease, metastases were found in the lungs, brain, and kidneys. Despite this, the patient had periods of remarkable response and quality of life. However, nearly five years from diagnosis, the patient elected to pursue supportive care and died from his cancer. This case report demonstrates the importance of repeat genomic analyses in the treatment of advanced cancer and timely access to targeted therapy. The clinical impact of utilizing a tumor agnostic treatment approach based on these genomic alterations has the potential to yield a strong response both in survival and quality of life.

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## Yassmin Behzadian

**Improving the Sustainability of Prescribing Practices within the Division of Respirology at the University of Western Ontario**

Yassmin Behzadian, Constance Mackenzie

**Background**: Metered Dose Inhalers (MDI) are an inhaler device that are commonly prescribed by Respirologists and other physicians, and which use hydrofluorocarbons (HFCs) propellants to deliver medications. HFCs are known greenhouse gasses when they are released into the atmosphere and have a high Global Warming Potential (GWP) as they trap substantially more heat than CO2 per unit mass. Non-MDI inhaler alternatives are available and may reduce the environmental impact of inhaler prescriptions. We therefore sought to decrease the number of MDI prescriptions made by the Department of Respirology at the University of Western Ontario. **Methods**: Posters outlining the relative carbon footprint and therefore environmental impact of various inhaler options were put up in various spaces throughout outpatient Respirology clinics. The number of prescriptions for MDIs made by the Respirology Department in the pre-intervention

and post-intervention periods were compared. **Results**: Results are pending at this time. **Conclusions**: As air quality worsens with global warming, patients with respiratory diseases suffer more exacerbations of their disease and further deterioration in their lung function, warranting more treatment with inhalers. This vicious cycle creates a safety gap in the care of our patients and planet. Reducing the number of MDI prescriptions in cases where equally effective non-MDI alternatives exist is a simple step that physicians can take to reduce the impact of our profession on our environment and consequently on our patients' health.

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## Yassmin Behzadian

**Improving Palliative Care Referrals for Patients with Advanced Cancer in Pleural Disease and Diagnostic Assessment Program Clinics**

Jaymee Shell, Shayan Kassirian, Yassmin Behzadian

**Background**: Palliative Care has been shown to decrease mortality, improve mood and quality of life, and reduce health care costs in patients with non-small cell lung cancer (NSCLC). However, barriers exist which prevent appropriate referrals to Palliative Care happening regularly in practice and as such, Palliative Care may be underutilized and many patients may not derive its potential benefits. Therefore, we sought to increase referrals of patients with locally advanced or metastatic cancer seen in the Diagnostic Assessment Program (DAP) and Pleural Disease Clinics to Palliative Care. **Methods**: A patient-centered brochure was designed and provided to patients with locally advanced and metastatic cancer. The number of appropriate patients with whom Palliative Care was discussed in the pre-intervention and post-intervention periods was compared. **Results**: Results are pending at this time.**Discussion**: The literature clearly demonstrates numerous benefits of referrals to Palliative Care in patients with advanced lung cancer. Nonetheless, our clinical experience demonstrated that Palliative Care referrals may be underutilized in appropriate patients. Using QI Methodology, we completed a root cause analysis to determine the potential barriers to Palliative Care referrals for our patients with locally advanced and metastatic cancer. Through three PDSA cycles, we created a patient-centered pamphlet to educate patients and families about the role of Palliative Care in their journey, with the aim of addressing some of the identified barriers to referrals.

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## Masooma Bhatti

**Strategies to negate inadequate pain management in the elderly hospitalized medicine inpatients**

Masooma Bhatti, Erin Spicer, Mark Goldszmidt

**Background**: Pain is common amongst hospitalized medicine patients and many rate their pain management as unsatisfactory. While guidelines exist for treating pain in special populations (e.g., post-operative, trauma and cancer), little attention has been paid to elderly medicine inpatients who typically have prolonged lengths-of-stay when pain is inadequately managed. In this population, understanding the unique factors contributing to suboptimal pain management and diminished functional abilities is necessary to develop targeted solutions. As part of a larger QI project, this pragmatic literature review is aimed to identify (1) predominant pain syndromes affecting elderly medicine inpatients, (2) barriers to adequately treating these patients, and (3) strategies for managing their pain. **Methods**: This is a pragmatic literature review. Due to the lack of published research on this particular population, our searches focused on gray literature

and published papers. **Results**: The predominant pain syndromes affecting the elderly population are compression fractures, non-operative fractures and spinal stenosis. Barriers to pain management included apprehensive attitudes among patients, communication issues, and lack of experience/knowledge amongst healthcare physicians. Several patient-centered but underutilized strategies were identified including use of non-medication-based adjuncts (compression, massage, heat, cold, etc.) and interventional radiologic approaches for compression fractures and epidural injections for spinal stenosis. Most also included the need for early and consistent mobilization.
**Discussion**: When combined with a local root cause analysis, the barriers identified in this literature review will serve as the basis for change ideas. The many underutilized pain control strategies described flag important opportunities for improvement initiatives.

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## Tanisha Birk

**A Case of Missed Pheochromocytoma**

Tanisha Birk, Kristin Clemens, Stan Van Uum

Pheochromocytomas are tumors of the adrenal medulla. They may occur spontaneously or in the context of various hereditary syndromes. The symptoms of pheochromocytoma can occur due to catecholamine excess or mass effect from the tumor. Pheochromocytoma is an important diagnosis to include in the work up of both resistant hypertension and adrenal incidentaloma. In the perioperative period, pheochromocytoma should be excluded as surgery can trigger a catecholaminergic crisis in which the release of excess catecholamines causes hemodynamic instability, end organ damage and potentially death. In the case presented, we are shown the potential perioperative complications that can occur in the presence of an undiagnosed pheochromocytoma that is taken to the operating room. A 63 year old woman presents for sentinel node biopsy after recent diagnosis of breast cancer. Previous imaging was done in order to evaluate for metastatic disease and showed an adrenal mass that was approximately 8cm in diameter. Biochemical evaluation was not completed preoperatively. The patient experienced intraoperative hypertension that was difficult to control as well as postoperative hypertension. The patient was admitted under Internal Medicine for hypertensive emergency after the procedure and the diagnosis of pheochromocytoma was made. Of note, the diagnosis of pheochromocytoma impacted the patient's management plan and the surgical plan for her breast cancer was adjusted given the new diagnosis. This case also serves as an excellent reminder of the lesser known triggers for catecholaminergic crisis. In this case, the intraoperative administration of dexamethasone was likely an exacerbating factor.

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## Garth Blackler

**Synovial macrophage activation mediates pain experiences in experimental knee osteoarthritis**

Garth Blackler, Yue Lai-Zhao, Joseph Klapak, Holly Philpott, Benoit Fiset, Logan Walsh, Elizabeth Gillies, C. Thomas Appleton

Synovial macrophages are thought to play a role in mediating joint pain in knee osteoarthritis (OA), but the underlying mechanisms are unknown. Our **Objective**s were to test whether synovial macrophages mediate knee OA pain experiences and investigate the role of macrophage activation via STAT signaling. Male Sprague Dawley rats underwent knee destabilization surgery

to induce experimental OA. RNA sequencing of sorted synovial macrophages was used to identify OA associated pathways. Liposomal clodronate or inhibitors of STAT1 or STAT6 were selectively delivered to synovial macrophages in a separate cohort of experimental OA animals. Evoked pain behaviors were assessed using pressure application measurement and electronic von Frey. Knee joint histopathology was performed to assess synovitis and cartilage damage. RNA sequencing identified a large role played by STAT signalling in synovial macrophages during experimental OA development. Macrophage depletion and STAT6 inhibition led to a marked improvement in pain behaviors compared to vehicle control at multiple timepoints. Synovial macrophage depletion reduced signs of synovial inflammation but led to increased fibrosis and vascularization, whereas STAT1 or STAT6 inhibition did not. Synovial macrophages play a key role in mediating pain experiences in joint destabilization-induced experimental knee OA. Selective drug targeting to synovial macrophages with STAT6 inhibitors may be a strategic approach to treatment of OA-related pain without accelerating joint damage.

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## Fabio Castrillon

**Glucagon-like peptide 1 receptor agonists in end-staged kidney disease and kidney transplantation: A narrative review**

Kristin K Clemens, Jaclyn Ernst, Tayyab Khan, Sonja Reichert, Qasim Khan, Heather LaPier, Michael Chiu, Saverio Stranges, Gurleen Sahi, Fabio Castrillon-Ramirez, Louise Moist

**Background**: Glucagon-like peptide 1 receptor agonists (GLP-1RA) improve glycemic control and weight loss in people with type 2 diabetes (DM2) and obesity. However, their metabolic effects in end-staged kidney disease (ESKD) and kidney transplantation have not been well-established. **Objective**: In this narrative review, we summarized the effects of GLP-1RA in end-staged kidney disease and kidney transplantation on measures of obesity and glycemic control, and examined adverse events and adherence with therapy. **Methods**: We implemented librarian-guided strategies to search for randomized controlled trials (RCTs) and observational studies on Medline, Scopus, EMBASE, PubMed, Google Scholar, conference abstracts and Clinicaltrials.gov. **Data synthesis**: In RCTs of DM2 patients on dialysis, 12 weeks of liraglutide treatment lowered HbA1c by 0.8%, reduced time in hyperglycemia by ~2%, lowered blood glucose by 2 mmol/L and weight by 1-2 kg, compared with placebo. In prospective cohort studies inclusive of ESKD patients, 12 months of semaglutide reduced HbA1c by 0.8%, and lowered weight by 8 kg. In small retrospective cohort studies of kidney transplant recipients with DM2, 12 months of GLP-1RA lowered HbA1c by 2%, and fasting glucose by ~3 mmol/L compared with non-use, with weight losses of up to 4 kg. Gastrointestinal (GI) side effects were most common, with a heightened risk of hypoglycemia in ESKD patients, particularly in insulin users. **Conclusions**: In RCTs and cohort studies of patients with ESKD and kidney transplantation, modest glycemic and weight benefits were described with GLP-1RA. GI side effects may limit adherence. Larger and longer-term studies of GLP-1RA remain important.

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RuoYan Chen

**Clinical Relevance and Prognostic Significance of Small-Vessel Inflammation in Temporal Artery Biopsies**

RuoYan Chen, Shervin Pejhan, Robert Hammond, Pari Basharat, Larry Allen, Lulu Bursztyn, Alain Proulx, Morgan Smith, Montana Hackett, Lillian Barra

**Introduction**: Temporal artery biopsy (TAB) is the standard of care for diagnosing Giant Cell Arteritis (GCA), a large vessel vasculitis that can lead to blindness and stroke. Only 50% of GCA cases have temporal arteritis (TA) on biopsy; however, small-vessel vasculitis (SVV) and angiitis of the vasa vasorum (AAV) have been reported. This study aims to investigate the relevance of SVV/AVV in TAB. **Methods**: Consecutive TAB were scored for inflammation between January and December 2018. Matching clinical data was collected from a retrospective chart review with a follow-up of 1-year post-biopsy. **Results**: Microscopy of seventy-two patients (mean age = 71 ± 10 years, 69% females) revealed 18 TA, 15 AVV, 5 SVV, 4 AVV+SVV, and 30 negative cases with no significant differences in age, sex, and comorbidities. All TA cases had concurrent small vessel inflammation on histopathology. At presentation, diplopia and jaw claudication were more common in TA than AVV/SVV ($p = 0.011$ and $p = 0.006$, respectively). C-reactive protein was higher in GCA patients ($p = 0.005$). The time on corticosteroids before TAB was lowest in TA and highest in those with a negative biopsy. At 1-year follow-up, 28% of patients with AAV and/or SVV had a GCA diagnosis compared to 14% with a negative biopsy ($p > 0.05$). **Conclusions**: The coexistence of TA and AVV suggests a role for small vessel vasculitis in GCA. However, less than 30% of patients with isolated small vessel disease developed GCA at 1-year. The presence of SVV/AVV on TAB must be interpreted with caution.

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RuoYan Chen

**Structural Cerebrovascular Sequelae and Cognitive Impairment in Anti-Neutrophilic Cytoplasmic Antibody-Associated Vasculitis**

RuoYan Chen, Fahad Hannan, Jeff Hamilton, Jonathan Thiessen, Michael Jurkiewicz, Jennifer Mandzia, Susan Huang, Lillian Barra

**Introduction**: Neuropsychiatric complaints has been reported in 30-60% of anti-neutrophilic cytoplasmic antibody (ANCA)-associated vasculitis (AAV) cases and is a significant contributor to reduced quality of life. Quantitative magnetic resonance imaging (qMRI) has the potential for detecting early abnormalities in brain perfusion but has not been previously studied in AAV. This study aims to assess the relationship between disease activity, cognition, and vascular abnormalities using multi-modal cerebral qMRI. **Methods**: Patients between 18- and 75-years old with AAV were recruited. They completed the Cambridge Brain Sciences (CBS) cognitive test and underwent a comprehensive 65-minute MRI containing qualitative and quantitative sequences. **Results**: Thirty-seven AAV patients (mean age = 53.07 ± 14.18 years, 57% females, mean disease duration = 6.93 ± 5.27 years) and 8 controls (mean age = 45.29 ± 19.36 years, 37% females) have been enrolled in the study from April 2021 to present. Significantly lower scores for a test measuring attention were noted in 10 AAV patients and for short-term verbal memory in 13 patients. qMRI revealed that the T2 relaxation time was significantly higher in the cingulate ($p < 0.001$), frontal ($p = 0.041$) and parietal lobes ($p= 0.022$) of ANCA-patients than controls (signifying increased water content from axonal loss and/or inflammation). These regions of the brain are responsible for attention and short-term memory.

**Conclusions**: Chronic cerebral inflammation and ischemic damage appear to affect cognition in AAV. Quantitative MRI may be a useful tool for investigating mechanisms contributing to AAV-related cognitive impairment.

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## Jodi Chiu

**A Hyperacute Presentation of Mature B-Cell Lymphoproliferative Disorder: A Case Report**

Jodi Chiu, Mark Crowther

**Background**: Mature B-cell lymphoproliferative disorders comprise a heterogeneous group of conditions, including chronic lymphocytic leukemia (CLL) and non-Hodgkin lymphomas. Their clinical course varies depending on the underlying diagnosis, although presenting manifestations are often mild with lymphadenopathy and constitutional symptoms.
Case Presentation: A 79-year-old woman presented with generalized weakness, gait instability, and dyspnea. She had a WBC 550 x109/L, hemoglobin 30 g/L, and platelets 49 x109/L. Electrolytes were consistent with tumour lysis syndrome (TLS). She had a metabolic acidosis, hyperlactatemia, and markedly elevated troponin. Peripheral blood smear demonstrated profound lymphocytosis. Bloodwork two years prior was normal. After aggressive red blood cell transfusion, she was managed for leukostasis with concurrent TLS. She received maintenance IV fluids, rasburicase, allopurinol, and escalating doses of prednisone (for lymphoreduction). TLS status was monitored with daily bloodwork. Incidental note of pseudohyperkalemia was made. Her flow cytometry eventually returned as a monoclonal B cell population (CD5+, CD10-, CD19+, CD23+), which is atypical for CLL, and raised concerns for peripheralizing Mantle Cell Lymphoma instead.
**Conclusion**: We review our approach to managing hyperleukocytosis in the setting of a mature lymphoproliferative disorder, including its associated hematologic emergencies of profound anemia, leukostasis, and TLS associated with evidence of systemic hypoperfusion. Clinicians should remain vigilant of non-specific signs and symptoms of leukostasis, particularly in mature B-cell lymphoproliferative disorders, where this presentation is rare and unexpected.

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## Jodi Chiu

**Are cervical cancer brachytherapy outcomes associated with pre-brachytherapy hemoglobin values and transfusion practice? An observational study comparing two large academic centres with divergent transfusion practices**

Taylor Dear, Jodi Chiu, David D-Souza, Alejandro Lazo-Langner, Eric Leung, Jeannie Callum, Ziad Solh

**Background**: Hemoglobin (Hb) thresholds for red blood cell (RBC) transfusion are well studied in many patient populations, but not in cervical cancer patients receiving radiation therapy where animal studies have suggested better outcomes with higher Hb. A recent survey showed that transfusion practice in Canada varies for this patient population due to lack of clinical evidence demonstrated in a recent systematic review. We hypothesized that disease-free survival and mortality are not different when cervical cancer patients are transfused to achieve Hb > 70 vs. 100 g/L. **Methods**: We conducted a retrospective observational cohort study from January 1, 2014 to December 31, 2018 including adult cervical cancer patients who underwent brachytherapy at London Health Sciences Centre (transfusion threshold Hb < 100 g/L) and Sunnybrook Health Sciences Centre in Toronto (transfusion threshold Hb <70 g/L). Patients were followed from date of first brachytherapy. Progression-free survival, overall survival, red cell

utilization, time to death, hospitalizations, complications, cause of death, and transfusion reactions were analyzed. **Results**: 336 patients were included:150 patients from London;186 patients from Sunnybrook. A total of 101 units of packed RBCs were transfused in London over the course of brachytherapy treatment, versus 19 in Toronto. Preliminary analysis shows there is no difference in disease-free survival and mortality for cervical cancer patients treated with brachytherapy when they are transfused liberally to achieve Hb >100 g/L compared to a restrictive threshold of 70 g/L. **Conclusion**: The practice of liberal transfusion in London leads to more RBC unit utilization with no clinical benefit.

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## Jodi Chiu

**Venous Thromboembolisms in Haematopoietic Stem Cell Transplantation**

Jodi Chiu, Brianna Ananthan, Matthew Lawrence, Mohamed Aly, Dhuvaraha Srikrishnaraj, Madeleine Weichel, Uday Deotare, Anargyros Xenocostas, Alejandro Lazo-Langner

**Background**: Venous thromboembolisms (VTEs) are a major cause of morbidity and mortality amongst allogeneic and autologous hematopoietic stem cell transplant (HSCT) patients. This remains understudied, with a paucity of established guidelines on thrombosis surveillance, prevention, and treatment in this unique population. Balancing risk of bleed and thrombosis remains challenging. We aimed to describe the incidence, predictors, and adverse events of VTE amongst patients at 90 days post-HSCT. **Methods**: We conducted a retrospective cohort study of adult patients who underwent HSCT for hematological malignancy between January 1, 2011 and December 31, 2021 at London Health Sciences Centre. Patients were followed from transplant until Day 90 post-transplant, or death. Baseline, transplant, laboratory, and cancer characteristics were analyzed. **Results**: 476 HSCT patients were included. 47 patients (9.8%) suffered from VTE within 90 days post-HSCT; 74.5% were catheter related. 9.43% of allogeneic, versus 10.09% autologous patients were diagnosed with VTE. 11.9% of allogeneic, versus 4.1% of autologous patients (p=0.001) suffered from bleed unrelated to anticoagulation. There was significant association of VTE post-HSCT with history of unprovoked DVT, previous treatment with L-asparaginase and steroids, infectious complications, >5 platelet transfusions, hospital admission >20 days, use of PICCs, and left-sided CVC placement. Mortality rate at 90 days amongst VTE patients was 14.89%, versus 3.27% in non-VTE patients ($p < 0.001$). **Conclusion**: The majority of VTE post-HSCT were catheter-related and were more frequently associated with use of PICCs. VTE prophylaxis or active surveillance could be considered in patients with the above-mentioned risk factors.

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## Bianca De Benedictis

**Hospitalised COVID-19 outcomes are predicted by hypoxaemia and pneumonia phenotype irrespective of the timing of their emergence**

Bianca De Benedictis, Brittany Salter, Laura Spatafora, Jessica Kapralik, Candice Luo, Steven Qiu, Laura Dawson, Mats Junek, Tyler Pitre, Aaron Jones, Marla Beauchamp, Rebecca Kruisselbrink, MyLinh Duong, Andrew P Costa, Jennifer Ly Tsang, Terence Ho

Despite the known clinical importance of hypoxemia and pneumonia, there is a paucity of evidence surrounding risk of mortality and short-term outcomes among hospitalised COVID-19 patients. **Objective**: Describe the prevalence and clinical course of hospitalized COVID-19 patients based on oxygenation and pneumonia status at presentation and determine the

incidence of emergent hypoxaemia or radiographic pneumonia. **Methods**: A retrospective study was conducted using a Canadian regional registry. Patients were stratified according to hypoxaemia/pneumonia phenotype and prevalence. Clinical parameters were compared between phenotypes using χ2 and one-way ANOVA. Cox analysis estimated adjusted Hazard Ratios (HR) for associations between disease outcomes and phenotypes. **Results**: At ED admission, the prevalence of pneumonia and hypoxaemia was 43% and 50%, respectively, and when stratified to phenotypes: 28.2% hypoxaemia+/pneumonia+, 22.2% hypoxaemia+/pneumonia-, 14.5% hypoxaemia-/pneumonia+ and 35.1% hypoxaemia-/pneumonia-. Mortality was 31.1% in the hypoxaemia+/pneumonia- group and 26.3% in the hypoxaemia+/pneumonia+ group. Hypoxaemia with pneumonia and without pneumonia predicted higher probability of death. Hypoxaemia <24 hours or ≥24 hours after hospitalisation predicted higher mortality and need for home oxygen compared with those without hypoxaemia. Patients with early hypoxaemia had higher probability of ICU admission compared with those with late hypoxaemia. **Conclusion**: Mortality in COVID-19 is predicted by hypoxaemia with or without pneumonia and was greatest in patients initially presenting with hypoxaemia. Emergence of hypoxaemia was predicted by radiographic pneumonia. Patients with early and emergent hypoxaemia had similar mortality but were less likely to be admitted to ICU. There may be delayed identification of hypoxaemia, which prevents timely escalation of care.

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## Luigi Del Sordo

**Impaired synovial macrophage-mediated efferocytosis in a rat model of post-traumatic knee osteoarthritis**

Luigi Del Sordo, Garth Blackler, Emily Sodhi, Matthew Grol, Bryan Heit, Tom Appleton

**Purpose**: Our lab has previously found that in patients with end-stage knee osteoarthritis (OA), the synovial apoptotic cell burden was significantly higher and that synovial-derived macrophage-mediated efferocytosis was impaired. Since uncleared apoptotic cells can promote inflammation, they therefore could contribute to the pain and/or joint damage caused by OA. Our Objectives were to determine the effect of efferocytosis impairment on structural and pain-related behavioural outcomes in a rat model of post-traumatic OA (PTOA). **Methods**: We performed an interventional, longitudinal study that compared four different groups based on pain scores taken at multiple time points throughout the study. Our sample consisted of 10-week-old male Sprague-Dawley rats that received either sham or PTOA surgery and either intervention (AnnexinV; blocks efferocytosis) or control (LacZ) intra-articular injections. Outcomes for this study included co-primary analyses for pain involving mechanical sensitivity at the target knee, and distal mechanical sensitivity at the hindpaw. **Results**: At 4 and 12 weeks post-PTOA induction surgery, AnnexinV induced a significant reduction in withdrawal threshold compared to LacZ. In contrast, at 4, 8, and 12 weeks post-sham surgery, the withdrawal threshold was not significantly different in both groups. Furthermore, there were no significantly different withdrawal thresholds at 4, 8 and 12 weeks using pressure application measurement analysis between all AnnexinV and LacZ groups. **Conclusions**: Overall, we found that efferocytosis impairment leads to worse distal pain-related behaviours in this rat model of PTOA. This data supports the key functions of the synovium and further emphasizes targeting synovial health in OA to improve outcomes.

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## Mithieu Derouet

**Establishment of human 3D in vitro mini-gut models to study cystic fibrosis**

M. Derouet, S. Asfaha

**Background**: Cystic Fibrosis (CF) is caused a genetic abnormality in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that encodes for a chloride channel. A defective CFTR channel **Results** in accumulation of sodium and water within the cells and this causes thickened mucus within the lungs and gut. The consequence of this is frequent airway infections, bowel obstruction and pancreatic insufficiency. Interestingly, CF patients are also known to have a higher risk of colorectal cancer (CRC), although the mechanism by which this occurs is unknown. In this study, we aimed to test the feasibility of generating mini-gut organoids from patients with CF in order to screen for phenotypic differences when compared to healthy controls. **Method**: We established 3D in vitro mini gut organoids using fresh human colonic biopsies from 2 healthy and 2 patients with CF. After establishment, we compared growth and responses to the cAMP agonist forskolin. The Forskolin Induced Swelling assay was used to examine the function of the CFTR channel. **Results**: Healthy organoid cultures were able to swell within 30 mins of addition of Forskolin. Organoids generated from CF patients, however, showed no noticeable swelling throughout the duration of the assay, consistent with the presence of a defective CFTR protein. **Conclusions**: We have conducted a proof of principle feasibility study of an in vitro colonic model that demonstrates that we can indeed grow organoids from patients with CF and that these can be used to study how CF alters the colonic epithelium and sensitize it to CRC.

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## Kaviya Devaraja

**Financial Aid Requests by Brain Tumor Patients in Ontario through GoFundMe**

Kaviya Devaraja, Jonathan Avery, Yajur Iyengar, Andy Zhang, Seth Climans

**Objective/purpose**: Numerous Ontario brain tumor patients suffer the unequal burden of responsibility to pay for treatments like oral chemotherapy. However, less is known about other direct and indirect financial costs due to their diagnosis. The purpose of this study was to analyze publicly-available data from GoFundMe, an online fundraising platform, to explore the financial needs of brain tumor patients. **Method**: A qualitative descriptive design drawing on thematic analysis was used to analyze GoFundMe requests to support individuals diagnosed with brain cancer in Ontario between 2014 and 2021. A coding framework was created to determine emerging themes using qualitative data analysis software NVivo 10.

**Results**: There were 195 fundraising requests. Requests described financial strain from the loss of income experienced by the patient and their caregivers to afford cancer treatments. Requests highlighted 1) an overall lack of awareness of how and where access financial aid and affordable psychosocial support; 2) concerns over the long-term financial well-being of bereaving family members; 3) A call for more public awareness of the financial burden and emotional distress experienced by of those impacted by brain cancer.

**Conclusions/clinical implications**: These GoFundMe requests highlight a connection between financial burden and emotional distress and an overall lack of awareness of where/how to seek financial and emotional support. These Results will serve as the foundation to advocate for and raise awareness of the financial assistance needed by brain tumor patients and their families.

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## Robert Dima

**Knee effusion-synovitis detected on ultrasound: biomarker of joint-level inflammation, or predictor of joint failure risk?**

Robert Dima, Trevor Birmingham, Holly Philpott, Mary-Ellen E.T. Empey, Aaron Fenster, C. Thomas Appleton

Inflammation of the synovial membrane, characterized by proliferation of synovial lining cells, mononuclear infiltration, and neo-vascularization, is an early pathological feature in knee OA and is thought to contribute to knee pain and accelerate joint damage. Due to its accessibility and non-invasive nature, effusion-synovitis seen on medical images is often used as a proxy measure of inflammation. However, effusion-synovitis is a composite of two separate pathological processes (effusion and synovial lining thickening) and recent work supports a fibrotic inflammatory profile among knee OA patients with low levels of effusion-synovitis as seen on ultrasound. As a result, the use of effusion-synovitis as a biomarker for joint-level inflammation may risk confounding by disease stage. Obesity and metabolic dysregulation manifesting as hypertension, hypercholesterolemia, hypertriglyceridemia, and hyperglycemia have been linked to increased local and systemic inflammation through multiple mechanisms, including M1 polarization of macrophages, release of pro-inflammatory adipokines, and altered lymphoid tissue architecture. Our Objective is to investigate whether effusion-synovitis represents an ordinal measure of joint-level inflammation. Our Methods will involve descriptive analysis of the distributions of ultrasound-detected synovial effusion and lining thickening between groups of knee OA patients with active knee OA with and without obesity, and with and without clinical and hematological evidence of metabolic dysregulation. We hypothesize that obese and metabolically dysregulated patients will demonstrate higher levels of effusion-synovitis on ultrasound imaging. We will also use adjusted linear regression to determine whether disease stage (degree of radiographic joint damage) is an interacting variable of the relationship between effusion-synovitis and obesity/metabolic dysregulation.

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## Emma Graham

**Surfactant dysfunction caused by vaping, with the addition of secondary insults**

Emma Graham, Sabrine Gehani, Lynda McCaig, Akash Tejura, Ruud Veldhuizen

**Introduction**: The use of e-cigarettes (ECs) remains a popular habit despite reports of vaping associated acute lung injury. EC aerosol comes into direct contact with pulmonary surfactant in the lungs. This critical mixture of lipids and proteins lines the alveolar surface and reduces surface tension upon exhalation, maintaining compliance. Surfactant dysfunction, associated with serum protein leak and oxidative stress, contributes to lung injury. We hypothesized that exposure to EC aerosol impairs pulmonary surfactant function, and thereby increases its susceptibility to protein inhibition or oxidative stress. **Methods**: Vaping was mimicked by exposing surfactant exposure to e-cigarette aerosol in a syringe. The functional impact was then tested on a constrained sessile drop surfactometer. In experiment 1 we tested compositionally different surfactant preparations to evaluate different surfactant components. In experiment 2 we tested post aerosol function following an additional insult via plasma proteins or oxidization. **Results**: In experiment 1, complete surfactant derived from a natural bovine source had significantly greater inhibition compared to exogenous surfactant. Both surfactants were inhibited compared to control. In experiment 2, plasma containing serum proteins significantly increased minimum surface tensions in aerosol exposed surfactant. Oxidization had an additive rather than synergistic effect

on inhibition of vaped samples. **Conclusion**: EC aerosols alter surfactant function through increases in minimum surface tension. This inhibition is amplified in the presence of serum proteins. Vaping impairs the pulmonary surfactant system and increases susceptibility to damage by secondary insults.

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## Fahad Hannan

**Voxel-based analysis of structural brain changes in thrombotic thrombocytopenic purpura post-remission using MRI**

Fahad Hannan, Patriquin CJ, Pavenski K, Jurkiewicz MT, Tristao L, Owen A, Kosalka P, Theberge J, Mandzia J, Thiessen J, Huang SHS

**Objective**: Immune-mediated thrombotic thrombocytopenic purpura (iTTP) is a rare disease caused by enzyme inhibition that leads to platelet aggregation and thrombosis. Despite treatment, patients experience an increased risk of cognitive impairment and depression. This study aims to understand the white matter changes in the brain caused by iTTP using advanced magnetic resonance imaging (MRI) to study white matter health and correlate them with neurocognitive changes. **Methods**: 20 patients with iTTP recruited 30 days after hematological remission and six healthy controls underwent a comprehensive MRI scan. Standard of care sequences and a multicomponent driven equilibrium steady-state observations of T1 and T2 (mcDESPOT) sequence were done to look for white matter changes. Additional tests included a cognitive test and depression scores to correlate with MRI findings. **Results**: Clusters of significantly increased voxels ($Z > 3.1$) were found mainly in subcortical and periventricular regions of the T1 maps, with clusters mainly residing in the cingulate and frontal region. Numerous clusters of significantly increased voxels ($Z > 3.1$) were found throughout the brain for T2 maps. Radiological findings found that 75% of patients had white matter hyperintense spots in aforementioned regions. These regions correlate with decreased cognitive scores and depression tests that indicated concentration difficulties and reduced short-term memory.
**Conclusion**: This study finds potential regions of interest, such as the frontal lobe and cingulate cortex, that show possible damage as indicated by increase T1/T2 signal. Future work will explore the use of diffusion tensor imaging to further investigate these regions to look for possible pathologies.

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## Mohammad Hmidan Simsam

**Efficacy of High Dose Tranexamic Acid (TXA) for Hemorrhage: A Systematic Review and Meta-analysis**

Mohammad Hmidan Simsam, Laurence Delorme, Dylan Grimm, Fran Priestap, Sara Bohnert, Marc Descoteaux, Rich Hilsden, Colin Laverty, John Mickler, Neil Parry, Bram Rochwerg, Christopher Sherman, Shane Smith, Jason Toole, Kelly Vogt, Sean Wilson, Ian Ball

**Background**: Standard dose (≤ 1g) tranexamic acid (TXA) has established mortality benefit in trauma patients. The role of high dose IV TXA (≥2g or ≥30mg/kg as a single bolus) has been evaluated in the surgical setting, however, it has not been studied in trauma. We reviewed the available evidence of high dose IV TXA in any setting with the goal of informing its use in the adult trauma population. **Methods**: We searched MEDLINE, EMBASE and unpublished sources from inception until July 27, 2022 for studies that compared standard dose with high dose IV TXA in adults with hemorrhage. We pooled trial data using a random effects model and considered

randomized controlled trials (RCTs) and observational cohort studies separately. Risk of bias and overall certainty of evidence was assessed using the GRADE approach.
**Results**: We included 20 studies with a combined total of 12,523 patients. Based on pooled RCT data, and as compared to standard dose TXA, high dose IV TXA probably decreases transfusion requirements (odds ratio [OR] 0.86, 95% confidence interval [CI] 0.76 to 0.97, moderate certainty) but with possibly no effect on blood loss (mean difference [MD] 43.31 ml less, 95% CI 135.53 to 48.90ml less, low certainty), and an uncertain effect on thromboembolic events (OR 1.33, 95% CI 0.86 to 2.04, very low certainty) and mortality (OR 0.70, 95% CI 0.37 to 1.32, very low certainty).
**Conclusion**: When compared to standard dose, high dose IV TXA probably reduces transfusion requirements with an uncertain effect on thromboembolic events and mortality.

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## Nafis Hossain

**Leveraging digital tools to support population health management and integrated care: A rapid scoping review**

Nafis Hossain, Sydney Neumeier, Rohan Kumar, Fahmida Islam, Jason Nie, Terence Tang

Digital tools are crucial to supporting population health management across sectors. They can be used to capture determinants of health to tailor services, segment populations, and enable outreach. We described evidence on how digital interventions can advance population health management, and provide recommendations of how to best implement these technologies. A rapid scoping review was conducted. The search strategy included keywords related to digital technology and population health management in integrated care models. Searches were performed in Medline, Embase, and Cochrane DSR, limited to high-income countries and published after 2000. Six reviewers were involved in the initial title and abstract screening, followed by full-text screening using Covidence. All articles in the full-text screening required agreement between two reviewers for inclusion, with conflicts resolved by a third reviewer or group consensus. 14,359 studies were identified in the database search. Following the initial title and abstract screening, 139 studies proceeded to the full-text review, and 52 studies are currently in the extraction phase. Preliminary Results reveal key themes; digital tools promote population health by: i) defragmenting care, ii) facilitating care coordination, iii) being multifaceted, and iv) improving health equity. Studies reporting positive Results use defined care coordination strategies. Subtypes of digital interventions appear to be more effective when used as combined (rather than standalone) interventions. This scoping review provides insights on the effective use of digital health tools in a population health context. This has implications for health system transformation initiatives for integrated care, to achieve quadruple aim and health equity.

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## Lynn Huong

**Evidence of Synovial Cell Stress and Mitochondrial Dysfunction in Knee Osteoarthritis**

Lynn Huong, Garth Blackler, Frank Beier, Tom Appleton

**Background**: Chronic synovitis is associated with increased pain and disease progression, but more research is needed to identify mechanisms driving osteoarthritis-related (OA) synovitis. Mitochondria have central roles in stress adaptation and immunometabolism. Emerging studies have shown that mitochondrial dysfunction contributes to the pathogenesis of chronic inflammation in diabetes and atherosclerosis. In OA, synovial macrophages are the chief immune cells driving inflammation, but little is known about their mitochondrial function and how cell stress

affects disease outcomes. Our Objective was to investigate the effects of the OA joint environment from various disease severities on macrophage mitochondrial function.
**Methods**: Synovial fluid samples were collected from patients with early-stage knee OA and healthy volunteers. Participants were classified into 2 groups: high disease activity (high pain, moderate/severe knee synovitis) and low disease activity (low pain, no/mild synovitis). Healthy blood-derived macrophages were conditioned with the synovial fluids before RNA isolation and mitochondrial staining. RNA sequencing was used to compare macrophage transcriptomic responses between disease activity groups. Immunofluorescence microscopy was used to measure mitochondrial reactive oxygen species (ROS) and morphology. **Findings**: RNA sequencing demonstrated that OA synovial fluid exposure increased macrophage cell stress and altered mitochondrial pathways, particularly in patients with high disease activity. Conversely, OA synovial fluid exposure increased ROS fluorescent intensity regardless of disease activity. Similarly, morphological analyses demonstrated that synovial fluid from both disease activity groups showed reduced and swollen mitochondrial networks. Overall, OA may lead to oxidative stress in synovial macrophages, highlighting the importance of targeting synovial health to improve OA outcomes.

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## Alvi Islam

**Pharmacological Strategies for the Management of Severe Alcohol-associated Hepatitis: A Systematic Review and Meta-analysis**

Alvi Islam, Claudia Alvizuri, Juan Pablo Arab

**Background**: Alcohol-associated hepatitis (AH) is part of the alcohol-associated liver disease (ALD) spectrum and represents the most critical form of its presentation. The one-month mortality of AH is estimated to be 20% and can be even higher in moderate to severe AH. To this day, therapies to treat severe AH are still lacking. Current pharmacological therapies include anti-inflammatories such as corticosteroids, pentoxifylline, zinc; antioxidants such as N-acetylcysteine; growth factors such as granulocyte colony stimulating factor; and other therapies including omega-5 fatty acid, anakinra or infliximab. Corticosteroids are used as first-line treatment for AH but survival improvement beyond 28-days has not been proven. Efficacy of other pharmacotherapy to treat AH outlined are unclear. The aim of this systematic review and meta-analysis is to determine the optimal pharmacological treatment for severe AH that Results in better survival outcomes. **Methods**: Literature search for eligible studies has been conducted in the following databases: MEDLINE, EMBRASE, CENTRAL. Two authors independently screened abstracts for eligibility and extracted relevant primary data. In brief, active comparator and placebo-controlled trials studying a pharmacotherapeutic intervention in severe AH were eligible for inclusion. A systematic review in accordance with Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) was conducted. **Results**: The primary clinical end point is overall mortality in AH. Secondary outcomes to be studied include mortality at 28 days, 90 days, rates of liver transplantation, and all-cause mortality. **Conclusion**: Full Results of the systematic review and meta-analysis are currently pending as data extraction and synthesis are actively being performed.

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## Xiaoyun Ji

**Junctophilin-2 prevents cardiomyocyte death by blocking MURF1-mediated Junctin ubiquitination and proteasome-dependent degradation**

Xiaoyun Ji, Yifan Huang, Rui Ni, Dong Zheng, Guo-Chang Fan, Douglas L Jones, Long-Sheng Song, Subrata Chakrabarti, Zhaoliang Su, Tianqing Peng

**Aims**: Junctophilin-2 is required for the development, maturation and integrity of the t-tubule system and the gating stability of RyR2 in cardiomyocytes. This study investigated whether and how junctophilin-2 maintained junctin, a scaffold protein stabilizing RyR2, to prevent cardiomyocyte death under stress. **Methods**: Cardiomyocytes were exposed to conditions of stress including palmitate, doxorubicin, or hypoxia/re-oxygenation. Adenoviral vectors were employed to manipulate expression of junctophilin-2 and junctin in cardiomyocytes. Molecular/cellular/biochemical analyses were conducted. **Results**: Different conditions of stress decreased junctophilin-2 expression through aberrant autophagy and concomitantly induced a reduction of junctin protein in cardiomyocytes. Over-expression of junctophilin-2 preserved the protein levels of junctin and attenuated cytosolic Ca2+ and apoptosis in cardiomyocytes under stress. Knockdown of junctophilin-2 reproduced the detrimental phenotypes of stress in cardiomyocytes. Notably, over-expression of junctin prevented cardiomyocyte death under stress whereas knockdown of junctin offset the protective effects conferred by junctophilin-2 over-expression. Mechanistically, junctophilin-2 blocked MURF1-junctin interaction thereby preventing junctin ubiquitination and proteasome-dependent degradation. Mass spectrometry analysis identified multiple ubiquitination sites on the junctin protein and the non-ubiquitinated junctin mutant (K8A/K102A/K107A/K140A) was resistant to degradation. **Conclusions**: This study uncovers an unrecognized role of junctophilin-2 in preventing junctin ubiquitination and degradation. Both junctophilin-2 and junctin represent two new survival factors of cardiomyocytes and thus, may be new therapeutic targets for cardiac protection.

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## Tharsan Kanagalingam

**Geriatrician Determinants of Choosing a First Practice: The Methodology of a survey for subspecialty trainees and new geriatricians**

Luxey Sirisegaram, Jasmine Mah, Sarah Best, Sallie Elhayek, José A. Morais, Marianne Lamarre, Jaspreet Bhangu, Jenny Thain, Michael Borrie

**Background**: The 2021 CGS Human Resource Committee (HRC) paper projected there will be a significant shortfall of geriatricians in 2030, particularly in rural and remote communities. These findings were presented at the CGS Strategic Retreat in May 2022. The CGS executive endorsed the suggestion that the HRC develop a survey for newly graduated geriatricians and subspecialty residents to determine the factors influencing the choice of their first specialist position. **Methods**: A consensus working group used a literature search and career planning knowledge to create a list of “specific factors”. These were grouped into domains and put in an anonymous RedCap survey tool for descriptive analysis. The emailed survey is available in English and French to new geriatricians 2021 & 2022 (~60) and subspecialty trainees graduating 2023 and 2024 (~60). **Results**: The literature search yielded 7 papers from 1996 – 2020 but none specific to geriatric medicine (GM). The 7 domains with specific factors of importance were: location, type of practice, support, and space, non-clinical opportunities, income model, lifestyle and recruitment. **Discussion**: This study is the first in Canada to examine specific factors and their relative importance in influencing the choice of trainees and new geriatricians in choosing their first

position. **Conclusion**: This survey will inform future trainees of the important factors that others have considered when career planning. The Results will also inform underserved communities about factors that could attract geriatricians.

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## Zoya Khandwala

**Calcium oxalate stones and vitamin D insufficiency in Canada: a scoping review of the literature**

Zoya Khandwala, Hassan Razvi, Stan Van Uum, Kristin Clemens

**Background**: The link between vitamin D and calcium oxalate kidney stones is unknown, particularly in a Canadian context. **Methods**: We conducted a scoping review of the medical literature to identify Canadian studies of adults aged 18 years and older with calcium oxalate stones. Our Objectives were twofold: 1. To examine the association between 25 hydroxyvitamin D, parathyroid hormone and calcium oxalate kidney stones, and 2. Understand the effect of vitamin D supplementation on clinical outcomes (e.g. biochemistry, imaging, stone formation). We searched Medline, Cochrane and Google Scholar between January and February 2023 using a librarian-developed search strategy. **Results**: We identified 28 relevant citations of which 5 studies appeared to meet inclusion criteria. The majority of studies were observational in design and included 200 to 400 patients. 25 hydroxyvitamin D insufficiency was highly prevalent in Canadians with calcium oxalate stones (more than 50% of stone formers). Where ascertained, a concomitant increase in parathyroid hormone was observed (i.e. secondary hyperparathyroidism). Most patients were normocalcemic in this setting. There were no studies to examine the effect of vitamin D supplementation on important clinical outcomes.
**Conclusion**: In some Canadian studies, an association between 25 hydroxyvitamin D and calcium oxalate stones has been observed, and with this, hyperparathyroidism. It may be useful to include 25 hydroxyvitamin D in metabolic screening. Further research on the therapeutic benefit of vitamin D in this patient population might also be helpful.

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## Pauline Kosalka

**The Association between aHUS and Cognitive Dysfunction using Magnetic Resonance Imaging for White Matter Assessment**

Pauline Kosalka, Hannan F, Thiessen J, Huang SHS, Pavenski K, Jurkiewicz MT, Tristao L, Owen A, Theberge J, Patriquin CJ

Atypical hemolytic uremic syndrome (aHUS) is a rare, life-threatening thrombotic microangiopathy caused by a defect in the alternative complement pathway. It is associated with renal failure and acute encephalopathy, but long-term neurocognitive effects are uncertain. Using MRI and neurocognitive tests, we can further evaluate the long term neurocognitive complication in aHUS. In this study, we analyzed microstructural chages in the cerebral white matter of patients with aHUS and assessed their neurocognitive testing Results. Six adult patients with aHUS in remission and 6 healthy controls were included. All patients were treated with complement blockade. They were followed for 12 months after study entry. All participants had consecutive MRI scans including standard-of-care scans as well as quantitative sequences to assess for white matter changes, along with concurrent cognitive testing. Participants were noted to have increased signal intensity in the frontal lobe, cingulate, insula, subcortical, and paraventricular structures compared with controls. This correlated with depression and increased impairment in

concentration, and short-term and verbal memory on neurocognitive testing. Patients had increased depression scores. In this study, patients with previous aHUS were found to have significant albeit nonspecific cerebral white matter abnormalities with impaired memory and concentration. Larger studies with longitudinal follow-up to assess these neurocognitive complications in aHUS patients are required.

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## Jami Kronick

**Metabolic Syndrome Increases the Risk of Late-Stage Knee Osteoarthritis: A Retrospective Cohort Study**

Jami Kronick, Surim Son, Tom Appleton, Trevor Birmingham, Andrew Appleton

**Background**: Given substantial epidemiological evidence for metabolic syndrome (MetS) as a risk factor for osteoarthritis (OA), it has been proposed that treating MetS may improve OA outcomes. However, it has not yet been established that MetS increases the risk of late-stage OA. To address this gap, our study compared the prevalence of early- versus late-stage knee OA (ES-KOA, LS-KOA) in patients with and without MetS. **Methods**: Data was obtained from 251 participants recruited for the Western Ontario Registry for Early Osteoarthritis (WOREO) Knee Study. To determine the association between MetS and KOA stage, Poisson regression with robust variance was performed. To determine whether MetS is associated with worse KOA pain as measured by the Knee Injury and Osteoarthritis Outcome Score (KOOS), multivariable linear regression with generalized estimating equation (GEE) was performed and stratified by KOA stage. **Results**: Participant characteristics were summarized using descriptive statistics. MetS prevalence was 28.2% in the ES-KOA group (KL grade 0-2) and 54.8% in the LS-KOA group (KL grade >2). Individuals with MetS had a 34% higher prevalence of LS-KOA, adjusting for all covariates. MetS had a lower mean KOOS than non-MetS indicating more severe pain in both ES and LS knees. However, the difference was only significant in ES knees. **Conclusions**: MetS increases the risk of LS-KOA independent of age. It is also associated with significantly worse pain in ES-KOA. Our Results indicate that treating MetS has the potential to improve patient outcomes by delaying radiographic progression and reducing symptoms.

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## Adrian Kuchtaruk

**Impact of Frailty Status on Readmissions after Impella Mechanical Circulatory Support**

Adrian Kuchtaruk, Rodrigo Bagur

**BACKGROUND**: Frailty is a common condition that is associated with significant morbidity and mortality in older adults. The impact of frailty on outcomes and readmissions after Impella mechanical circulatory support (MCS) remains uncertain. **OBJECTIVES**: To evaluate the impact of frailty on hospital readmissions and outcomes during after Impella MCS. **METHODS**: Frailty status was assessed using the Hospital Frailty Risk Score (HFRS) for patients ≥65 years old who required Impella MCS between 2016-2020 using the U.S. Nationwide Readmission Database. Patients with an HFRS >5 were considered frail. **RESULTS**: Among 16,004 patients who required Impella MCS, 54% were considered frail. At 30-days, 14% were readmitted, among these, 58% had frailty versus 42% did not (P<0.001). Of the 6,497 participants available for the 31-180-day analysis, 28% were considered frail, and increased readmissions were observed among frail compared to not frail individuals (34% versus 21%, P<0.001). After adjusting for age, sex, and comorbidities, frailty was associated with increased readmissions at 30-days (OR: 1.29; CI: 1.19-

1.40; P<0.001), and 31-180-days (OR: 2.07; CI: 1.85-2.32; P<0.001), and prolonged length-of-stay during 30-day (OR: 1.04; CI: 1.02-1.06; P<0.001) and 31-180-day (OR: 1.05; CI: 1.02-1.07; P<0.001) readmissions. Notably, frailty was not associated with higher mortality during readmissions at 30-day (OR: 1.26; CI: 0.84-1.91; P=0.27), but it was at 31-180-day (OR: 2.20; CI: 1.20-4.04; P=0.01). **CONCLUSIONS**: Frailty is common among older adults requiring Impella MCS and is associated with increased rates of 30- and 31-180-day readmissions.

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## Frederikke Larsen

**DNA hypomethylation inhibits colitis-associated colorectal cancer**

Frederikke Larsen, Hayley J. Good, Alice E. Shin, Mathieu Derouet, Liyue Zhang, Christina Castellani, Samuel Asfaha

**Background**: Colorectal cancer (CRC) is the second leading cause of cancer death in Canada with a major risk factor being chronic inflammation. We previously described a colitis-associated cancer (CAC) model in which tumors arise from DCLK1+ cells following loss of APC and colitis induction. Interestingly, both colitis and CAC are associated with DNA methylation changes. Moreover, DNA hypomethylation has recently been shown to lead to a viral mimicry response. Thus, we hypothesize that DNA hypomethylation leads to a viral mimicry response that inhibits CAC. **Method**: Dclk1/Apcf/f and Dclk1/Apcf/f/Dnmt1f/f mice was administered tamoxifen followed by dextran sodium sulfate (DSS) to induce CAC. Fourteen weeks later, we assessed tumor number and size. In a separate cohort of Dclk1/Apcf/f mice, we compared tumor number amongst mice treated with 5-AZA-2'-deoxycytidine (5-AZA) versus vehicle. The effect of 5-AZA and DSS on DNA methylation was assessed using the Infinium Mouse Methylation BeadChip Array on colonic epithelial cells. RNA expression of transposable elements and type-I interferon genes was measured as a readout of a viral mimicry response. Lastly, we inhibited the viral mimicry response by crossing Dclk1/Apcf/f/Dnmt1f/f mice to MAVS knockout mice and examining tumor number. **Results**: DNMT1 loss or 5-AZA treatment inhibited colonic tumorigenesis and led to DNA hypomethylation and upregulation of gene expression of transposable elements. Additionally, increased expression of type-I interferon genes was observed. Knockout of MAVS reversed the anti-tumor effect observed with DNMT1 loss.
**Conclusions**: Our findings demonstrate that DNA hypomethylation reduces CAC formation through activation of a viral mimicry response.

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## Bishoy Lawendy

**A Nationwide Study of Acute Gastroenterology related Hospitalizations During the Coronavirus Pandemic in the United States; Trends and Outcomes**

Bishoy Lawendy, Muni Rubens, Philip N. Okafor

**Background and Aims**: COVID-19's impact on acute gastrointestinal presentations requiring hospitalization remains unclear at the population level in the United States. Our study aimed to describe inpatient gastroenterology outcomes during the first year of the pandemic (2020), with 2018 and 2019 as comparator years, using the National Inpatient Sample. **Methods**: We analyzed trends in hospitalizations, length of stay, and inpatient mortality for gastrointestinal presentations (luminal, biliary, infectious, inflammatory, and pancreatic diseases) between 2018-2020 using regression modeling. Relative change (RC) described the trend between time periods, and statistical significance was set at $P < 0.05$. **Results**: In 2020, there were significantly lower rates

of hospitalization for most acute GI conditions relative to 2019. However, we observed an increase in all-cause mortality (0.9% in 2019 and 1.1% in 2020, p<0.001) and hospital costs for patients hospitalized with acute presentations of GI-related conditions in 2020 relative to 2019. Furthermore, we observed increased mortality in patients with acute pancreatitis, Variceal upper GI bleeding, ulcerative colitis, and acute cholangitis who were also COVID-19 positive. A month-to-month trend analysis showed that in 2020, the lowest number of admissions for all conditions was during April, coinciding with lockdowns ordered by most state governments throughout the country. **Conclusions**: In general, acute GI-related hospitalizations decreased in 2020; however, hospital costs and mortality increased compared with the pre-pandemic period in 2019. These findings suggest that COVID-19 had an impact on acute GI-related hospitalizations and highlights the importance of continued research to better understand the relationship between COVID-19 and GI-related conditions.

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## Alexandre Le-Nguyen

**Role of azathioprine in the management of Immune Thrombocytopenia: A Single Centre Retrospective Study**

Alexandre Le-Nguyen, Cyrus C. Hsia

Immune thrombocytopenia (ITP) is an autoimmune disease involving the formation of autoantibodies against platelets and resulting in potential bleeding complications. Patients with ITP unfortunately often have a refractory and relapsing disease course. Despite new advancements in therapies, such as thrombopoietin-receptor agonists (TPO-RA) and splenic tyrosine kinase (Syk) inhibitors, the need for further treatment options remains. This paper will aim to investigate the role of azathioprine at a single centre at a tertiary care centre and compare it to the existing literature surrounding azathioprine as a therapeutic agent in relapsed or refractory ITP, and determine if it is an effective treatment modality in patients in the era post TPO-RAs. This will be a single center, retrospective study.We have analyzed seven papers published between 1984 and 2021 evaluating azathioprine as a treatment modality for relapsed or refractory ITP. Each study evaluated 24 to 90 patients (mean = 53), and patients were treated with either weight-based or fixed doses of azathioprine (usually 1-2 mg/kg/day or 150 mg daily) with or without concomitant drugs. Treatment duration ranged from 90 days to 84 months and response rates ranged from 38 to 75%. Common recorded side-effects included gastrointestinal symptoms, leukopenia and hepatobiliary laboratory abnormalities. We will assess all adult patients diagnosed with refractory or relapsed ITP who have received azathioprine between Jan 1, 2009 and Dec 31, 2022. We will assess the rate of utilization, timing, dosing, safety and efficacy of azathioprine in this patient population.

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## Jordan LeSarge

**Interventions to Reduce Sedentary Behaviour in Adults with Type 2 Diabetes: A Systematic Review and Meta-Analysis**

Siobhan Smith, Babac Salmani, Jordan C. LeSarge, Kirsten Dillon-Rossiter, Harry Prapavessis

Reducing sedentary behaviour (SB) may be a more feasible/sustainable behaviour change than physical activity (PA) in adults with type 2 diabetes (T2D) that could lead to improved cardiometabolic health. This review is the first to summarize, synthesize the effectiveness of, and appraise the quality of interventions that reduced and/or broke up SB in adults with T2D. This

review followed PRISMA guidelines, was registered on PROSPERO (CRD42022357281), and included all published interventions that aimed to reduce and/or break up SB in adults with T2D. A comprehensive systematic database search (PubMed, EMBASE, Scopus, Web of Science, PsycINFO, SPORTDiscus, CINAHL, and Cochrane Library) was conducted on 16/09/2022. Risk of bias was assessed with Cochrane risk of Bias Tools. Twenty-two articles were included in the review. The meta-analysis of short-term SB interventions found significant improvement in the standard mean difference (SMD) for continuous interstitial glucose measured for 24-hours after the SB intervention compared to control (SMD:-0.823,95%CI:-1.252,-0.394,p<0.001). Similarly, there was a significant improvement in the SMD for postprandial interstitial glucose after the SB intervention compared to control (SMD:-0.347,95%CI:-0.584,-0.110,p=0.004). Seven out of eight longer-term SB interventions improved at least one measure of SB compared to control. Five out of five longer-term SB interventions improved at least one cardiometabolic biomarker compared to control. This review suggests that reducing SB, independent of PA, can improve glycemic control in adults with T2D. It also suggests that SB may be a more feasible/sustainable behaviour change than PA.

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## Danning Li

**Time of Declaration of Donor Brain Death to Cross-Clamp Time vs. Cardiac Transplant Outcome at LHSC**

Danning Li, Stuart Smith

**Background**: Cardiac transplant is a treatment for severe heart failure refractory to medical therapy. As of 2021, there are 135 patients pending cardiac transplant in Canada. Thus, it is important to assess the various factors that potentially affect cardiac transplant outcomes, especially in context of high procedure cost, as well as the difficulty of finding suitable donors.
**Methods**: 163 cardiac transplants at LHSC from 2012 to 2022 were analyzed, with the time between declaration of donor brain death to cross-clamp time in the operating room dichotomized at 72hr. Statistical analysis was completed to assess transplant outcome, defined as graft loss within 90 days. Other potential factors were analyzed, including donor and recipient BMI, age, and gender. **Results**: 145 cases had <72hr between pronouncement and cross-clamp time, with 14 graft failures. 18 cases had >72hr between pronouncement and cross-clamp time, with 6 graft failures. Overall graft failure rate is 9.66% in <72hr group and 33.33% in >72hr group, with statistical significance (P=0.0114) by Fisher's exact test, with a odds ratio of 4.679. Age, gender, BMI of donors and recipients were statistically non-significant in affecting overall outcome. **Conclusion**: Time between pronouncement of donor brain death and aortic cross-clamp in the operating room affects cardiac transplant outcome significantly, with increased time correlating with increased graft failure rate. Donor and recipient age, BMI, and gender do not significantly affect outcome. Reducing this time may positively affect cardiac transplant outcome, and further investigation is needed for other possible factors.

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## Eden Liu

**Cervical Spine Management and Outcomes in Rheumatoid Arthritis Patients in the Perioperative Setting - A Single Center Experience**

Eden Liu, Catherine Gnyra, Kathryn Myers

**Background**: Patients with rheumatoid arthritis (RA) can have cervical spine (c-spine) involvement that causes instability. During the act of intubation, manipulation of the c-spine can result in worsening instability, resulting in adverse neurological outcomes or death. **Methods**: We performed a scoping review of the available literature looking at the perioperative management of the c-spine in patients with RA. Additionally, we performed a quality assessment of our local practice for patients with RA. Adult patients at LHSC with a formal diagnosis of RA, that were seen in the Pre-Admission Clinic (PAC) by an Internist prior to their surgery were included in the study. Outcome measures included documented assessment of the c-spine, c-spine imaging, delivery of anesthesia, Method of intubation, and immediate adverse neurological outcomes. **Results**: (Preliminary data) A total of 1987 unique articles were identified with the help of a librarian, of which 36 were included in our scoping review. In 2022, there were a total of 1756 patient encounters in our PAC, with 81 patients having RA. 53 had some form of c-spine imaging preoperatively, but only 28 had the appropriate imaging done. 27 patients were intubated with 11/27 using video laryngoscopy. 13/81 patients had an unstable c-spine. No adverse outcomes noted. **Conclusions**: Based off the scoping review, perioperative neurological complications are exceedingly rare. With increasing use of biologics and video laryngoscopy, most patients with RA do not require cervical spine imaging preoperatively. At LHSC, only 65% of RA patients had c-spine imaging preoperatively, of which 47% was completed incorrectly.

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## Jessica Liu

**Sodium-glucose cotransporter-2 inhibitor-associated erythrocytosis: A retrospective cohort study**

Jessica Liu, Benjamin Chin-Yee, Ian Chin-Yee, Jenny Ho, Bekim Sadikovic, Cyrus C. Hsia

**Background**: Sodium-glucose cotransporter-2 (SGLT-2) inhibitor use is an underrecognized cause of erythrocytosis and the natural history of this condition remains uncertain. In this study, we report clinical outcomes in patients with SGLT-2 inhibitor-associated erythrocytosis who continued, discontinued, or underwent dose changes to their SGLT-2 inhibitor. **Methods**: We retrospectively reviewed all patients referred to our centre for erythrocytosis between August 1, 2015 and May 20, 2021 who had JAK2 mutation testing and were taking an SGLT-2 inhibitor. Patients who were JAK2 mutation positive or who were on concomitant testosterone were excluded. Descriptive statistical analysis was performed. **Results**: Eighty-two of 891 patients were included in the study. Sixteen patients (19.5%) received treatment for erythrocytosis. Overall, median hemoglobin increased by 20 to 28 g/L on an SGLT-2 inhibitor from baseline, with a median peak hemoglobin of 182 to 185.5 g/L. Twenty patients (24.4%) discontinued SGLT-2 inhibitors and two patients (2.4%) underwent dose reduction. In this group, the majority (81.8%) showed normalization or return to baseline of hemoglobin. In patients who continued with no dose changes, half (50.0%) showed normalization or return to baseline of hemoglobin levels, while the rest had stabilization of elevated hemoglobin levels. Five patients (6.1%) developed thromboembolic events while on an SGLT-2 inhibitor; all five patients had other cardiovascular risk factors. **Conclusion**: SGLT-2 inhibitor-associated erythrocytosis may lead to potentially

unnecessary investigations and treatments. Further investigation is required to characterize the safety of this medication class and the risk of thromboembolism in this population.

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## Haitao Lu

**CfDNAs worsen heart transplantation by inducing ZBP1-mediated PANoptosis**

Haitao Lu, Zhuxu Zhang, Xuyan Huang, Patrick McLeod

**Background**: Transplant rejection is associated with various forms of programmed cell death. Donor-derived cell-free DNAs (dd-cfDNAs) are novel biomarkers for monitoring allograft rejection, which was confirmed by endomyocardial biopsy to allograft samples. However, current reports have not illustrated the injuries induced by cfDNAs to heart transplantation rejection yet as cfDNAs cause tissue injuries through various cell death pathways.
**Methods**: We conduct cell death assays in human cardiovascular endothelial cells with purified cfDNAs treatment. Then we tried to determine whether cfDNAs promote cell death by activating various DNA sensors. Next, we used coIP to determine how cfDNAs-DNA sensors axis induces cell death. Continuously, we used Western blotting to measure key molecules for pyroptosis, apoptosis or necroptosis termed PANoptosis (a crosstalk among pyroptosis, apoptosis and necroptosis). **Results**: We found markedly elevated cell death levels with cfDNAs treatment. PCR and blotting Results showed ZBP1 has a significant increase. In addition, ZBP1 silencing reduced cell death in cfDNAs-treated cells. Interestingly, coIP Results showed ZBP1 interacts with RIPK3 and ADAR1. which are the essential complexes inducing cell death. Furthermore, we found that GSDMD (p30), caspase 7(p20), and pMLKL, key molecules of pyroptosis, apoptosis or necroptosis, showed a significant increase in cfDNA-treated cells. Surprisingly, their protein levels were reduced in ZBP1silencing cells treated with cfDNA. Interestingly, the protein level of ADAR1 was increased in ZBP1 silencing group. **Conclusion**: cfDNAs induce cell death by activating ZBP1 to initiate cell death. CfDNA-induced PANoptosis predicts histological injuries outcome and may mechanistically propagate dd-cfDNAs-induced heart allograft rejection.

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## Hamza Mahmood

**Retrospective Case Series of HELLP syndrome with AKI**

Hamza Mahmood, Cassandra Fayowski, Rayyan Mahmood, Susan Huang, Dongmei Sun

**Background**: Hemolysis, elevated liver enzymes and thrombocytopenia (HELLP) syndrome is a severe, multi-system process occurring in 0.5-0.9% of pregnancies. 1 Acute kidney injury (AKI) has previously been described to affect 7-25% of cases of HELLP syndrome in older series. 2 The resulting complications from HELLP related AKI range from full renal recovery, to need for renal replacement therapy, to death. 2 It is unclear what the incidence and consequences of AKI in HELLP syndrome is in our institution. We sought to conduct a case series on patients at our institution with HELLP syndrome complicated by AKI. **Methods**: This is a retrospective case series conducted at London Health Sciences Centre and St. Joseph's Health Care, on all pregnancies with a diagnosis of HELLP from January 2001 to October 2020. Potential participants were identified using ICD-10 codes for preeclampsia and HELLP syndrome both from admission diagnosis and discharge diagnosis. In addition, investigator's case files were used. Charts were screened by two independent physicians. Data abstraction from patients' hospital charts was done to identify cases as patients with HELLP syndrome with AKI, Descriptive statistics and graphs were used to describe the cohort. **Results**: A total of 1862 charts were obtained for

screening. Thirty-one charts were identified as cases of HELLP with AKI. Four cases required renal replacement therapy, with only two cases not returning to normal renal function. One patient died, representing a mortality rate of 3% at our institution.

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## Aminmohamed Manji

**The impact of aging on pulmonary microvascular endothelial cell barrier function**

Aminmohamed Manji, Sanjay Mehta, Lefeng Wang, Cynthia M. Pape, Sean E. Gill

Elderly individuals have elevated morbidity and mortality during conditions of lung injury, though the underlying mechanisms are ill-defined. Lung injury is associated with damage to pulmonary microvascular endothelial cells (PMVEC) and the cell-cell junctions between them, leading to a compromised vascular barrier, fluid and protein leakage within the tissue, and respiratory dysfunction. Our pilot data showed increased pulmonary vascular leak in aged vs. young mice during lung injury. We hypothesized that aging contributes to PMVEC barrier dysfunction due to impaired cell-cell junction integrity. To address this, PMVEC isolated from young and aged mice were cultured in vitro, until a confluent monolayer was formed. Barrier integrity was assessed by Evans blue-labelled albumin leak across monolayers, as well as immunofluorescence staining of the adherens junction protein, VE-cadherin. Localization of leak was visualized using the fluorescently labelled macromolecule, NeutrAvidin. Proteomics analysis was conducted to identify differentially enriched pathways in young and aged PMVEC. Compared to young, endothelial monolayers from aged mice exhibited a significant increase in albumin leak associated with augmented VE-cadherin disruption. NeutrAvidin staining localized to paracellular regions with VE-cadherin discontinuity was increased in aged PMVEC, suggesting a direct association between leak and junctional disruption. Proteomics analysis revealed pathways implicated in endothelial barrier dysfunction, including oxidoreduction regulation, that were altered in aged PMVEC. We will next target protein pathways dysregulated in aged PMVEC to potentially rescue age-induced barrier dysfunction. These findings may highlight molecular pathways involved in predisposing aged individuals to worsened outcomes during lung injury, which can aid in therapeutic development.

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## Yehia Moharrem

**Expansion of human mesenchymal stromal/stem cells on decellularized adipose tissue scaffolds preserves primitive cell phenotype and enhances pro-angiogenic secretory function**

Yehia Moharrem, Gillian I. Bell, Tyler T. Cooper, Lauren E. Flynn, David A. Hess

**INTRODUCTION**: Due to limited treatment options for individuals with critical limb ischemia (CLI), cellular-based therapies have been investigated to induce collateral blood vessel regeneration. Bone marrow-derived mesenchymal stromal/stem cells (BM- MSC) have shown pre-clinical success in animal models of CLI as they possess pro-angiogenic and immunomodulatory secretory functions. However, clinical translation has been hindered by inadequate expansion and poor survival in the ischemic limb after injection. This project aimed to characterize the phenotype and pro-angiogenic secretory function of human BM-MSC cultured on decellularized adipose tissue (DAT) bioscaffolds as an expansion and delivery platform. **METHODS**: Human fat samples were decellularized through an established detergent-free treatment protocol and then processed to generate DAT coatings. BM-MSC seeded onto DAT coatings were assessed in vitro

for cell survival, proliferation, surface marker phenotype, mass spec-based proteomic analyses, and pro-angiogenic secretory function. In vivo function was characterized via the Directed in vivo Angiogenesis Assay (DIVAA). **RESULTS**: Compared to cells grown on tissue-culture plastic (TCP), DAT coatings increased BM-MSC proliferation and regenerative marker expression (Aldehyde dehydrogenase and CD271). Conditioned media (CM) generated by BM-MSC cultured on DAT coatings significantly increased human endothelial cell survival under starvation conditions in vitro, and proteomic analysis of the CM showed enrichment with factors associated with wound healing and angiogenesis in the BM-MSC expanded on DAT relative to TCP. Similarly, BM-MSC cultured on DAT coatings increased endothelial cell infiltration in DIVAA inserts implanted in NOD/SCID mice. **CONCLUSION**: BM-MSC expansion on DAT coatings represents a promising approach to retain primitive phenotype and enhance pro-angiogenic secretory function.

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## Ahmed Mokhtar

**Validation of a stroke preventive algorithm in a digital healthcare platform: VIRTUES Antithrombotic Algorithm**

Ahmed Mokhtar, Pavel Antiperovitch, Marco Herrera, Thea Lee, Nellie Kamkar, Anthony S.L. Tang

**Introduction**: VIRTUES (Virtual Integrated Reliable Transformative User Driven E-Health System) is a digital health platform to provide guideline-directed cardiovascular management recommendations remotely to patients and their healthcare providers. To accomplished this, a team of clinicians, research assistants and computers programmers extract from national and international practice guidelines recommendations for various clinical scenarios and build a decision-team algorithm that accounts for patient's characteristic, clinical status, and medical information. We plan to develop these care pathway algorithms for several cardiovascular and related conditions. The first of these is the care pathway for the management of patients needing antithrombotic treatment. **Objectives**: To test the accuracy of the antithrombotic algorithm against (1) a group of experts, and (2) against a group of trainees. **Methods**: The antithrombotic algorithm was designed to incorporate 12 common clinical scenarios that require primary and secondary thromboembolic and myocardial ischemic prevention. A total of 12 experts are asked for their expert anti-thrombotic recommendations for each clinical scenario. In addition, 20 healthcare trainees of various levels (PGY 3-5) will be asked to provide clinical answers to the best of their knowledge. Validation will be determined based on the responses provided from the healthcare providers and degree of matching with guideline-based recommendations. **Results**: Pending **Conclusion**: To be determined once Results are obtained.

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## Ahmed Moustafa

**Vascular and Cardiac Ultrasound as the Primary Imaging Tool to safely deliver pacing leads while implanting Single Chamber Cardiac Implantable Electronic Devices: RADICAl USE investigators**

Ahmed Moustafa, Samuel Triemstra, Ahmed T. Mokhtar, Saketh Saravu, Viwe Mtwesi, Lorne J. Gula, Peter Leong-Sit, Jaimie Manlucu, Allan C. Skanes, Raymond Yee B, Anthony Tang

**BACKGROUND**: Conventional cardiac implantable electronic devices (CIEDs) implantation requires the use of fluoroscopy, and heavy personal radiation protection. Risks include pocket

hematoma, pneumothorax, lead dislodgement, and perforation of the right ventricle. There are long-term risks of malignancy with prolonged use of radiation and mechanical injuries associated with heavy protection equipment for the operators. We aimed to study the utilization of ultrasound for the entire procedure to implant single-chamber devices. **METHODS**: The RADICAI USE study (Reduction or Elimination of Radiation Use in Single Chamber Cardiac Devices using ultrasound) was a prospective, single-arm and multi-operator study in which patients awaiting a single-chamber CIED were enrolled. A fluoroscopic cut-off time of 20 seconds was used to define success (Group A) or failure (Group B) of using ultrasound for the entire duration of the pacemaker implant. Patients were followed up at 1 week, 1 month and 1 year post implant. **RESULTS**: 63 patients received CIEDs with a mean age of 79.5 ± 13.8 years (95% CI = 76.1 – 82.9). Ultrasound use was successful in implanting CIEDs (Group A) in 53 (84.1%) patients, with no significant change in procedural time including ultrasound setup time, mean 65.2 ± 20.2 (60.2 -70.2) minutes. Significant reduction in fluoroscopic time (5.8 ± 4.5s vs 109.5 ± 92.9s, p = 0.004). 2 lead revisions were needed with 1 unrelated to ultrasound use, otherwise no procedural adverse events. **CONCLUSION**: Ultrasound-guided implantation of CIEDs is feasible and safe to perform, reducing the need to have fluoroscopic guided implantation and subsequent risks of higher radiation exposure.

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## Rui Ni

**DDIT3 promotes necroptosis by blocking MK2 and increasing p38 MAPK activation**

Rui Ni, Ting Cao, Xiaoyun Ji, Angel Peng, Zhuxu Zhang, Guo-Chang Fan, Subrata Chakrabarti, Zhaoliang Su, Tianqing Peng

DNA damage-inducible transcript 3 (DDIT3) is well-known to induce apoptosis under endoplasmic reticulum stress. Here, we report an unrecognized role of DDIT3 in promoting necroptosis in cardiomyocytes under oxidative stress.Conditions of oxidative stress including incubation with hyperglycemia or doxorubicin elicit DDIT3 expression and initiate RIPK1/ RIPK3/MLKL necroptosis signaling and cell death in cultured-adult cardiomyocytes, which are attenuated by a selective RIPK3 inhibitor. Deletion of DDIT3 prevents oxidative stress-induced necroptosis signaling and necroptotic cell death in cardiomyocytes whereas over-expression of DDIT3 sufficiently induces necroptosis and apoptosis in cardiomyocytes and non-cardiomyocytes including endothelial cells and tumor cells. Characterizing the functional domains of DDIT3 reveals that its N-terminus accounts for necroptosis whereas its C-terminus elicits apoptosis. Further mapping the N-terminus of DDIT3 identifies a 10-amino acid region (from Glu 19 to Val 28) accounting for necroptosis. Mechanistically, the N-terminus of DDIT3 binds MAPK-activated-protein-kinase 2 (MK2) thereby directly blocking p38 MAPK-mediated MK2 activation while inhibition of MK2 activation prevents RIPK1 phosphorylation at Ser321 (inactive-RIPK1) thereby promoting RIPK1 autophosphorylation at Ser166 (active-RIPK1), leading to necroptosis. Notably, constitutive activation of MK2 inhibits DDIT3-induced necroptosis. Lastly, over-expression of DDIT3 or its N-terminus sufficiently induces cardiac cell necroptosis as determined by Evans blue staining assay, phosphorylated MLKL staining and serum cardiac troponin I, whereas deletion of DDIT3 prevents hyperglycemia or doxorubicin-induced cardiac necroptosis and improves myocardial function in mice.These findings identify DDIT3 as a novel driver of necroptosis and strengthen the potential of DDIT3 as a therapeutic target for cardiac protection.

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## Freeman Paczkowski

**The Practice and Clinical Utility of Trace Metal Testing for Hematology Patients: A Retrospective Cohort Study**

Freeman Paczkowski, Yehia Moharrem, Benjamin Chin-Yee, Vipin Bhayana, Matthew Nichols, Ian Chin-Yee, Cyrus Hsia

**Introduction**: Deficiencies/toxicities in trace metals may be associated with hematologic changes and are included in the work-up of cytopenias. This study examined the utility of lead, copper, and zinc testing in hematology patients to optimize future clinical practice.
**Methods**: A retrospective chart review was performed on all adult Hematology patients who underwent testing for lead, copper, and zinc ordered by hematologists between 01/01/2017-12/31/2021 at LHSC. Primary outcomes were indications for testing, frequency of abnormal Results, and intervention rates. Secondary outcomes included correlation of these metal levels to hematologic parameters to characterize affected patients. **Results**: The final cohort consisted of 187 patients (66M, 121F, mean age 57.7+/-18.6). The most common indication for ordering each metal was anemia. Abnormal Results were identified for 17/85 (20%) of patients tested for lead, 68/168 (40.5%) zinc (all deficiencies; 79% within 20% of normal lower limit), and 24/169 (14.2%) copper (deficiencies and toxicities). Treatment was initiated for 1/17 (5.9%) patients with abnormal lead, 7/68 (10.3%) zinc, and 1/24 (4.2%) copper. Zinc levels were significantly lower in patients with an elevated CRP vs. normal CRP (7.46±1.03ug/L vs 8.6±0.88ug/L, p=0.0008). **Conclusion**: Abnormal levels of these three metals were relatively common, yet intervention rates were low. This suggests that slightly abnormal Results identified did not lead to changes in management. Additionally, the association of lower zinc levels with CRP suggests that zinc may be a negative acute phase reactant. Thus, clinicians should exercise caution in interpreting low zinc levels in the context of an inflammatory condition.

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## Hasib Rahman

**Propofol sedation does not improve measures of colonoscopy quality – Findings from a large population-based cohort study**

Hasib Rahman, McDonald C, Cocco S, Hindi Z, Chakraborty D, French K, Siddiqi O, Blier M, Brahmania M, Wilson A, Guizzetti L, Yan B, Jairath V, Sey M

**BACKGROUND and AIMS**: Propofol is commonly used for sedation during colonoscopy. We assessed the impact of colonoscopy on quality metrics in a population-based cohort study.
**METHODS**: All colonoscopies performed at 21 hospitals in Ontario during an 18-month period using either propofol or conscious sedation were evaluated. The primary outcome was adenoma detection rate (ADR) and secondary outcomes were sessile serrated polyp detection rate (ssPDR), polyp detection rate (PDR), cecal intubation rate (CIR), and perforation rate. **RESULTS**: A total of 46,634 colonoscopies were performed by 75 endoscopists (37.5% by gastroenterologists, 60% by general surgeons, 2.5% by others), of which 16,408 (35.2%) received propofol and 30,226 (64.8%) received conscious sedation. Patients who received propofol were more likely to have a screening indication (49.2% vs 45.5%, p<0.0001) and performed at a non-academic center (32.2% vs 44.6%, p<0.0001). Compared to conscious sedation, the use of propofol was associated with a lower ADR (24.6% vs. 27.0%, p<0.0001) but not ssPDR (5.0% vs. 4.7%, p=0.26), PDR (41.2% vs 41.2%, p=0.978), CIR (97.1% vs. 96.8%, p=0.15) or perforation rate (0.04% vs. 0.06%, p=0.45). On multi-variable analysis, propofol sedation was not significantly associated with ADR (RR=0.90, 95% CI 0.74-1.10, p=0.30), ssPDR (RR=1.20, 95%CI 0.90-1.60,

p=0.22), PDR (RR=1.00, 95% CI 0.90-1.11, p=0.99), or CIR (RR=1.00, 95%CI 0.80-1.26, p=0.99). **CONCLUSION**: The use of Propofol sedation was not associated with better or worse colonoscopy quality metrics in comparison to conscious sedation.

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## Marina Sanchez-Latorre

**Association Of Dual-Task Gait Performance And Falls Across The Cognitive Spectrum**

Marina Sanchez-Latorre, Frederico Pieruccini-Faria, Manuel Montero-Odasso

**Background**: Gait and cognitive impairment are independent risk factors for falls. Gait slowing while walking and talking (i.e. dual-task gait cost) is a risk factor for cognitive decline. However, the role of dual tasking on fall risk assessment remains unclear across cognitive statuses.
**Objective**: To examine the association between dual-task gait cost (DTC) and falls risk across the cognitive spectrum. **Methods**: Participants from the Gait and Brain Study had their gait assessed during usual and dual-task conditions. Cognitive status was assessed by trained clinicians using standardized neuropsychology battery during face-to-face interviews. Associations of DTC at baseline with incidental fall events (a fall and a fall with injury) across cognitive statuses were examined using separate Cox-regression models for each DTC condition(predictor) adjusted for baseline covariates. **Results**: 382 patients (mean age 72.3±6.66 years; 59% women) were analyzed, and divided into controls (n=123), subjective cognitive impairment (SCI; n=67) and MCI (n=192) with a maximum follow-up duration of 87 months. Increased DTC at baseline was significantly associated with an earlier fall with injury during the follow-up (HR,11.04; 95%CI 1.2-101.1; p=.034). No significant associations were found with all falls across the cognitive spectrum. **Conclusion**: Increased DTC while naming animals is an index of future injurious falls in older adults with MCI. Cognitive inability to control gait performance in complex situations may contribute to falls with worse consequences. Our findings may help improve and facilitate the fall risk screening of patients with MCI through an effective yet simplified walking test.

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## Clara Schott

**Utility Of Genetic Assessment In Chronic Kidney Disease Patients: A Canadian Prospective Cohort**

Clara Schott, Ava Pourtousi, Logan R. Van Nyatten, Samantha Colaiacovo, Cadence Baker, Dervla M. Connaughton

**Background**: Genetic kidney disease (GKD) is more prevalent than previously considered. Genomic testing using gene-panel or exome sequencing (ES) can confirm GKD through detection of mutations in genes known to cause kidney disease (KD). Unfortunately, widespread integration into clinical practice has been hampered by small studies and selective populations predominately performed in research settings. **Objective**: To use gene-panel and ES to identify genetic aetiologies of renal disease in a Canadian cohort with CKD and to assess the clinical impact of genetic diagnosis on patient specific outcomes. **Methods**: We analysed data from a cohort of patients (n=216 families, n=314 patients) referred to a renal genetic clinic between September 2019 and December 2022. Testing strategy was firstly to perform gene-panel testing, and if negative or unsuitable, ES was performed. Testing was performed for the detection of mutations in genes suspected to cause the specific subtype of KD in each patient.

**Results**: We identified a causative mutation, classified as pathogenic or likely pathogenic, in 22% of families (n=48/216 families). Gene panel testing detected the underlying molecular cause of KD in 34% of patients tested (n=41/122). In patients whom gene-panel was negative or not possible (n=113), ES analysis was performed. ES confirmed diagnosis in 20% of patients (n=23/113). **Conclusion**: We show that in a Canadian cohort of adults referred to a renal genetic clinic, genomic testing has utility by confirming the cause of genetic kidney disease in 22% of families. Genetic sequencing also has significant impacts on clinical management and patient outcomes.

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## Clara Schott

**Reclassification Of Genetic Diagnosis: Need For Structure In The Re-Evaluation Of Genetic Findings**

Clara Schott, Samantha Colaiacovo, Cadence Baker, Dervla M. Connaughton

**Background**: Constant advances and emerging data in genomic medicine causes classification of genetic findings to be dynamic. In kidney disease (KD) alone, the number of single gene disorders are increasing, with over 600 genes described thus far. The American College of Medical Genetic guidelines suggest that all new data should be incorporated into the genetic evaluation as it becomes available. Currently, there are no protocols guiding when and how often to reevaluate genomic data. We present a case which highlights the importance of periodic genetic re-evaluation in a living donor. **Case**: A 45-year-old female donated her left kidney as a non-directed altruistic donor. At the time of donor assessment, her creatinine was normal (60-70mmol/L), however, she had persistent microscopic hematuria and a positive family history, so testing was performed. This revealed a variant of unknown significance (VUS) in COL4A4 c.3307G>A, p.G1103R. Since a VUS is not considered a clinically actionable finding, she elected to proceed with donation. Unfortunately, 5-years post-donation, she had progressive rise in creatinine (125 umol/L), and her son developed kidney disease, warranting variant reanalysis. New clinical data supported pathogenicity of this variant, reclassifying to pathogenic, supporting a familial diagnosis of Alport Syndrome. **Conclusion**: We show that reevaluation of patient genomics can lead to reclassification of previously identified variants, which can have significant clinical implications for the patient and family. This case highlights both the importance of re-analysis and clinical implications of establishing a genetic diagnosis for family screening and decision making for transplants.

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## Jenna Schulz

**Changes in knee synovial fluid markers in osteoarthritis are associated with changes in gait biomechanics following high tibial osteotomy**

Jenna Schulz, Holly T Philpott, Trevor B Birmingham, Codie A Primeau, Kristyn M Leitch, Frank Beier, J. Robert Giffin, C. Thomas Appleton

It is unclear if altering gait mechanics can alter joint biology in knee osteoarthritis (OA). Therefore this study explored the associations between changes in knee synovial fluid biochemical markers and gait biomechanics after medial opening wedge high tibial osteotomy (HTO). Twenty-six patients with medial compartment knee OA and varus alignment underwent three-dimensional gait analysis and synovial fluid aspiration before and one year after HTO. The top biomarkers that increased [endothelial growth factor (EGF), platelet derived growth factor (PDGF-BB) and

fibroblast growth factor 2 (FGF-2)] and decreased [tumor necrosis factor-alpha (TNF-α) and interleukins (IL)-1B and -6)] after surgery were used to determine biological responder and non-responder groups. A series of mixed effects polynomial regressions compared external knee adduction moment (KAM, outcome) between the responders and non-responders over 100% of stance (predictor) for each biomarker, adjusting for body mass index and OA radiographic stage. This was repeated for the knee flexion moment (KFM). The largest differences were observed for EGF, where KAM differed between the responders and non-responders from 0-97% of stance, with the greatest decrease (unstandardized β [95% CI]) in the responder group occurring at 28% of stance ( 17.62 Nm [-20.08; -15.08]). For KFM, the two groups differed from 62-86% of stance, with the greatest increase in the responder group occurring at 76% of stance (15.90 Nm [2.84; 28.96]). These Results suggest a biological response after HTO associated with greater decreases in KAM and greater increases in KFM during walking, consistent with the ability to alter mechanobiological processes in knee OA.

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## Malcolm Sherwood

**Evaluation of Triple Therapy using Magnetic Resonance in Asthma (ETHA). An interim analysis**

Malcolm Sherwood, Alex Biancaniello, Lisa Cameron, Kiran Kooner, Christopher Licksai, Constance MacKenzie, David McCormack, Marrisa McIntosh, Narinder Paul, Maksym Sharma, Paulina Wyskiewicz, Cory Yamashita, Grace Parraga

**Background**: Long acting muscarinic antagonists (LAMA) are considered add on therapy for severe asthma according to 2022 GINA guidelines. This study investigates the potential role of LAMA in moderate Asthma, by examining the efficacy of a triple therapy (LAMA, Long Acting Beta Agonist (LABA), inhaled corticosteroid (ICS)), once a day puffer (umeclidinium, vilanterol, fluticasone furoate -UMEC/VI/FF) in patients with established asthma on low/medium dose maintenance ICS/LABA therapy. **Methods**: 14 participants were switched onto UMEC/VI/FF from their previous LABA/ICS puffer. At baseline and at 6 weeks follow up these participants had functional MRI, pulmonary function tests, clinical questionnaires and inflammatory markers taken. Initial outcomes examined were measures from spirometry, plethysmography, oscillometry, multiple breath nitrogen washout, fractional exhaled nitrogen oxide, and scores from the Asthma Control (ACQ), Saint George's Respiratory (SGRQ), and Asthma Quality of Life (AQLQ) questionnaires. The final analysis will look at hyperpolarized 129Xe MRI ventilation defect percent. **Results**: At 6 weeks after being initiated on UMEC/VI/FF triple therapy inhaler, participants had an improvement in clinical status: a mean improvement of 6.19 on SGRQ (MCID = 4), 0.514 on AQLQ (MCID = 0.5), and 0.226 on ACQ (MCID = 0.5). Quantitatively they had an improvement in measures of airway obstruction (FEV1 improved by 266mL), small and large airway resistance (improvement of 0.41 cmH2O/L on small airway oscillometry) and gas trapping (6.75% reduction in RV/TLC). **Conclusions**: This interim analysis of ETHA shows benefit from UMEC/VI/FF triple therapy in moderate asthmatics.

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## Igor Sljivic

**Feasibility and outcomes of outpatient Cytarabine Consolidation Chemotherapy used in a 6-day model in Acute Myeloid Leukemia patients at LRCP**

Igor Sljivic, Uday Deotare

**Introduction**: The last decade has seen consolidation therapy for acute myeloid leukemia (AML) move to outpatient settings. The standard or care involves high-dose cytarabine (HDAC) or intermediate dose cytarabine (IDAC), twice daily for three alternating days. At the London Regional Cancer Program (LRCP), we have transitioned the administration of outpatient cytarabine to a once-daily regimen over 6 consecutive days. The safety of a longer duration interval of cytarabine is unknown. This study aims to assess the safety and feasibility of a 6-day, once daily protocol of high-dose (HDAC-16) and intermediate-dose cytarabine (IDAC-16) consolidation therapy. **Methods**: This is a retrospective chart review of outpatients receiving AML consolidation therapy at LRCP from January 1, 2019, through November 1, 2022. The primary **Objective** was to determine the incidence of hospitalization, delays, and neutrophil recovery rates after cycles of 6 days, once-daily HDAC or IDAC. **Results**: Forty-five patients received 89 cycles of cytarabine; 55.6% of patients were male, with a median age of 57 years. Our incidence of hospitalization (31%), as well as 2-year all-cause survival in HDAC-16 (57.1%) and IDAC-16 (83.3%), is consistent with the reported literature. There was no difference in delays or relapse rates between HDAC-16 or IDAC-16 groups. Time to neutrophil recovery was unchanged with respect to age or cytarabine dosing. **Conclusion**: Outpatient administration of HDAC and IDAC once daily over 6 consecutive days is both safe and feasible. Moving to a once daily administration schedule would alleviate logistical and/or accessibility hurdles in outpatient oncology clinics.

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## Virginia Solitano

**Reliability and responsiveness of histologic disease activity indices in Crohn's Disease**

Virginia Solitano, David F. Schaeffer, Malcolm Hogan, Rish K. Pai, GY Zou, Reet K. Pai, Niels Vande Casteele, Claire E. Parker, Julie Remillard, Britt Christensen, Remo Panaccione, Bruce E. Sands, Geert D'Haens, Brian G. Feagan, Christopher Ma, Vipul Jairath

The operating properties of histologic indices are poorly characterized in Crohn's disease (CD) and no validated index exists. We assessed the reliability and responsiveness of histologic indices/items, developed an exploratory index, and compared different Methods of scoring.Using baseline and week 12 histologic image sets from the EXTEND trial, blinded central readers scored 4 histologic indices (Global Histologic Activity Score [GHAS], Geboes Score [GS], Robarts Histopathology Index [RHI], and Nancy Index [NHI]) and 3 items identified by an expert panel. Reliability and responsiveness were evaluated for a global score, colonic score and ileal score using the intraclass correlation coefficient (ICC) and area under the receiver operating curve (AUC). Change was defined using treatment assignment and improvement in histologic disease activity as measured on a VAS. Exploratory indices were developed using backward stepwise linear regression analysis. Paired histologic images were analysed from 55 subjects. Inter-rater reliability was substantial to almost perfect (ICC=0.73-0.85) and responsiveness was small to large (treatment assignment AUC=0.50-0.65; VAS AUC=0.71-0.94). The GHAS, GS, RHI, and NHI reached the minimum threshold for reliability (ICC ≥0.4) and responsiveness (AUC ≥0.56) regardless of whether the global and colonic scores were calculated using the worst affected segment, average of the included segments, or sum of the included segments. Three exploratory indices (global index, colonic index and ileal) were developed, and they highly correlated with the

GHAS, GS, RHI, and NHI, with correlation coefficients ≥0.80.The 4 existing indices were similarly reliable and responsive in measuring CD histologic activity.

## Virginia Solitano

### HLA-DQA1*05 Genotype and Immunogenicity to Tumor Necrosis Factor-alpha Antagonists: A Systematic Review and Meta-analysis

Virginia Solitano, Antonio Facciorusso, Dermot P.B. McGovern, Tran Nguyen, Ruben J. Colman, Lily Zou, Brigid S. Boland, Silje W. Syversen, Kristin Kaasen Jørgensen, Christopher Ma, Alessandro Armuzzi, Aze Wilson, Vipul Jairath, Siddharth Singh

Identifying patients at high risk of immunogenicity is important when selecting tumor necrosis factor-(TNF) antagonists in patients with immune-mediated inflammatory diseases (IMIDs). We evaluated the association HLA-DQA1*05 genotype and risk of immunogenicity with TNF antagonists. Through a systematic review till 14 July, 2022, we identified studies in patients with IMIDs treated with TNF antagonists, which reported the risk of immunogenicity and/or secondary loss of response in patients with HLA-DQA1*05 variants. Primary outcome was risk of immunogenicity. We performed random effects meta-analysis and used GRADE to appraise certainty of evidence. On meta-analysis of 13 studies (3,756 patients, median follow-up, 12m; 41% with variants), HLA-DQA1*05 variants were associated with 75% higher risk of immunogenicity compared to wild type [relative risk (RR), 1.75 (95% CI, 1.37-2.25)] with considerable heterogeneity (I2=62%) (low certainty evidence). Positive and negative predictive value of HLA-DQA1*05 variants for predicting immunogenicity was 30% and 80%, respectively. Proactive therapeutic drug monitoring, but not concomitant use of IMMs, IMIDs- and TNF antagonist-type, modified this association. Patients with HLA-DQA1*05 variants experienced 2.2-fold higher risk of secondary loss of response [six cohorts; RR, 2.24 (1.67-3.00), I2=0%] (moderate certainty evidence). Variants in HLA-DQA1*05 are associated with an increased risk in immunogenicity and secondary loss of response in patients with IMIDs treated with TNF antagonists. However, the positive and negative predictive value is moderate, and decisions on concomitant use of IMMs to prevent immunogenicity should be individualized based on all factors that influence drug clearance.

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## Robbie Sparrow

### Risk and Causes of Repeat Emergency Department Visit after Internal Medicine Consultation and Discharge from the Emergency Department

Robbie Sparrow, Mark Goldszmidt, Erin Spicer

**Background**: While causes of readmission have been well studied for patients discharged from the Emergency Department (ED) or Internal Medicine (IM) wards, an overlooked population are patients who receive an IM consultation in the ER and are discharged home without admission. Understanding the rate and predictors of hospital revisits for this population will assist in designing effective strategies to prevent revisits and allow IM physicians to make better-informed decisions about which patients to discharge from the ED. **Methods**: The population were patients referred to IM for consultation and then discharged from University Hospital's ED between August 2017 and December 2022. London Health Sciences Centre Decision Support extracted anonymized records for patients meeting these criteria. The primary outcome was an ER revisit within 14 days of index IM consultation. Analyses were performed using R statistical software. **Results**: Of the 1278 included patients, 26.4% revisited the ER and 9.5% were admitted to hospital within 14

days. Pneumonia, delirium, and COPD exacerbation were the most prevalent initial diagnoses. Patients with UTI (32.4%), COPD exacerbation (29.9%), heart failure (32.6%) and drug-related visits (41.2%) had the highest frequency of revisit. Receiving a CT, MRI or ultrasound was associated with a lower rate of ER revisit (19.2% vs. 27.9%, p <0.001). **Conclusion**: A quarter of patients returned to the ER within 14 days, which represents substantial cost and resource utilization. Several factors were found to influence the likelihood of revisits. This data will be used to guide quality improvement initiatives aimed at reducing avoidable revisits.

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## Scott Strum

**Real world experience of cemiplimab in the treatment of refractory locally- advanced and metastatic cutaneous squamous cell carcinoma**

Scott Strum, Seth Climans, Victoria Adelaide Purcell, Morgan Black, Scott Ernst

**Background**: Limited real-world data exists on the treatment of refractory locally advanced (non-metastatic disease no longer amenable to surgical intervention or radiation therapy) or metastatic cutaneous squamous cell carcinoma (SCC) with cemiplimab to date. The **Objective** of this study was to characterize demographic and clinical outcomes of these patients within a regional cancer program. **Methods**: Retrospective analysis of adult patients with refractory locally advanced (LA) and metastatic cSCC treated with cemiplimab at the London Regional Cancer Program. Patient demographics and treatment characteristics were reported, as well as Kaplan–Meier (KM) estimates of progression free survival (PFS) and overall survival (OS).
**Results**: Forty (40) patients were included. 15 (38%) had LA disease, and 25 (62%) had metastatic disease. Kaplan–Meier analysis revealed median OS was not reached (NR) for LA patients, but was 10 months (95% CI 3.25 months–NR) for metastatic patients. Median PFS was 25.3 months (95% CI 7.29 months–NR) for LA patients, 7.1 months (95% CI 3.02 months–NR) for metastatic patients. Estimated probability of OS at 12 months for all patients was 58.6% (95% CI 43.2%–79.4%), and PFS was 45.3% (95% CI 30.4%–67.5%). Reasons for treatment discontinuation were death from any cause (44%), disease progression (22%), cemiplimab side effects (4%), and other causes (30%). **Conclusion**: Estimates of OS and PFS were lower than corresponding phase I and II clinical trials. However, toxicity was tolerable. Thus, cemiplimab remains a safe and effective therapy in patients with refractory LA and metastatic cSCC.

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## Man Ger(Margaret) Sun

**Unmet need in the treatment of polymyalgia rheumatica and giant cell arteritis**

Man Ger (Margaret) Sun, Janet Pope

For decades, aside from prednisone and occasional use of immune suppressive drugs such as methotrexate, there was little to offer patients with polymyalgia rheumatica (PMR) and giant cell arteritis (GCA). However, there is a great interest in various steroid sparing treatments in both these conditions. This review aims to provide an overview of our current knowledge of PMR and GCA, examining their similarities and distinctions in terms of clinical presentation, diagnosis, and treatment, with emphasis placed on reviewing recent and ongoing research efforts on emerging treatment. Multiple recent and ongoing clinical trials are demonstrating new therapeutics that will provide benefit and contribute to evolution of clinical guidelines and standard of care for patients with GCA and/or PMR.

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## Kathryn Taberner

**A Case of Renal Hemosiderosis in Cold Agglutinin Disease Managed Successfully with Rituximab**

Kathryn Taberner, Cyrus Hsia, Andrew House, Aaron Haig

Renal hemosiderosis in the context of severe intravascular hemolysis is typically associated with paroxysmal nocturnal hemoglobinuria (PNH). Cases of renal hemosiderosis have been reported in sickle cell anemia, primary hemochromatosis, and prosthetic heart valves. We report the first case of a patient with cold agglutinin disease who developed renal hemosiderosis due to severe intravascular hemolysis which was successfully managed with rituximab. We present the case of a 71-year-old female who presented to clinic with a history of fatigue, tea-coloured urine, and anemia. Labs demonstrated low hemoglobin, elevated reticulocyte count, lactate dehydrogenase (LDH), total bilirubin, and low haptoglobin. Agglutination was seen on peripheral blood smear, and cold agglutinin screen was positive. Urinalysis was positive for protein and blood, however, the patient's renal function was normal throughout her clinical course. A renal biopsy was completed and abundant hemosiderin pigmentation in the tubular epithelium was seen, with no features of glomerulonephritis. These biopsy findings were consistent with renal tubular hemosiderosis. The patient was successfully managed with 4 courses of rituximab, with normalization of her hemoglobin and reticulocyte count. Cold agglutinin disease is an autoimmune condition where IgM-mediated red cell destruction typically leads to extravascular hemolysis. It accounts for 15% of autoimmune hemolytic anemia and has relatively mild intravascular hemolysis in comparison to PNH, which is why renal hemosiderosis is uncommon. There has been one report of renal hemosiderosis occurring with cold agglutinin disease, but this was associated with heavy alcohol intake.

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## Cheng-Chun Tai

**CYP2C19 Rapid and Ultra-rapid Metabolizers on chronic PPI therapy for Refractory Gastroesophageal Reflux Disease exhibit Greater Esophageal Mucosa Inflammation and Reduced Lower Esophageal Sphincter Resting Pressures**

Cheng-Chun Tai, Samantha Medwid, Keith McIntosh, Nilesh Chande, Richard B. Kim, Jamie Gregor

**BACKGROUND**: Despite numerous studies demonstrating suboptimal proton-pump inhibitors (PPIs) responses among CYP2C19 rapid and ultra-rapid metabolizers with Gastroesophageal Reflux Disease (GERD), the extent of esophageal acid exposure in such patients remain unclear. **METHODS**: This was a retrospective study of 56 patients with PPI refractory GERD who underwent CYP2C19 genotype testing for PPI metabolism, esophagogastroduodenoscopy, high-resolution esophageal manometry and ambulatory pH study. Patients were divided into two groups: normal metabolizer/intermediate metabolizer/poor metabolizer (NM/IM/PM) group and rapid metabolizer/ultra-rapid metabolizer (RM/UM) group, with 37 patients (23 NMs, 13 IMs, and 1 PM) and 19 patients (18 RMs and 1 UM), respectively. Chi-Square or Fisher's exact test was used to analyze categorical variables and independent samples T-Test for comparing means. **RESULTS**: In the RM/UM group, more had Grade C/D reflux esophagitis (6/19, 31.6% vs 3/37, 8.1%, P=0.049) and metaplasia of the esophagus (9/19, 47.4% vs 4/37, 10.8%, P=0.006). More required empirical dilatation for nonobstructive dysphagia (9/19, 47.4% vs 3/37, 8.1%, P=0.001) and more likely to have a hypotensive lower esophageal sphincter (10/19, 52.6% vs 6/37, 16.2%, P=0.011) and overall reduced mean lower esophageal sphincter resting pressure (mean±SD:

14.53±13.68 mmHg vs 22.94±13.79 mmHg, P=0.035; Normal=13-45 mmHg). Both groups had similar DeMeester scores (mean±SD: 31.36±38.98 vs 22.57±25.02, P=0.31; Normal < 14.7) as PPIs were discontinued before ambulatory pH study. **CONCLUSION**: CYP2C19 rapid and ultra-rapid metabolizers on PPI for refractory GERD tend to have greater esophageal mucosa inflammation, reduced lower esophageal sphincter resting pressures and are more likely to require empiric esophageal dilatation.

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## Misa Tanaka

**Sleep disorders in primary systemic vasculitis**

Misa Tanaka, Osvaldo Espin Garcia, Kathy Speechley, Saverio Stranges, Lillian Barra

**Background/Objective**: Primary systemic vasculitis (PSV) consists of disorders characterized by inflammation and the destruction of blood vessels, leading to ischemic damage in multiple organ systems. Current treatments for vasculitis have significantly increased survival rates of PSV patients. For survivors, poor sleep quality is a critical issue for health-related quality of life (HRQoL). Sleep deprivation increases risk of chronic diseases, such as hypertension, cardiovascular disease and mental illness. However, there is a lack of information about sleep quality among PSV patients. The **Objective** of this study is to determine the prevalence of clinical sleep disorders among PSV patients. We will also explore factors associated with disordered sleep. **Methods**: We designed an online survey and recruitment materials with input from a patient-partner. Study subjects were recruited from the Vasculitis Patient-Powered Research Network, an international longitudinally survey-based study of PSV patients aged 18 years and older and their caregivers. Cross-sectional data was collected from Feb 1st to March 31st, 2023. **Results/Conclusions**: As of March 20th, 2023, there were 1,003 PSV participants enrolled and 938 who had completed the survey. Participants included: 439 with granulomatosis with polyangiitis (44%), 140 with eosinophilic granulomatosis with polyangiitis (14%), 100 with microscopic polyangiitis (10%), 117 with large vessel vasculitis (12%) and 207 (20%) with various other types of vasculitis. This is the largest study investigating quality of sleep in PSV. This presentation will present Results including the burden of sleep disorders in PSV, risk factors and consequences of poor sleep in this population.

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## Priya Thandrasisla

**Infective Endocarditis in Women Who Inject Drugs**

Priya Thandrasisla, Janica Adams, Cara Spence, Stuart Skinner, Esfandiar Shojaie, Michael Silverman

**Background**: In Canada, women make up 32.7% of people who inject drugs (PWID), but clinical characteristics and outcomes of intravenous drug use (IDU) complications in women are poorly described. We aimed to identify clinical characteristics and outcomes of infective endocarditis (IE) in women who inject drugs (WWID). **Methods**: We conducted a retrospective cohort study of males and females with IE admitted to one of five tertiary care hospitals in London, Ontario, and Regina, Saskatchewan, Canada between April 2007 and March 2018 (n=762). Sex differences in clinical characteristics of PWID were examined using Peason's chi-squared test and Wilcoxon rank sum test. Differences in one- and five-year mortality between male and female PWID were determined using multivariable Cox regression models.

**Results**: Women comprised 51.2% of PWID with IE (220/430) and 30.4% of non-PWID with IE (101/332). Female PWID with IE were younger than male PWID (P<.001), were more likely to have right-sided IE (P<.001), and 5.0% were pregnant on admission. Female PWID with IE living in urban areas had a significantly higher rate of five-year mortality than those in rural areas (P=.01). Addictions counselling was associated with lower mortality, and mortality was lower in a center with inpatient addiction counselling compared to one offering only post-discharge referrals. **Conclusions**: Despite making up a minority of PWID, women are overrepresented amongst cohorts of PWID with IE. The reasons for increased susceptibility to IE need further study. Inpatient addiction support services, reproductive counselling, and enhanced social support of WWID in urban areas must be prioritized.

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## Jaspreet Toor

**Association of Arthritis with Immune Responses in the Collagen-Induced Model of Rheumatoid Arthritis**

Jaspreet Toor, Shujun (Lucy) Dong, Sofya Ulanova, Garth Blackler, Ewa Cairns, Lillian Barra

**Background**: Over 1% of Canadians suffer from rheumatoid arthritis (RA), a systemic autoimmune disease characterized by painful joint swelling, inflammation, and damage. These symptoms result following a breakdown of immune tolerance against proteins containing two post-translational modifications, citrulline and homocitrulline. This dysfunction causes the production of RA-specific T and B cell responses, including autoantibodies known as anti-citrullinated protein antibodies (ACPA) and anti-homocitrullinated protein antibodies (AHCPA). There is no cure for RA, and RA-specific treatments are critically needed because current symptom management relies on systemic immunosuppression which is associated with significant side effects. **Problem**: New treatments for RA are typically tested in DBA/1J mice, using the collagen-induced arthritis (CIA) model. However, it remains unclear if CIA joint derangements are associated with RA-specific autoimmune responses in this strain. **Objective**: We investigated if joint swelling, inflammation, and damage are related to immune responses against citrulline and homocitrulline in DBA/1J CIA mice. **Method**: DBA/1J mice were either immunized with type II collagen (CII) or PBS, or remained as un-injected naïves, and were sacrificed 49 days later (N = 18). **Results**: Consistent with published literature, only CIA mice developed joint swelling, inflammation, and damage, as well as anti-CII antibodies. However, we detected ACPA reactivity and citrulline/homocitrulline T cell responses in CIA and negative controls. **Significance**: This finding demonstrates that RA-specific immune responses do not associate closely with joint symptoms in DBA/1J CIA mice, suggesting that this model may have limited value in preclinical trials of RA-specific therapeutics.

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## Matthew Turk

**Non-pharmacological interventions in the treatment of rheumatoid arthritis: a systematic review and meta-analysis**

Matthew Turk, Yideng Liu, Janet E. Pope

**Purpose**: To investigate the role of non-pharmaceutical therapies on disease activity in rheumatoid arthritis through systematic review and meta-analysis. **Methods**: A review of EMBASE and MEDLINE was performed from inception until Feb 23, 2019. Only randomized controlled trials which assessed oral, non-pharmacological interventions (e.g. diets, vitamins, oils,

herbal remedies, fatty acids, supplements, etc.) in adult patients with rheumatoid arthritis, that presented clinically-relevant outcomes (defined as pain, fatigue, disability, joint counts, and/or disease indices) were included in our meta-analysis. Data were analysed as mean differences between active and placebo and forest plots were performed. Heterogeneity was evaluated using I-squared statistics while funnel plots and Cochrane's risk of bias assessment evaluated bias. **Results**: 8170 articles were identified in the search and 51 were RCTs were included. The mean difference in DAS28 was significantly improved in experimental group treated with diet (-0.46 [-0.91 , -0.02], p=0.04), xx supplements (-0.77 [-1.17 , -0.38], p <0.001), xx vitamins (-0.52 [-0.74 , -0.29], p <0.001), and fatty acids (-0.19 [-0.36 , -0.01], p= 0.03). Other clinical metrics such as SJC, TJC, HAQ, SDAI, ACR20, and self-reported pain were decreased in the treatment groups. There was significant reporting bias in the studies. **Conclusion**: Some non-pharmacological therapies may modestly improve some clinical outcomes in patients with rheumatoid arthritis. Many identified studies lacked full reporting. Further clinical trials that are well-designed, adequately powered, and sufficiently report ACR improvement criteria or EULAR response criteria outcomes are needed to confirm the efficacy of these therapies.

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## Sofya Ulanova

**Investigating T Cells in a Mouse Model of Rheumatoid Arthritis**

Sofya Ulanova, Ewa Cairns, Lillian Barra

**Background**: Rheumatoid Arthritis (RA) is an incurable autoimmune disease affecting 1 in every 100 Canadians. Two main types of immune cells involved in RA progression are B and T cells. In RA, these cells respond to an amino acid called homocitrulline. Although B-cell activation to homocitrulline has been studied before, less is known about T cells. **Objective**: To study T cells responding to homocitrulline in a mouse model of RA. **Methods**: Male and female mice (n=4-6) were immunized with homocitrullinated peptides (HomoCitJED) or saline as a control. Draining lymph nodes and spleens were collected on days 10 and 100 post-immunization, and T-cell subtypes were investigated using flow cytometry. **Results**: On day 10, there were significantly higher proportions of pro-inflammatory T helper 1 (Th1) cells and activated T helper 17 (Th17) cells in HomoCitJED vs. PBS-immunized mice, mimicking what is seen in RA. By day 100, all HomoCitJED-immunized mice developed ankle swelling, indicative of arthritis. In these mice, we also observed a significant increase in activated T cells, mainly consisting of Th17 cells differentiated into Th1-like cells that are known to be involved in the pathogenesis of autoimmune diseases. Additionally, there was evidence of chronic antigen stimulation with a higher proportion of exhausted T cells that correlated strongly with ankle swelling. **Conclusion**: T cell responses to homocitrullinated antigens are pro-inflammatory and may contribute to chronic autoimmunity in RA. This research can identify new targets for RA medications to help patients live pain-free and high-quality lives.

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## Venkat Vaibhav

**The role of 5-lipoxygenase (5-LO) expressing cells in colitis-associated colorectal cancer**

Venkat Vaibhav, Samuel Asfaha

**Introduction**: Patients with prolonged ulcerative colitis (UC) exposure are 20% more likely to develop colorectal cancer (CRC). Tuft cells, a rare epithelial cell type within the intestinal crypt, may be the origin for colitis-associated cancer (CAC). To study this, I will be using a new

transgenic mouse model 5-LO-GFP-DTR-CreERT2, wherein tuft cells are marked by 5-lipoxygenase (5-LO) expression. Due to the abundance of genetic tools, this can be an effective mouse model for studying CAC. **Methods**: 1) Characterize the location of 5-LO+ cells within the intestinal epithelium and bone marrow. Immunofluorescent staining of the colon and bone marrow (BM) was conducted to quantify the number of GFP+ cells. 2) Determine whether 5-LO+ epithelial cells give rise to colitis-associated CRC. 5-LO-GFP-DTR-CreERT2 mice crossed to APC fl/fl mice were treated with three doses of 6mg tamoxifen, followed by five days of 2% DSS to induce colitis. 14 weeks following DSS treatment, the mice were sacrificed for histology, tumor number and size. **Results**: Immunofluorescent staining of the colon and BM shows frequent endogenous GFP fluorescence with 7 GFP+ cells per 100 crypts and 15% of total cells, respectively. For the tumor experiments, two tumors were generated (n=4) and verified through histology. The tumor-bearing mice will be analyzed further to optimize the protocol for tumor generation. **Discussion**: Characterizing the location and frequency of 5-LO+ cells in the colon and BM has established the foundation for future colitis and CAC experiments. Further experiments will be conducted to elucidate the mechanism of 5-LO-derived tumor formation.

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## Akshay Varghese

### Dunnigan Familial Partial Lipodystrophy Type 2 (FPLD2): A Longitudinal Case Series of the World's Index FPLD2 Family

Akshay Varghese, Robert Hegele

Dunnigan familial partial lipodystrophy type 2 (FPLD2; MIM 151660), first described in 1974, is the most common heritable lipodystrophy syndrome with a global prevalence of ~1 in 60,000. FPLD2 is a dominant condition characterized by redistribution of subcutaneous adipose stores with insulin resistance, hypertriglyceridemia and hepatic steatosis. We report 30-year follow-up of the world's index FPLD2 family. A 48-year-old woman and her 28- and 26-year-old daughters were first seen in 1991 for dyslipidemia and FPLD2 diagnosed clinically. From their DNA the causal gene was mapped, namely LMNA on chromosome 1q22 encoding nuclear lamin A/C, and the first pathogenic variant p. Arg482Gln was identified. The mother had been diagnosed retrospectively with FPLD2 at age 40. She had undertaken no specific preventive measures for most of her life. She had hepatosteatosis at 22, cirrhosis by 35, along with type 2 diabetes, a coronary artery bypass at 53, eventually dying from colon cancer at 65. The daughters, who share the LMNA genotype were diagnosed in their twenties. Each proactively undertook healthy diets and regular exercise. They had annual clinical and metabolic assessments. The older sister is currently 61 and only started rosuvastatin at 58; she takes no diabetic medications and her HbA1c is 5.6%. The younger sister is now 58 and only started taking metformin at age 54. Both sisters maintain excellent blood lipids, glucose and blood pressure with no liver function abnormalities. These observations suggest that in FPLD2, metabolic deterioration is mitigated with early diagnosis, lifestyle intervention and regular follow-up.

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Sudheer Vuyyuru

**Patients with Crohn's disease and permanent ileostomy are universally excluded from clinical trials: A systematic review**

Sudheer Vuyyuru, Florian Rieder, Virginia Solitano, Tran M. Nguyen, Eileen Crowley, Neeraj Narula, Siddharth Singh, Christopher, Vipul Jairath

**Background**: There is a paucity of research in patients with Crohn's disease (CD) and permanent ileostomy (PI). We performed this study to investigate whether patients with CD and PI were eligible to participate in clinical trials. **Methods**: MEDLINE, Embase, and the Cochrane library (CENTRAL) databases were searched from inception to April 2022 for randomized, placebo-controlled induction and maintenance trials of biologics and small molecules in adult patients with active CD. The primary outcome was a proportion of trials that included patients with CD and PI. **Results**: Eighty-one studies (induction:58 and maintenance:23) which enrolled 22000 participants were included (Table 1). The majority were phase 2 trials (n=41, 50.6%), 86.4% (n=70) evaluated efficacy and safety of biologics and the remaining studies (n=11, 13.6%) evaluated oral small molecules. Amongst the induction trials, 39 (67.2%) specifically stated that they excluded patients with an ostomy and the remaining studies (n=19, 32.8%) did not comment. For maintenance trials, 16 (69.6%) stated that they excluded patients with an ostomy and the remaining seven (30.4%) studies did not comment. Twenty-one induction studies and thirteen maintenance studies reported the proportion of patients with prior intestinal resection which ranged from 2.4% to 51%. No clinical trial included patients with a PI. **Conclusion**: Patients with CD and PI have been excluded from pharmaceutical trials of biologics and small molecules to date. There is an urgent need to identify barriers to enrolment and develop eligibility and outcome measures that enable inclusion of these patients into clinical trials.

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Sudheer Vuyyuru

**Comparative Efficacy of Advanced Therapies for Achieving Endoscopic Outcomes in Crohn's Disease: A Systematic Review and Network Meta-Analysis**

Sudheer Vuyyuru, Tran M. Nguyen, Mohammad Hassan Murad, Neeraj Narula, Talat Bessissow, Guangyong Zou, Jeffrey D McCurdy, Laurent Peyrin-Biroulet, Silvio Danese, Christopher Ma, Siddharth Singh, Vipul Jairath

**Background**: We conducted a network meta-analysis to compare the efficacy of advanced therapies for achieving endoscopic outcomes in patients with moderate to severe CD. **Methods**: MEDLINE, Embase, and Cochrane CENTRAL databases were searched from inception to May 16, 2022, to include phase II and III randomized controlled trials (RCTs) in adults with CD treated with advanced therapies. Primary outcome was endoscopic response after induction therapy, and endoscopic remission after maintenance therapy. Random-effects network meta-analysis using a frequentist approach was performed, with estimated relative risk (RRs), 95% CI values and p-score for ranking agents. We used GRADE to ascertain certainty of evidence. **Results**: Twenty RCTs were included. On network meta-analysis JAK1 inhibitors (RR 3·49[1·48-8·26]) and anti-IL23p19 (RR 2·30[1·02-5·18]) agents were more efficacious than anti-integrin agents (moderate certainty of evidence), and JAK1 inhibitors (RR 2·34[1·14-4·80]) were more efficacious than anti-IL12/23p40 agents for inducing endoscopic response (moderate certainty of evidence). JAK1 inhibitors and anti-IL-23p19 ranked highest for induction of endoscopic response. For maintenance of endoscopic remission, all drug classes were superior to placebo. On comparative efficacy, TNF antagonists (RR 4·63[1·01-21·27]) and JAK1 inhibitors (RR 2·51[1·02-6·15]) were

more efficacious than anti-integrins for maintaining endoscopic remission (moderate certainty of evidence). **Interpretation**: In network meta-analysis, JAK1 inhibitors and anti-IL23p19 agents may be most effective amongst advanced therapies for inducing endoscopic response. Future head-to-head trials will further inform positioning of different therapies for the management of CD.

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## Sudheer Vuyyuru

**Long washout periods between biologics mandated by regulators for inflammatory bowel disease clinical trials are unnecessary**

Sudheer Vuyyuru, Meagan Archer, Tran M. Nguyen, Melanie Beaton, Vipul Jairath

**Background**: Regulatory authorities mandate prolonged washout period between biologics in patients with inflammatory bowel disease (IBD) which is not an evidence-based recommendation. We performed this study to assess safety of early biologic switch compared to late switch in patients with IBD. **Methods**: In this retrospective study, we compared patients with IBD who underwent early switch (≤30 days) compared to late switch (>30 days) in a tertiary center between Jan 2014 and July 2022. The primary outcome was difference in rate of any infection at 6 months following the switch. **Results**: A total of 128 switches took place in 94 patients (ulcerative colitis = 31; Crohn's disease = 63), of which 51 were early biologic switches and 77 were late switches. There were no significant differences between the two groups in baseline characteristics. The median time to switch in the early switch group was 20 days (IQR: 13-22) compared to 42 days (range: 35-66) in the late switch group. The proportion of patients with infectious complications in first 6 months following switch in the early switch group was 6.8%, compared to 8.9% in the late switch group (P = 1.00). Furthermore, there was no observed difference in the rates of short or long-term non-infectious adverse events. On univariable analysis, there was no single factor associated with development of infections at 6 months after switch. **Conclusion**: Our Results indicate that early switch between biologics is safe irrespective of the type of switch. Therefore, a prolonged washout period between two biologics is unnecessary.

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## Kathleen Winger

**A scoping review on electronic health records ability to help or hinder inter-professional or intra-professional collaboration in the workplace.**

Kathleen Winger, Chelsea Norris, Karina Marie Kaberi, Kristen A. Bishop, Erin Spicer, Mark Goldszmidt

**Introduction**: Communication and collaboration are essential to creating better care for patients in-hospital. With the rise of Electronic Health Records (EHRs), there has been debate as to whether the incorporation of health care technology has enhanced or hindered workflow dynamics within an inpatient setting. **Methods**: Arksey and O'Malley's (2005) five-stage framework was used to synthesize the current knowledge base related to how EHRs support or constrain inter-professional and intra-professional collaboration in the inpatient setting. Of the 4314 articles retrieved from searching five databases and through citation tracking, 32 articles met the inclusion criteria and were included. **Results**: Of the 32 articles identified most involved surveys, questionnaires, or interviews. These were completed by health care professionals (HCPs) including nurses, physicians, and pharmacists, and focused on assessing attitudes towards EHRs. One study used observational Methods to explore how EHRs functioned in the real world. Few articles focused on specific features geared to improving issues like cognitive burden EHRs

created for HCPs through lab alert systems, templates to auto-regulate instructions and electronic white boards to provide over-arching information on patient's hospitalization. Across the 32 articles, there was no clear conversation such that findings of one study were building on findings from the others. **Conclusion**: EHRs improved clinical documentation availability, but this inconsistently translated to improved collaboration. Moreover, EHRs routinely caused fragmentation of patient data forcing HCPs to spend more time documenting, finding, and interpreting, which in turn decreased face-to-face communication. Certain features were found to overcome some of these barriers.

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## Ha Ryun Yang

**Anemia associated with Decreased Plasma Zinc Levels is Likely Secondary to Acute Inflammation**

Ha Ryun Yang, Matthew Nichols, Cyrus Hsia, Vipin Bhayana, Benjamin Chin-Yee, Ian Chin-Yee

**Introduction**: Zinc (Zn) is an important trace metal for hematopoiesis, and deficiencies in Zn can result in anemia. Many conditions can disrupt metal concentrations in the body, such as impaired absorption. Plasma Zn is also a negative acute-phase reactant, decreasing with systemic inflammation. We aimed to determine the effects of Zn deficiency on hematopoiesis and define risk factors for deficiencies. **Methods**: We performed a retrospective cohort study on 606 patients (age>18 years), 303 each from Zn deficient (<9.4 umol/L) and Zn normal groups. We recorded plasma zinc, hemoglobin, malabsorptive pathologies (celiac disease, Crohn's disease, pancreatic insufficiency, short gut, and gastric bypass), PPI usage, serum albumin, and serum c-reactive protein (CRP). Mean hemoglobin levels (single-sided t-tests) and mean measurements of risk factors between zinc deficient and zinc normal patients (double-sided t-tests) were compared. We also examined the relationship between Zn plasma concentration across risk factors. **Results**: A deficiency in plasma Zn is associated with significantly lower hemoglobin concentrations ($p < 0.001$), lower albumin ($p < 0.001$) and higher CRP ($p < 0.001$). No significant relationships were identified with malabsorption or PPIs ($p > 0.05$).
**Significance**: Decreased plasma Zn is associated with systemic inflammation through low albumin and high CRP in keeping with Zn as a negative acute-phase reactant. Although patients with low plasma Zn had lower hemoglobin, the lack of correlation suggests that Zn deficiency was not a cause, rather reflected a common factor: inflammation. In evaluating patients with anemia, plasma Zn should be interpreted cautiously with signs of inflammation.

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## Samuel-Caleb Yeung

**Impact of age on microvascular endothelial cell barrier function in sepsis and acute respiratory distress syndrome**

Samuel-Caleb Yeung, Aminmohamed Manji, Cynthia Pape, Lefeng Wang, Sanjay Mehta

Sepsis, defined as organ dysfunction due to a dysregulated host response to infection, often affects the lungs and leads to acute respiratory distress syndrome (ARDS). Sepsis is the most common cause of mortality in intensive care units (ICUs) and disproportionately affects elderly individuals that have worsened outcomes compared to younger patients. During sepsis, injury of pulmonary microvascular endothelial cells (PMVEC) occurs, leading to barrier dysfunction and the accumulation of protein-rich edema fluid within the lung. Pilot studies involving single-cell RNA sequencing and proteomic analysis of isolated PMVEC suggest that increased apoptosis may be

a mechanism for enhanced septic dysfunction of “aged” PMVEC. Thus, we hypothesize that aging exacerbates septic pulmonary microvascular endothelial dysfunction due to increased PMVEC death. To address this hypothesis, we will utilize an in vitro model of sepsis in which PMVEC isolated from young (3-month-old) and aged (22-months-old) mice will be stimulated with cytomix, which is an equimolar combination of cytokines known to be relevant in sepsis - tumor necrosis factor-α, interleukin-1β, and interferon-γ. PMVEC apoptosis will then be quantified by AnnexinV+/FLICA+/TUNEL+ staining. Additionally, the time course and extent of PMVEC apoptosis will be correlated with barrier dysfunction by monitoring PMVEC monolayer electrical resistance in real time using the ECIS system. This study will provide some of the first evidence of age-dependent differences in septic PMVEC dysfunction and also address the potential mechanistic role of augmented PMVEC apoptosis, thereby providing the foundation for future therapeutic studies.

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## Carly Yim

**A Presentation of Diabetic Ketoacidosis in Gestational Diabetes**

Carly Yim, Selina Laura Liu, Tamara Spaic

Diabetic ketoacidosis (DKA) is a diabetic emergency characterized by wide anion gap acidosis, presence of serum and/or urine ketones and, frequently, uncontrolled hyperglycemia. In pregnancy, DKA more commonly occurs in women with pre-existing diabetes, usually type 1 diabetes, and is exceptionally rare in women with gestational diabetes mellitus (GDM). We report a case of a 37-year-old woman in her second pregnancy presenting in DKA at 29+3 weeks gestation shortly after diagnosis of GDM 4 days earlier with 75 gram oral glucose tolerance test (OGTT). She presented to hospital at 29+3 weeks gestation with a 2-day history of polyuria, polydipsia, dizziness, and decreased oral intake without nausea or vomiting. Her admission labwork was consistent with DKA. She was treated with IV fluids and insulin and initiated on multiple daily injections of insulin. Other than pregnancy, no clear precipitating factor was found. Her serum insulin and C-peptide levels were inappropriately low, anti-glutamic acid decarboxylase and anti-islet cell antibodies were negative. Abdominal ultrasound did not suggest any findings of acute pancreatitis. Workup for Cushing's syndrome was negative. Following discharge, she remained significantly insulin resistant with suboptimal glycemic control. Due to increased insulin resistance in pregnancy, DKA can progress more rapidly compared to nonpregnancy. Given increased rates of perinatal morbidity and mortality associated with DKA, treatment and monitoring should be promptly initiated. A high index of suspicion is especially important given that DKA is a rare presentation in GDM. Other precipitating factors of newly decompensated diabetes should also be ruled out.

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## Zina Zein Abdin

**Modeling the Effects of $\Delta^8$-THC on Endothelial Cells using Human Induced Pluripotent Stem Cells**

Zina Zein Abdin, Kerry-Ann Nakrieko, Michelle Si, Md Abrar Kashfi Jahin, Aleksandra Leligdowicz, Grace Parraga, Geoffrey Pickering, Mark Chandy

Cannabis is the most used recreational drug. Clinical studies have found that daily cannabis use is associated with a 33% increased risk of developing coronary artery disease. Δ8-tetrahydrocannabinol (Δ8-THC) is an unregulated psychoactive cannabinoid whose popularity

increased by 257% from 2019 to 2020. It is an isomer of Δ9-THC, the most abundant psychoactive component of cannabis that causes endothelial dysfunction via the cannabinoid receptor 1 (CB1). Endothelial dysfunction is implicated in the pathogenesis of atherosclerosis and is characterized by inflammation and oxidative stress resulting in reduced bioavailability of nitric oxide (NO) and increased permeability. Given the increase in popularity of Δ8-THC, it is necessary to investigate its potential cardiovascular effects. To address this, primary endothelial cells (ECs) and human-induced pluripotent stem cell-derived ECs (hi-PSC-ECs) were used. hi-PSC-ECs provide an unlimited supply of ECs and are free from environmental exposures that could confound the Results, making them an ideal model for studying toxicity. We hypothesize that Δ8-THC will induce endothelial dysfunction. First, iPSC-ECs were treated with increasing concentrations of Δ8-THC and Δ9-THC, and cell viability was measured. Preliminary data demonstrated that Δ8-THC is cytotoxic at physiologic concentrations. Next, iPSC-ECs will be treated with Δ8-THC, inflammation, and oxidative stress will be quantified using qPCR, NO bioavailability will be measured, and EC function will be interrogated using Electric Cell-substrate Impedance Sensing (ECIS). The long-term effects of Δ8-THC use may not be apparent for several decades. Therefore, the proposed study will help provide information about the safety of this newly popular cannabinoid.

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## Zhubo Zhang

**Prevalence and treatment of iron deficiency in end-stage renal disease at London Health Sciences Centre**

Zhubo Zhang, Joey Liu, Mohammad Faraz, Dilraj Sanghera, Omar Assiri, Abdulaziz Bari, Michael Chiu

**Background**: Iron deficiency is common in patients with end-stage renal disease (ESRD). Despite multiple guidelines since 2008 addressing the treatment of iron deficiency in these patients, no standardized protocol exists across LHSC. **Methods**: As part of a quality improvement initiative , we first collected baseline laboratory data between July and December 2022 to identify the prevalence of iron deficiency. Then, we administered an online survey to nephrologists and nephrology nurse practitioners at LHSC between January and February 2023. The survey explored iron deficiency treatment approaches, reasons for holding iron supplementation, and perceived barriers to standardization. **Results**: From the baseline data collection, 195 out of 470 (41%) patients were iron deficient based on Kidney Disease Improving Global Outcomes criteria and 48 (10%) had anemia, defined as a hemoglobin less than 95 g/L. 23 out of 26 practitioners (88%) responded to the survey. All support developing a standardized local protocol for treatment of iron deficiency. 20 respondents (87%) currently have their own approaches to treatment, although their approaches varied between three major strategies. The most common reasons for delaying iron supplementation include active infection, patient hesitancy or refusal, and risk of iron overload. The most common reported barrier to standardization was the lack of consistency between guidelines. **Conclusion**: Iron deficiency is present in a significant amount of ESRD patients at LHSC and there exists substantial practice variability with regards to its treatment. This study provides a starting point for further studies to clarify and eliminate barriers to a standardized protocol across LHSC.

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## Pei Jun Zhao

**The Impact of Low-Density Lipoprotein Equation Changes on Cholesterol Treatment in Canada**

Pei Jun Zhao, Robert Hegele

**Background**: In cardiovascular disease prevention, low-density lipoprotein cholesterol (LDL-C) values guide treatment for lowering cholesterol level. After 50 years of clinical laboratories using the Friedewald LDL-C equation, the Canadian Society of Clinical Chemists recently recommended adoption of the new and more accurate Sampson / U.S. National Institutes of Health (NIH) LDL-C equation. Here, we estimate the anticipated population-level impact of this equation change. **Methods**: We compared lipid profiles from the Canadian Health Measures Survey (CHMS) year 2019 to those from the National Health and Nutrition Examination Survey (NHANES) years 2017 to 2020. Then, based on 10,828 participants in the latter, we calculated the impact of changing the LDL-C equation from the Friedewald to the Sampson. **Results**: Sampson- and Friedewald-equation LDL-C values are strongly correlated ($r = 0.99$, $P < 0.001$), but differences between them increase with both higher triglyceride and lower LDL-C values. We evaluated the impact of these discordances using LDL-C treatment thresholds from the 2021 Canadian Cardiovascular Society lipid guidelines. Among patients who take cholesterol-lowering medications, the Sampson equation reclassifies 3.3% more patients (95% confidence interval 2.2% to 4.9%), or about 123,000 individuals, as meeting the criteria for treatment intensification. **Conclusion**: Although changing the LDL-C equation used from the Friedewald to the Sampson affects only a small proportion of the population, an estimated 123,000 Canadians who are taking cholesterol-lowering medications may need to intensify treatment to lower their cholesterol level, due to small absolute changes around guideline threshold values of LDL-C.https://pubmed.ncbi.nlm.nih.gov/36700190/

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Scan the QR code to complete the **Participant Evaluation** form online.

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