UNIVERSITY OF ALBERTA

DEPARTMENT OF MEDICINE
FACULTY OF MEDICINE & DENTISTRY

ME2 MAJUMDAR RESEARCH & QUALITY IMPROVEMENT DAY

& QI DAY

MAY 14, 2026. 08:00 AM

Scientific Research Abstracts

Integrative imaging and transcriptomics implicate neutrophils in microvascular no-reflow after stroke

Sima Abbasi-Habashi, Mike Clarke, Yonglie Ma, Maria Guadalupe C. Real, Gabrielle M. Siegers, Glen C Jickling, Ian R Winship1
Supervisor: Dr. Glen Jickling

INTRODUCTION

Microvascular no-reflow persists in a substantial proportion of ischemic stroke patients despite successful large-vessel recanalization and is associated with poor neurological outcomes. Increasing evidence suggests that neutrophil-driven inflammation contributes to post-stroke microvascular obstruction, yet the molecular mechanisms linking immune activation to vascular dysfunction remain poorly defined. To address this gap, we investigated immune–vascular interactions after stroke using integrated vascular imaging, transcriptomics, and translational genomic analyses.

METHODS

Transient middle cerebral artery occlusion (MCAO) was induced in mice to model ischemic stroke. Cerebral perfusion and microvascular function were assessed longitudinally using laser speckle contrast imaging and two-photon microscopy at baseline, early reperfusion, and 24 hours. Neutrophil depletion experiments were performed to determine the contribution of neutrophils to vascular dysfunction. Bulk RNA sequencing was used to characterize transcriptional responses to stroke and neutrophil modulation, followed by differential expression and pathway analyses to identify immune and signaling pathways associated with microvascular impairment. Translational relevance was further explored through analysis of single nucleotide polymorphisms (SNPs) in human stroke cohorts.

RESULTS

Stroke produced marked reductions in cortical perfusion and microvascular flow following reperfusion. Neutrophil depletion significantly preserved cortical perfusion, reducing the ischemia-induced perfusion decline from approximately 60% in untreated animals to about 30%, and nearly doubling early microvascular blood flow (red blood cell flux ~72% vs ~33%). Intravital imaging revealed neutrophil-mediated capillary obstruction and capillary stalls that directly impaired microvascular perfusion. Transcriptomic analyses demonstrated suppression of inflammatory mediators including Il1b, Mmp8, Lcn2, Tlr2, Cd14, and Cxcl2, together with preservation of regulatory pathways involving Mef2c and modulation of signaling networks including phosphodiesterase (PDE)-related pathways.

CONCLUSIONS

These findings identify neutrophil-mediated immune signaling as a key driver of microvascular no-reflow after stroke. By integrating vascular imaging, transcriptomics, and human genomic analyses, this study provides a translational framework linking experimental mechanisms with genetic variation in patients, highlighting immune–vascular pathways as potential therapeutic targets and biomarkers for improving reperfusion therapies and stroke outcomes.

Disparities in Ferritin Testing and Identification of Iron Deficiency Anemia Among Reproductive-Age Women with Venous Thromboembolism: A Retrospective Population-based Matched Cohort Study

Nazanin Abolghasemi Taree1, Linda Sun2, Cynthia Wu2
Supervisor: Linda Sun & Cynthia Wu

INTRODUCTION
Background: Iron deficiency anemia (IDA) is associated with venous thromboembolism (VTE) risk and anticoagulant complication. However, patterns of IDA screening and correction following VTE diagnosis remain poorly characterized. Aims: To determine the rate of ferritin and hemoglobin testing and prevalence of IDA in reproductive-age women with and without VTE.

METHODS
Methods: Population-based retrospective cohort study using linked administrative data. We included all reproductive-age women (aged 19-49 years) diagnosed with VTE (2012-2022), using validated diagnostic algorithms based on ICD diagnostic and imaging codes. Cases were matched in 1:3 ratio with population controls by age, socioeconomic quintiles, pregnancy and the Charlson comorbidity index. The index date was the VTE diagnosis for cases and the matching date for controls. We analyzed testing rates and IDA prevalence in several periods: the acute VTE window (-7 to +7 days), pre-VTE periods (7 days-12 months, 12-24 months, 24-36 months prior), and post-VTE periods (+7 days-12 months, 12-24 months, 24-36 months after index). IDA was defined as hemoglobin <120 g/L (or <110 g/L if pregnant) and ferritin <30 µg/L (<70 µg/L if CRP >10 mg/L), with all performed within the same analysis period. Differences between cases and controls were assessed using Chi-squared test. Changes over time were assessed using the Mann-Kendall trend test.

RESULTS
Results: We included 2,887 cases and 8,661 controls (Table 1). Baseline anemia and IDA were prevalent in 8.9% and 3.6% of women within 12 months prior to VTE, respectively. IDA prevalence was significantly higher in cases than controls at 12-months prior (OR 2.77, 95% CI 2.11-3.63) and within 12-months post-index (OR 4.41, 95% CI 3.26-5.98). This gap persisted until 24-36 months post-index (Figure 1). Hemoglobin testing rates were low during acute VTE (27.4%) and within 12 months after (27.7%). Ferritin testing occurred in only 12.3% during acute VTE and 49.4% within 12 months. Testing rates declined significantly over time for both groups.

CONCLUSIONS
Conclusion: Women with VTE experience suboptimal hemoglobin and ferritin testing despite higher IDA prevalence at diagnosis compared to matched controls. Alarmingly, a meaningful reduction in IDA prevalence took 12-24 months following acute VTE. This temporal decline suggests heightened clinical management, anticoagulant discontinuation/modification, or a spurious finding (e.g. reduced surveillance rates, death as competing risk).

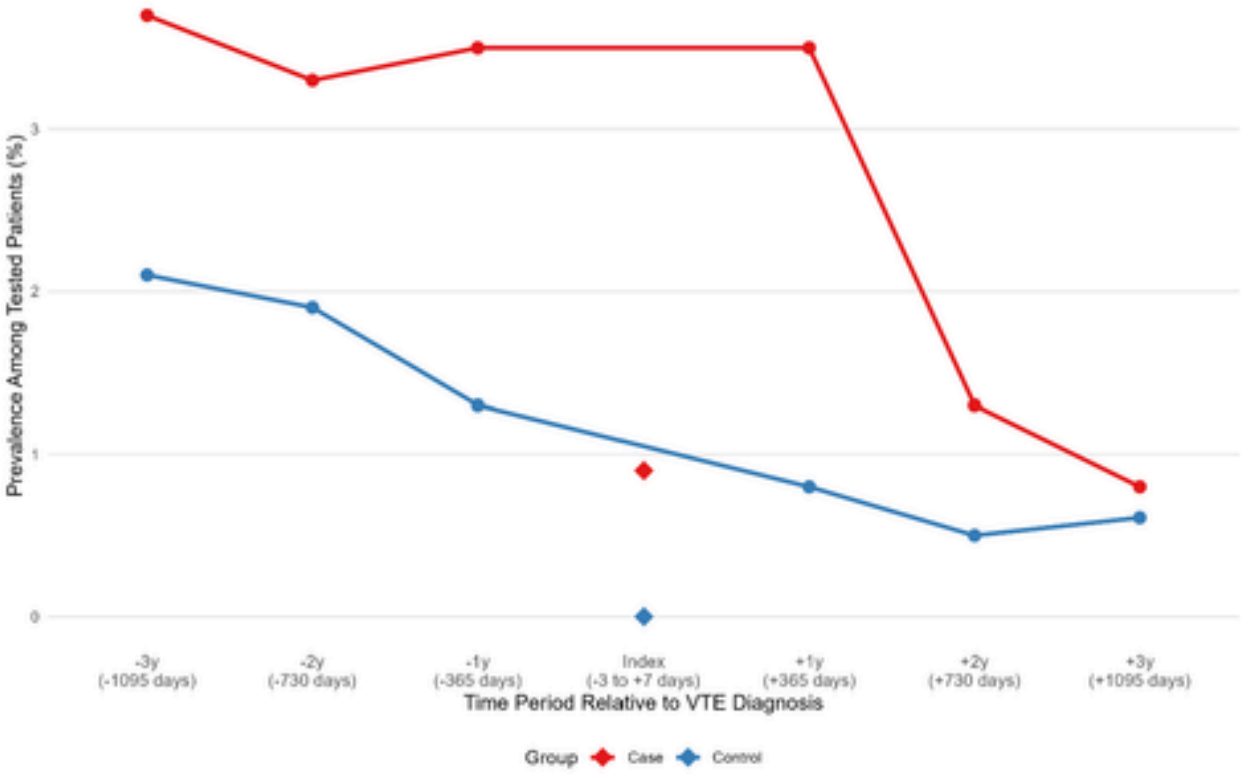


Figure 1: Prevalence of Iron Deficiency Anemia in Cases and Matched Controls Before and After Index Date Among Reproductive-Age Women

Chronic Rhinosinusitis - How are Alarmin Cytokines Involved?

Sarah Almas, Hazel Marriott, David Cote, Paige Lacy
Supervisor: Paige Lacy

INTRODUCTION

Airway epithelial cells play an integral role in host defence, immune reactions, and modulating chronic diseases. These cells initiate signalling pathways that result in the production of alarmin cytokines (thymic stromal lymphopoietin (TSLP), interleukin (IL)-25, and IL-33) during the natural host response. Continuous stimulation of these pathways may result in chronic inflammation and epithelial dysfunction, underlying the pathogenesis of diseases such as chronic rhinosinusitis (CRS). However, the expression of these cytokines from different regions of the nasal cavity in patients remains yet to be elucidated.

Here, we aim to compare alarmin cytokine production from paranasal sinuses in patients with CRS compared to healthy controls. We hypothesize that nasal epithelial samples from CRS patients express elevated alarmin cytokines from all cavities.

METHODS

Patients with CRS (n=18) and controls (n=12) were recruited during initial consultation at a tertiary rhinology practice and completed a pre-operative questionnaire grading their symptom severity. Paranasal sinus specimens were obtained during functional endoscopic sinus surgery for patients with CRS. For control patients, brushings of accessible sinus cavities were obtained during septoplasty, rhinoplasty, or endoscopic sinonasal mass removal surgeries. Cytokine expression was identified via flow cytometry.

RESULTS

Epithelial cell brushings from the paranasal sinuses revealed high levels of expression of IL-25, IL-33, and TSLP in patients with symptomatic CRS. TSLP was consistently elevated in the maxillary posterior sinuses of patients with CRS compared with controls (unadjusted $p = 0.009$ for TSLP, $p = 0.34$ for IL-25, and $p = 0.52$ for IL-33). We also observed differential alarmin cytokine expression from distinct regions of sinus cavities.

CONCLUSIONS

Identifying distinct profiles of key alarmin cytokines driving symptomatology in CRS highlights targets for pharmaceutical interventions that aim to manipulate innate immune mechanisms. Understanding the differential cytokine release from paranasal sinus cavities can guide both surgical and medical management of patients with CRS.

Forecasting long-range blood glucose in hospitalised type 2 diabetes patients: a comparative study of predictive modelling techniques

Leen Alzebdeh, Anna Lam, Jianfei Zhang, Russ Greiner
Supervisor: Dr. Anna Lam

INTRODUCTION

In-hospital hyperglycemia is associated with longer stays and higher complications, but insulin therapy to control it risks life-threatening hypoglycemia. Specialized diabetes teams improve outcomes yet lack capacity, especially in community and remote hospitals. Machine learning (ML)-based insulin decision support has shown promise, but existing models are not optimized for electronic health records (EHR). Our model enhances in-hospital diabetes management by predicting blood glucose (BG) at routine measurement times, enabling proactive therapy adjustments.

METHODS

We used retrospective EHRs from 1,279 type 2 diabetes patients admitted for cardiovascular surgery to the Mazankowski Heart Institute (2019–2024). We developed ML models to forecast BG before three daily meals and bedtime using BG, demographic, and visit information. The dataset comprised irregularly sampled time series—a major challenge for long-range forecasting. We propose a modelling approach that effectively processes EHR to provide accurate BG forecasts for clinical decision support.
Evaluated models included regression, tree-based, and deep learning methods. Performance was assessed using mean absolute error (MAE), root mean square error (RMSE), mean absolute percentage error (MAPE), and Clarke Error Grid Analysis (CEGA).

RESULTS

Our best model, XGBoost, achieved an average MAE of 1.49 mmol/L (26.8 mg/dL), outperforming a naïve forward-fill baseline by 33%. CEGA showed 97.8% of predictions fell within clinically acceptable zones (A and B) (Table 1). Averaged errors per encounter reached a MAE of 1.33 mmol/L and 98.5% fell within clinically acceptable zones.

CONCLUSIONS

Routinely collected EHR data alone can power accurate, clinically safe blood glucose forecasts. XGBoost achieved near-optimal clinical accuracy (97.8% in zones A/B), demonstrating that ML-driven prediction is ready to enable proactive, individualized inpatient diabetes care. Critically, this approach integrates directly into existing EHR workflows for real-time forecasting or pairs with an insulin recommender—closing the loop from prediction to action.

Table 1 Model errors across all evaluated ML models, all errors are validation and in mmol/L unless otherwise specified. Reported as metric ± SD.

Metric	Baseline	XGB	SGD	REGR	TFT	TCN	Ensemble
Train MAE	2.23 ± 0.03	1.10 ± 0.02	1.66 ± 0.02	1.86 ± 0.02	3.09 ± 0.04	1.31 ± 0.04	1.00 ± 0.02
MAE	2.23 ± 0.10	1.49 ± 0.06	1.69 ± 0.08	1.87 ± 0.06	1.56 ± 0.08	1.79 ± 0.08	1.52 ± 0.06
gMAE	4.47 ± 0.37	1.98 ± 0.15	2.46 ± 0.22	2.92 ± 0.17	2.12 ± 0.22	2.83 ± 0.24	2.06 ± 0.19
RMSE	3.14 ± 0.15	2.51 ± 0.21	2.32 ± 0.12	2.49 ± 0.10	2.21 ± 0.12	3.90 ± 0.47	2.15 ± 0.10
gRMSE	5.33 ± 0.35	2.99 ± 0.19	3.37 ± 0.25	3.57 ± 0.19	3.20 ± 0.26	3.90 ± 0.47	3.10 ± 0.22
MAPE (%)	25.8 ± 1.0	17.4 ± 0.5	19.7 ± 0.5	23.2 ± 0.6	17.6 ± 0.6	21.0 ± 1.0	17.5 ± 0.5
gMAPE (%)	52.8 ± 4.1	25.5 ± 1.6	30.6 ± 1.7	40.0 ± 2.2	25.3 ± 1.9	35.6 ± 3.3	25.9 ± 1.9
CE (%)	93.3 ± 0.7	97.8 ± 0.3	97.1 ± 0.5	97.3 ± 0.4	97.4 ± 0.4	96.6 ± 0.6	97.6 ± 0.4

VALIDATION OF THE SAURIN CLASSIFICATION IN A NORTH AMERICAN PATIENT COHORT UNDERGOING VIDEO CAPSULE AND ENTEROSCOPY FOR OBSCURE BLEEDING

Naik Arbabzada, Jeff Reeve, Shawn Wasilenko, Kunihiko Oguro, Sergio Zepeda Gomez, Brendan Halloran
Supervisor: Dr. Brendan Halloran

INTRODUCTION

The evaluation of patients with obscure gastrointestinal bleeding (OGIB) frequently involves video capsule endoscopy (VCE) and/or CT enterography (CTE) followed by enteroscopy (including balloon assisted enteroscopy (BAE) and push enteroscopy) for lesion characterization and therapeutic intervention, yet standardized reporting systems are seldom used. The validated Saurin scoring system is used to characterize lesions seen on VCE based on their bleeding potential – P0-P3 with clinically significant lesions scoring P2 or higher. To our knowledge, there is no published literature in its application to North American patient cohorts.

Aim: We aim to assess and validate the Saurin classification in a cohort of patients who have undergone both VCE and BAE. Our objectives are to evaluate the concordance between VCE and enteroscopy for clinically significant lesions (P2 or higher) based on Saurin scoring.

METHODS

We performed a retrospective review at a quaternary centre (University of Alberta Hospital) which included adult patients with OGIB who underwent VCE followed by enteroscopy (push or BAE) from January 2010 to May 2024. All procedures were reviewed, and a Saurin score was assigned to both VCE and enteroscopy reports.

RESULTS

A total of 119 patients underwent a VCE followed by enteroscopy with a median age of 65 (range 20-92) and a male predominance (n=71, 60%) totaling 140 pairings. There were 24 P1, 89 P2 and 25 P3 lesions on VCE accounting for a diagnostic yield of 98.5% (n=138/140) with 76.3% (n=87/114) accuracy in predicting clinically significant lesions confirmed by enteroscopy ($p<6.2x10-7$; OR 10.5) with a false negative rate of 6.5%. The most common diagnosis was vascular lesions (n=85, 61%). In 18 P2 vascular lesions on VCE (12.9%), the subsequent enteroscopy was unremarkable (7 normal studies and 11 P1 lesions). The pooled diagnostic yield of enteroscopy was 87.1% (n=122/140) and its therapeutic yield was 55% (n=78/140). Within the therapeutic subgroup, the yield was considerably higher for P2 and P3 classified lesions compared to those classified as P1 or lower (81% vs 4%, $p<2.2x10-16$).

CONCLUSIONS

The Saurin scoring system is a tool which works well when applied to this North American cohort of patients. If enteroscopy had been performed only in patients with high-risk VCE findings (P2 and P3), we would have spared 26 patients (21.8%) from an invasive procedure while missing only six cases with significant lesions.

Validated scoring should become a standardized part of small bowel endoscopy reporting to help improve patient outcomes and resource utilization. Prospective studies are required for further validation.

Limited nesting stress in mice as a model to study neuroimmune relationships in postpartum depression.

Marie Armbruster, Ritu Mann-Nüttel, Shivani Mandal, Karen-Anne McVey Neufeld, Paul Forsythe
Supervisor: Dr. Paul Forsythe

INTRODUCTION
Postpartum depression (PPD) is a mood disorder that affects the ability of mothers to engage with and care for their infants. Stress exposure is known to be a major predisposing factor for PPD, while immune factors, particularly the balance between pro-inflammatory and immunoregulatory cells, are also hypothesized to influence development of the disorder. Here we assessed limited nesting (LN) in mice, with or without depletion of T regulatory cells (Tregs), as a potential model to investigate the relationship between stress and the immune system in PPD.

METHODS
Dams and their pups were provided standard nesting or LN, with or without anti-CD25 treatment to deplete Tregs. Maternal behaviour and pup-directed interactions were evaluated together with assessment of gene expression changes in selected brain regions and the peripheral lymphocyte profile.

RESULTS
LN exposure led to a significant increase in aggressive behaviour towards the pups and altered grooming in the splash test. These effects on behaviour were associated with brain region specific changes in expression of several genes related to depression and maternal behaviour and with increased levels of Tregs in the periphery. When LN was combined with anti-CD25 antibody treatment there were further deficits in nursing behaviour and changes in the brain circuitry related to lactation and stress. Moreover, we found that levels of pro-inflammatory Th17 cells were positively correlated with maternal aggressivity, independent of the anti-CD25 treatment.

CONCLUSIONS
Our study indicates that LN in mice may be a useful model for studying neuroimmune relationships in certain aspects of PPD. Our findings with this model suggest that post-partum regulatory immune changes may mitigate effects of stress on brain circuitry associated with maternal behaviour, lactation and stress. Conversely, pro-inflammatory Th17 cells may contribute to the aggressivity observed in LN exposed mothers and should be investigated further for their role in stress induced negative maternal behaviour.

Understanding the beliefs, management practices, and barriers associated with the management of non-fistulous urinary incontinence among older women in rural Ghana: results from a feasibility study

Prosper Asaana, Saima Rajabali, Gifty Aninanya, Hawa Malechi, Najawa Mutawakil, Patricia Akweongo, Adrian Wagg
Supervisor: Dr. Adrain Wagg

INTRODUCTION
Urinary incontinence (UI) is a prevalent, highly stigmatized yet underreported global health issue that disproportionately affects women. Despite UI's global impact, UI research in African countries remains underprioritized. This study sought to understand UI in rural Ghana in order to lay the foundation for co-creating a culturally appropriate UI management program.

METHODS
This qualitative, exploratory study employed a community-based participatory research (CBPR) approach, partnering with Ghanaian partners and rural Ghanaian women to generate experiential knowledge on non-fistulous UI. Participants aged 50 or older provided written informed consent before participating in digitally recorded, semi-structured, in-depth interviews (IDIs) or Focus Group Discussions (FGDs). IDIs and FGDs were conducted in Dagbani, transcribed verbatim, translated into English and subsequently de-identified for conventional content analysis.

RESULTS
Data saturation was attained after 16 IDIs and 7 FGDs. Data analysis yielded 164 codes, which were collapsed into 19 categories and 5 themes. 1. Knowledge and Beliefs reflected Ghanaian women's understanding of UI, their beliefs about its causes, and the strategies they currently employ to manage the condition. 2. UI as a taboo: Ghanaian women described UI as a "sickness" that must be hidden since exposure risked stigmatization, gossip, and shame. 3. Daily Realities: Concerns about involuntary leakage negatively affected various aspects of womenâ€™s daily lives, such as their religious practices, marital intimacy, participation in employment, and social activities. 4. Openness to doing something: Women demonstrated readiness not only to support initiatives addressing UI in rural Ghana but also to actively work with the research team as patient partners to find a cure for UI. 5. Forms of trust and support: In navigating life with UI, women demonstrated resilience and hopefulness in defeating the condition via faith in God and the research team, as well as support from family members and community networks.

CONCLUSIONS
This study lays the foundation for developing a culturally appropriate continence management program.

Categories	Themes	Illustrative Quotes
Shame Stigma Secrecy	**UI as a Taboo Subject** This theme reflects women's wishes to keep the condition secret due to the level of shame and stigma associated with it.	Urinary incontinence is a bad sickness. You lose respect, and you are not free. You cannot do what you like. I have seen and heard about this condition **(GH-IDI-004)** I told you we keep this condition a secret, so I have never heard that someone goes for treatment of this condition **(GH-IDI-012).**
Willingness to engage/support Suggestions for the research team Want a cure Talk more about it	**Openness and willingness to do something about it** This theme reflects women's desire to engage and support the search for a cure	We have partnered like that by God's grace. As you have come, we will not waste your effort of coming. So, we have part1: Categoriesnered already. May god help you, and by the time you come back, we will all be home **(GH-FGD-005)** If you are sick and you fail to tell anyone, how can someone know you need help? If the support comes, the chief in this community will use it to help them. He will give it to those with the condition **(GH-IDI-007).**
Causes of UI Knowledge of UI No knowledge about UI No Cure Management practices	**Knowledge and beliefs about UI and its management:** This theme reflects women's understanding of UI and its management	When you open up to someone about this, they tell you it is because you are old and that it comes with old age. They do not consider it to be a sickness **(GH-FGD-003)** Some other people experience it in an attempt to lift something a little heavy. Some other people also experience it when they laugh aloud **(GH-IDI-014)**
Reliance on the researcher Reliance on God Support from family, friends, and colleagues	**Forms of trust and support in managing UI** This theme reflects who and what women depend on to deal with UI.	The help is within your ability. I already told you that we do not know anything. We are illiterates. The knowledge will come from you. You will show the way to help treat the challenge **(GH-IDI-013)**. If the family loves one another, they can help her look for the cure. If they do not love each other, they will not stop talking about it and yet they will not do anything about it **(GH-IDI-004).**
Challenges in practicing religious duties Social Issues Financial Considerations Marital problems	**Daily Realities of Living with UI** This theme reflects the challenges women with UI face on a daily basis as they navigate the realities of living with the condition.	If you are undertaking the pilgrimage to Mecca and you urinate like that, you can not go **(GH-FGD-002)**. I am not able to observe my Islamic prayers even though the mosque is standing outside my house. This situation is not good because imagine you have been able to walk to the mosque, but you can not go because of urination **(GH-IDI-007).** I was a traditional midwife, but because of this condition, I had to stop **(GH-IDI-007)**. I do not sleep with him anymore. That is our challenge. I fear going to him because of this challenge. I fear that I can go to him, and this challenge will occur **(GH-FGD-001).**

The management of urinary incontinence in rural Ghana: the perspectives of primary health care workers operating rural CHPS compounds

Prosper Asaana, Saima Rajabali, Gifty Aninanya, Hawa Malechi, Najawa Mutawakil, Patricia Akweongo, Adrian Wagg
Supervisor: Dr. Adrain Wagg

INTRODUCTION
Urinary Incontinence (UI) is a prevalent, underreported condition that impairs women's quality of life. In rural Ghana, where access to specialist care is limited, the burden is pronounced. It is essential that primary health care providers (PHCPs) present in rural communities to be fully equipped to provide first-line continence services. This study assessed PHCP's capacity to assess and manage UI.

METHODS
This qualitative, exploratory study employed a community-based participatory research (CBPR) approach, partnering with Community Health Officers and Community Health Workers. Participants provided written informed consent before participating in digitally recorded Focus Group Discussions (FGDs). FGDs were conducted in English and Dagbani, transcribed verbatim, and translated by professional translators. All transcripts were de-identified for conventional content analysis.

RESULTS
Data saturation was attained after 5 FGDs. Data analysis yielded 205 codes, which were collapsed into 19 categories and 5 themes. 1. Support and willingness to co-create: This theme reflects PHCP's openness to the idea of, and willingness to actively support, the co-creation of a continence management program. 2. Perspectives on collaboration, engagement, and discourse: PHCPs encouraged active collaboration between the research team and community stakeholders to ensure the intervention's accessibility. 3. Determinants of continence care seeking: Cost, confidentiality, preferences, trust, and confidence in providers' ability to treat UI influenced health seeking. 4. Knowledge, beliefs, and perceptions of UI: While some PHCPs had some knowledge about UI, is causes, and management, others misattributed the condition to witchcraft or aging. Both also reported inadequate training in UI. 5. Community Continence Care Services and Health System Challenges: PHCPs acknowledged systemic healthcare challenges and a profound lack of government focus on UI.

CONCLUSIONS
PHCPs play a critical role in rural primary health care. Their willingness to partner presents a promising foundation for an intervention that builds local health capacity while addressing UI in underserved commmunities.

Table 1: Categories, Themes, and Illustrative Quotes.

Categories	Themes	Illustrative Quotes
• Needs and support • Willingness to take action • Willingness to treat everyone • Community support for the intervention/willingness to participate	**Support and willingness to co-create**	Yes, it is necessary. It is even necessary you involve we the volunteers because most of them will come to the volunteers with their health-related challenges. So, there should be a program including us (volunteers) and the women so that you can occasionally identify the extent of the sickness in our communities … You have to come and educate us. It has been in the system for a long time, but we do not consider it **(GH-FGD-CHW-003).** Okay, frankly speaking, with this particular condition, we don't normally talk about it. So, now that you have drawn our attention to it, I think we'll consider it, and we'll try as much as possible. When we go to the communities, we will do more investigations, we'll talk to especially the aged **(GH-CHO-FGD-002)**
• Suggestions for the research team • Suggestions for collaboration • How to engage women on UI • Advocacy for a more public Discourse on continence	**Perspectives on collaboration, engagement, and discourse**	We are grateful for this meeting. I was wondering why we were called, but it turned out to be about the health of our mothers. We are asking you to make any available treatment affordable so that whoever has this condition can afford it **(GH-FGD-CHW-005).** With this one, unless we engage the local authority, I mean the local authorities, the chiefs, the imams, and the pastors, they are with them. If we can educate them, they will take the message very well. Once we go back and tell the women, with the support of the health workers, I think they will buy into the idea, they will come out **(GH-FGD-CHO-001).**
• Health-seeking behaviors • Factors that impact health-seeking • Who Women Prefer, Trust, and Discuss UI with	**Determinants of continence care seeking**	They believe that someone is behind it. That's why I say sometimes they say it's from the house (spiritual). Yes. So most of the time, they even prefer using the local drugs. It helps more than the exotic ones. Yes. **(GH-FGD-CHO-001).** You can not go to the hospital empty-handed, so they prefer the traditional healer. All they need to go to the traditional healer is cola **(GH-FGD-CHW-003).**
• Beliefs and perceptions (Community) • Knowledge and beliefs regarding UI and its management • Challenges to living with continence • Previous Training • Current practices and approaches to UI Management/Care	**Knowledge, beliefs, and perceptions of UI practices and challenges**	A few months ago, I encountered one woman with such a condition. And for her… she was thinking it is a spiritual thing to her because she used not to experience it. And when she started experiencing it, she and her husband were rather looking at it spiritually. And her reason was not, though I educated her that that its not the cause, that the husband has married one woman to come and act with her. And that has caused it. Yes. So, I try to let her know that it's just like you have developed a condition, not because of somebody. So, they should remove the spiritual aspects and handle it. **(GH-FGD-CHO-002).** Yes. It affects them in their social and economic lives. I've seen a woman selling tomatoes in the market. She can't go. Or maybe if she's doing any business. She can't go while she's wetting herself. Sometimes when it happens like that, she just remains in the house. They don't do any business again **(GH-FGD-CHO-001).**
• Continence Services or Service Providers in the community • Systemic Health Care Challenges regarding UI	**Community continence services and health system challenges**	In our culture, it will not be appropriate for a man to go and ask someone's wife something that is private. The reproductive parts are immoral. Religiously you are not also supposed to do that **(GH-FGD-CHW-005).** I will also say that the government is not focusing more attention on that area. If you look at these facilities, they are been provided by the government. If the government wants to make its focus in that area, it will provide facilities for that and it will be available in our society. So, the government is not focusing on that area that is why we don't have it in that area **(GH-FGD-CHW-005).**

A Novel Progeria Disease Model: Identifying Critical Genetic Targets Against Human Aging and Aging-Related Diseases

Marina Beshara, Ph.D. (Candidate)
Supervisor: Dr. Terra Arnason & Dr. Troy Harkness

INTRODUCTION

Rare human diseases offer crucial insight into biological mechanisms and cellular processes. Hutchinson-Gilford Progeria Syndrome (HGPS) is a rare and fatal premature aging disorder caused by mis-splicing of the LMNA gene, producing progerin, a mutant lamin A protein. Progerin accumulation disrupts nuclear architecture, increases genomic instability, and accelerates cellular aging, resulting in premature aging phenotypes in children. Patients have shortened life expectancy, typically dying from cardiovascular complications such as myocardial infarctions or strokes during adolescence. Because HGPS shares molecular features with normal aging, identifying genetic regulators of progerin effects may reveal mechanisms of aging and age-related diseases.

METHODS

We developed a novel HGPS model in Saccharomyces cerevisiae expressing human progerin under a galactose-inducible promoter. A yeast deletion library was screened to identify genes that modify progerin-dependent growth phenotypes. Progerin expression was analyzed by Western blotting, cellular responses by immunofluorescence, confocal microscopy localization, and DNA damage assays (Rad52 repair foci).

RESULTS

Preliminary results demonstrated that progerin expression reduced chronological lifespan in yeast. Progerin expression produced conserved molecular phenotypes, including impaired cellular growth and increased markers of DNA damage, validating yeast as a model for HGPS. Genetic screening identified components of the conserved Hog1 MAPK stress-response pathway as key modifiers of progerin defects. Deletion of HOG1 or PTP2 suppressed progerin-associated growth defects and reduced progerin accumulation, whereas deletion of STE50 exacerbated growth impairment. In addition, progerin expression increased Rad52 DNA-repair foci, indicating elevated double-strand break formation and genomic instability.

CONCLUSIONS

S. cerevisiae is a powerful and established platform for genetic screening to identify pharmacological targets relevant to human disease. Deletion of Hog1 (mammalian p38 MAPK orthologue) suppresses progerin accumulation and associated growth defects. We plan to translate these discoveries in patient-derived fibroblasts, identifying novel pharmacological targets to maintain cellular function, promote genomic stability, and extend lifespan in HGPS and normal aging.

Novel Pathways for Apc10 Degradation in Saccharomyces cerevisiae

Dylan Bunko, Rachel Harris, Troy Harkness
Supervisor: Dr Troy Harkness

INTRODUCTION

The Anaphase Promoting Complex (APC) is an E3 ubiquitin ligase conserved throughout the eukaryotic domain. The APC serves as a regulator in critical cellular functions such as cell cycle control, nutrient and stress signaling, genomic stability and overall cellular proteostasis. Apc10, a core catalytic subunit of the APC, in Saccharomyces cerevisiae is known to have high rates of turnover in the cell. Aging is associated with loss of Apc10 stabilization within the cell, associated with a host of molecular phenotypes characterized as hallmarks of aging. Our lab has shown that peptides may act to stabilize Apc10 and restore overall APC activity in cells with phenotypic expressions associated with aging. Understanding pathways responsible for Apc10 degradation plays a pivotal role in elucidating the mechanistic action of these therapeutic peptides.

METHODS

Through a systems genetics approach I studied the effects of gene knockouts in suspect pathways for Apc10 degradation. Among the possible candidates were genes associated with the Skp/Cullen/F-Box (SCF) complex, the SUMO3 complex, autophagy and APC activating proteins resulting in auto-ubiquitination. Then using a cell cycle arrest and release along with protein translational inhibition I analyzed rates of Apc10 degradation through western blot across set time point collections in wildtype and various knockout mutants.

RESULTS

Through process of elimination I believe I may have potentially narrowed down the candidate pathways towards the SCF. Current work is focused on creating mutations in essential genes of the SCF that allow us to block potential Apc10 degradation while maintaining cell viability.

CONCLUSIONS

Further work is needed to elucidate the exact pathway by which Apc10 is degraded in the cell. Insight into this novel pathway may provide better understanding of the mechanisms of studied peptide therapeutics in our lab that act to combat cellular aging hallmarks at the molecular level.

Pharmacist-Physiotherapist Collaborative Care for Knee OA: Comprehensive Review of Recruitment Efforts for a Community-Based Pragmatic RCT

Dr. Ross Tsuyuki, PharmD, MSc; Dr. Allyson Jones, PT, PhD; Jill Hall, BScPharm, ACPR, PharmD; Dr. Claire Barber, MD, PhD, FRCPC; Dr. Doug Klein, MD, CCFP, MSc
Supervisor: Dr. Ross Tsuyuki

INTRODUCTION
Knee osteoarthritis (OA) is often underdiagnosed, with many individuals relying on over-the-counter pain medications. As accessible healthcare providers in the community, pharmacists can screen for knee OA and facilitate multidisciplinary care. A pharmacist-physiotherapist collaborative model was proposed to support community-based knee OA management. Within the context of the primary study, we discuss recruitment strategies for this pragmatic randomized controlled trial (RCT).

METHODS
Nineteen urban and rural pharmacies in Alberta were partnered with eight local physiotherapy clinics. Pharmacists will recruit a total of 125 patients to be randomized into either the intervention or conservative care group. The intervention includes a comprehensive pharmacist assessment, medication review, and referral to physiotherapy for an evidence-based 6-week group exercise program for knee OA (GLA:D). The conservative care group receives a brief pharmacist assessment, non-prescription recommendations, and an education pamphlet, with a crossover offered at 3 months. Follow-up for both groups occurs at 3 and 6 months post-intervention or baseline. After the trial launched, recruitment was anticipated to take 3 months; however, it has been slower than expected. Our objective is to determine the reasoning for delayed recruitment and how it can be supported.

RESULTS
New recruitment strategies included brief study information leaflets to provide to existing patients with OA risk factors, posting recruitment materials around the community, and leveraging an online booking system at some pharmacies. Additionally, visiting high-recruiting sites informed strategies for other locations, with planned follow-up via email/phone to implement identified action items. The COM-B model was used to inform visit questions and identify behavioural drivers. The efficacy of these methods is being evaluated.

CONCLUSIONS
Supporting pharmacists in recruitment efforts is essential for implementing pragmatic RCTs in community settings. Achieving the target sample size is critical to generate meaningful findings that can inform future models of care for chronic conditions like OA.

Correlating biophysical properties of TDP-43 aggregates with clinical phenotypes in amyotrophic lateral sclerosis

Maddison Charlton, Satish Nemani, Leonardo Cortez, Helen Huang, Valerie Sim
Supervisor: Dr. Valerie Sim

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a clinically heterogeneous neurodegenerative disease, varying in upper and lower motor neuron involvement, site of onset (limb vs bulbar), and progression rate. Despite this variability, most ALS cases share a common pathological hallmark: cytoplasmic inclusions of transactive response DNA-binding protein 43 kDa (TDP-43). Whether pathology arises from TDP-43 mislocalization, aggregation or both remains unclear. TDP-43 aggregates are also observed in frontotemporal dementia (FTD) and limbic-predominant age-related TDP-43 encephalopathy (LATE), with evidence suggesting that distinct TDP-43 conformations may affect different disease phenotypes. Drawing on parallels from prion diseases, we plan to investigate whether TDP-43 aggregates exhibit distinct biophysical properties that correlate with clinical phenotypes.

METHODS

TDP-43 aggregates were isolated from the frontal cortex of ALS patient brains with different phenotypes and compared with LATE and control brain samples. A protocol was optimized to isolate pathological TDP-43, with confirmation using antibodies targeting total and phosphorylated forms. Aggregate size distributions were assessed using asymmetric flow field-flow fractionation (AF4). Seeding efficiency was measured using real-time quaking-induced conversion (RT-QuIC) with a truncated TDP-43 substrate.

RESULTS

Western blot analysis detected phosphorylated TDP-43 (pTDP-43) in some, but not all, ALS samples, suggesting a difference in phosphorylation patterns. Bands corresponding to pTDP-43 (Ser409/410) were observed at ~20–25 kDa in some samples, while all samples showed total TDP-43 at 43 kDa. RT-QuIC revealed variability in seeding efficiency, with LATE samples exhibiting faster seeding than ALS and control samples. Fractionated ALS samples showed improved seeding compared to P2 fractions. AF4 analysis indicated larger size ranges in some LATE compared to ALS samples.

CONCLUSIONS

These findings suggest that TDP-43 aggregates differ in biophysical properties across disease states, potentially supporting the hypothesis that conformational variation may contribute to clinical heterogeneity in TDP-43 in ALS. Ongoing work includes probing additional phosphorylation sites (Ser403/404, Ser379) to further characterize biochemical differences among samples.

Disparities for Tremor and Dystonia Patients Accessing Deep Brain Stimulation: An Explanatory Sequential Mixed Methods Study

Shaina Corrick, Janis M. Miyasaki, Ashley Hyde, Sabrina Poonja, Bashir Daud Shah, Eric Noyes, Pouria Torabi, Kevin Yen, Gail Dimapilis, Tejas Sankar, Alex Rajput, Aleksander M. Vitali, Bukola Salami, Fang Ba
Supervisor: Dr. Fang Ba

INTRODUCTION
Deep brain stimulation (DBS) is an established therapy for tremor and dystonia in appropriately selected patients. However, disparities in DBS access exist, particularly among women and racialized populations, and are less studied compared with Parkinson disease. While barriers influencing DBS utilization in these groups remain underexplored, identifying disparities is essential to ensuring equitable healthcare access.

METHODS
A sequential explanatory mixed methods design was conducted with a retrospective chart review and telephone survey at two Canadian centers followed by semi-structured qualitative interviews, analyzed using thematic analysis.

RESULTS
The retrospective chart review included 152 patients. Despite a higher proportion of females referred, more males ultimately underwent DBS implantation. The vast majority (>85%) of both referred and implanted patients were White and Canadian born. Implanted patients were more commonly referred by subspecialist neurologists. Levels of education, marital status, geography, and household income were not associated with DBS access. Sixteen tremor and dystonia patients participated in the qualitative interviews, with key themes identified: (1) 'Just a Shaky Gal' – A Gendered Lens to DBS Decision-Making, (2) Pushing for More – Self-Advocacy in the Community and the Role of Community Health Service Providers in Facilitating DBS Access, and (3) Hidden Layers - Ethnicity, Cultural and Other Demographic Considerations for DBS.

CONCLUSIONS
The DBS referral and implantation for tremor and dystonia was characterized by ethnicity, sex and gender, and referral-based disparities. These findings highlight the need for targeted efforts to improve equitable access to DBS for women and racialized populations, as well as information to providers in the community.

Impact of Cor Pulmonale in Patients Hospitalized for Acute Exacerbations of COPD A Population-Based Retrospective Cohort Study in Alberta

Alex E. Crentsil1,2, Paul Ronksley3,4, Michael K. Stickland1,2, Chuan Wen5,6, Kahir Rahemtulla1,2, Jason Weatherald1,2*, Grace Y. Lam1,2,7
Supervisor: Dr. Grace Lam

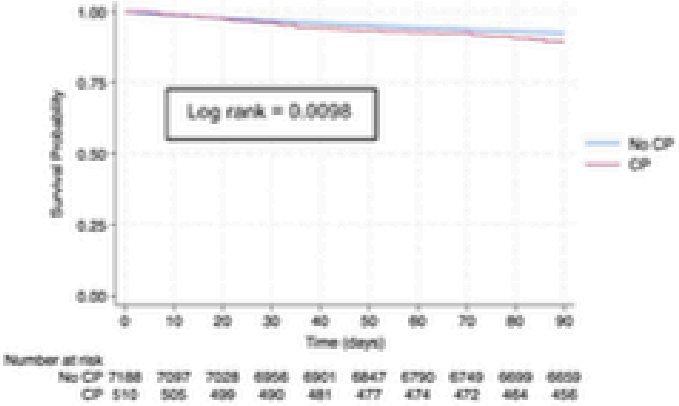
INTRODUCTION
Cor pulmonale (CP) is right heart dysfunction caused by pulmonary hypertension in chronic lung diseases, which may represent a high-risk group after an acute COPD exacerbation (AECOPD). However, there are limited population-level data on how CP affects the risk of mortality and rehospitalization after AECOPD discharge.

METHODS
Using linked administrative databases from Alberta, Canada, we performed a population-based retrospective cohort study that included adults aged 35 and older with an index hospitalization for AECOPD between November 1, 2018, and December 1, 2019. We used a validated case definition for AECOPD using ICD-10 and ICD-9 codes along with prior medical claims. The exposure of interest was CP, defined as the presence of ICD-10 code I27 or ICD-9 code 416.9 in any claim within five years prior to the initial hospitalization but post COPD diagnosis. The primary outcome was all-cause mortality within 90 days of index hospitalization discharge. Secondary outcomes included COPD-related and all-cause rehospitalization within 90 days. We used adjusted Cox regression models accounting for age, sex, urban/rural residence, neighbourhood income, Charlson Comorbidity Index, hospital length of stay during initial hospitalization, ICU admission during index hospitalization, and number of emergency visits for AECOPD in the prior year.

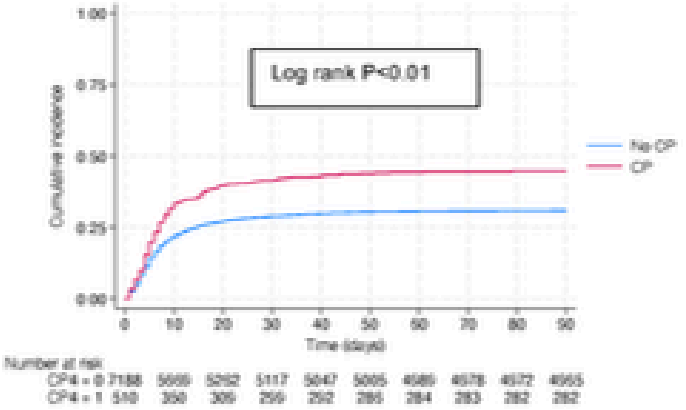
RESULTS
Among 7,698 patients hospitalized with AECOPD, 510 [6.6%] had CP. Baseline characteristics were similar between groups although patients with CP were less likely to have rural residency (19.6% vs. 23.5%, p=0.04) and had slightly longer index hospitalization duration (median 6 vs. 5 days, p<0.01). CP was associated with higher 90-day mortality (10.59% vs. 7.42%, p=0.009, adjusted HR [aHR] 1.50, 95% CI 1.12–2.02, p<0.01) and increased risks of COPD-specific (aHR 1.85, 95% CI 1.54–2.23, p<0.01) and all-cause rehospitalization (aHR 1.49, 95% CI 1.28–1.72, p<0.01). Results were similar using a Fine-Gray model to account for death as a competing risk for rehospitalization.

CONCLUSIONS
Among patients hospitalized with AECOPD, CP was associated with an increased risk in 90-day post discharge all-cause mortality and recurrent rehospitalizations early post discharge. Future work integrating clinical, biomarker, and imaging data in future studies may clarify mechanisms and guide targeted interventions.

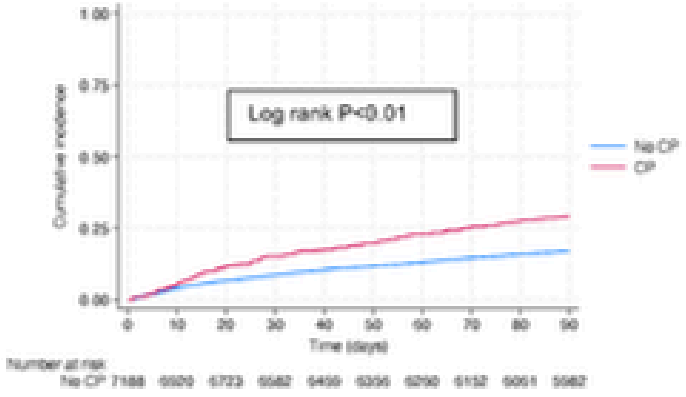
A. All-Cause Mortality



B. COPD-Related Rehospitalization



C. All Cause Rehospitalization



Family Members' Perspectives Towards Alberta's Compassionate Intervention Act

Avnit Dhanoa, Boogyung Seo, William Rioux, Dylan Viste, S. Monty Ghosh
Supervisor: Sumantra Monty Ghosh

INTRODUCTION

Legislation in North America allowing for involuntary care of substance use disorders (SUD) has emerged in recent years, including Alberta's Compassionate Intervention Act, which was passed in 2025. This policy marks a significant shift in addiction treatment by mandating substance use care and giving family members a central role in initiating treatment decisions. Given the complex nature of mandatory treatment, it is essential that the perspectives of those directly impacted inform its implementation. In this study, we explored family members' perceptions of the legislation and identified areas for consideration.

METHODS

Semi-structured interviews with 18 participants were conducted. Participants had to reside in Alberta and have a family member with lived experience of SUD. Qualitative thematic analysis was performed.

RESULTS

4 key themes were identified: 1) the importance of integrating mental health support within treatment for achieving meaningful recovery; 2) emphasis on aftercare, as recovery doesn't end at discharge; 3) worries about the involvement of police officers causing more negative encounters; and 4) family voices need to be represented in policy decisions. Although family members held differing opinions toward the legislation, these themes emerged consistently across perspectives, demonstrating shared concerns and priorities regardless of stance.

CONCLUSIONS

Across varying perspectives, participants consistently pointed to the need for more holistic care that includes mental health support, stronger post-discharge services, reconsideration of police involvement, and greater inclusion of family input in policymaking. As Alberta advances mandatory SUD treatment policies, it is imperative that policymakers meaningfully engage those with lived experience in decision-making processes. Doing so can help ensure that addiction policies are responsive to the realities of people who use substances and the families who support them.

Combination treatment more effective than single agent for Eosinophilic Esophagitis: long term Histologic, Endoscopic and Quality of life outcomes from a prospective cohort in Alberta

Poshika Dhingra, Farhan Zahid, Michaela Quon, Dayoung Kim, Ravdip Dhaliwal, George Tadros, Aydin Herik, Jingru Helen Ha, Igor Stukalin, Michelle Buresi, Dorothy Li, Matthew Woo, Eva Mak, Ryan Rosentreter, Christopher Ma, Brooke Maracle, Milli Gupta
Supervisor: Dr. Milli Gupta

INTRODUCTION
Eosinophilic esophagitis (EoE) is a chronic immunologic disorder managed with proton pump inhibitors (PPIs), topical corticosteroids (TCS), elimination diets, biologics, with endoscopic dilation. Real world data comparing treatment and quality of life (QoL) impact are limited.

METHODS
Adults with EoE enrolled prospectively from 2011–2025 were evaluated for demographics, treatment exposures, histology, EREFS scores, dilation history, and EoE-QoL-A scores. Outcomes were analyzed using Wilcoxon signed-rank testing, Spearman correlation coefficients, and logistic regression.

RESULTS
Among 178 adults (median age 40 years, 69.7% male; median follow-up 7.3 years), patients trialed a median of 2 therapeutic classes. Treatment patterns included PPIs (30.1%), TCS (8.5%), dietary elimination (5.7%), combination therapy (38%), biologics (4%), other therapies (4.5%), and no therapy (9.1%). Peak eosinophil counts declined significantly from 40 to 7 eos/hpf ($p<0.001$). Deep and standard histologic remission was strongest with PPI plus diet (OR 5.54 and 7.35), followed by PPI plus TCS and PPI monotherapy. Regional modeling suggested that PPI monotherapy preferentially improved proximal disease, PPI plus TCS provided greater benefit in mid/distal disease, and PPI plus diet achieved more uniform reductions across esophageal segments. Common dietary eliminations were dairy, gluten, and wheat; soy, nuts, eggs, and fish were less frequent. No specific elimination profile was superior unless combined with a PPI. EREFS scores improved from 2.39 to 2.00 ($p<0.001$), driven mainly by reductions in inflammatory features. Stricture prevalence decreased from 30.7% to 21.6% ($p=0.059$), with fewer dilations over time. Atopy was present in 92%, including 55% with at least two conditions. QoL improved significantly (2.83 to 3.04, $p<0.001$), but did not correlate with histologic or endoscopic response.

CONCLUSIONS
In this Canadian cohort, EoE outcomes improved substantially over long-term follow-up. Combination therapy, particularly PPI plus diet, showed the greatest benefit, while QoL improvement appeared independent of objective inflammatory measures.

ACCURATE DETERMINATION OF DRUG BINDING AFFINITIES AND BINDING KINETICS IN NMR-BASED TITRATIONS

Kuldeep P Dodia, Sarah Donnelly, Allen Yeung, Thomas Dumont, Vahid Lotfikalajahi, Philip B Liu, Hacer Karatas Bristow, Peter M Hwang
Supervisor: Dr. Peter M Hwang

INTRODUCTION

Drug discovery efforts frequently produce lead compounds with high hydrophobicity and poor water solubility. Dose response curves often level off prematurely due to poor water solubility, giving a false impression of drug saturation of the protein and calculation of artificially small dissociation constants. In solution NMR spectroscopy, protein signals are broadened by exchange processes between free and bound states, making it possible to extract binding kinetics data that is relatively free from such measurement errors.

METHODS

We titrated 5 different compounds into a chimeric construct for human cardiac troponin. NMR signals during the titration showed characteristic broadening due to drug binding and release. We wrote MATLAB scripts that modelled NMR signal intensity and position during the drug titrations using the Bloch-McConnell equations. There were 4 fitting parameters used: kon, koff, drug solubility, and protein scaling factor.

RESULTS

Our MATLAB scripts could precisely determine koff and a protein scaling factor for our NMR-based drug titrations. However, there were a range of values for kon and drug solubility, though their product was relatively constant. By assuming similar kon values, it is possible to discern solubilities and relative binding affinities for any family of drug-like small molecules binding to a particular protein target.

CONCLUSIONS

NMR could become an essential method for drug development based on its ability to determine drug binding kinetics that are not susceptible to binding affinity determination artefacts due to low drug solubility.

Beyond Frailty Screening: An Integrated Acute Geriatric Medicine Model to Improve Hospital Flow

Michael Grossi, Michelle Valpreda, Ashif Rahman, Aatif Hussain, Gurkirat Gill, Judy Peng, Elena Kumar, Anthony Anugom, Karen Leung, Martin Moran, Jean Triscott, Winnie Sia, Jason Chan, Naheed Rajabali
Supervisor: Dr. Naheed Rajabali

INTRODUCTION
Older adults with frailty and multimorbidity represent a growing proportion of acute hospital admissions and are associated with prolonged length of stay (LOS) and increased healthcare utilization. Despite this, frailty identification alone has not consistently improved inpatient flow, highlighting a gap between risk stratification and care delivery. We describe the implementation of an integrated Acute Geriatric Medicine model at a tertiary care centre and evaluate its impact on hospital LOS.

METHODS
This is a longitudinal, real-world evaluation of a phased acute care model at the Royal Alexandra Hospital from 2012–2025. The model evolved through: (1) expansion of acute care capacity and higher-acuity admissions, and (2) integration of geriatric medicine principles, including frailty-informed decision-making, into acute Internal Medicine care. Annual Acute Length of Stay to Expected Length of Stay (ALOS/ELOS) ratios were obtained from institutional data and examined over time.

RESULTS
ALOS/ELOS ratios improved from 1.39–1.60 in the pre-integration phase (2012–2016) to 1.18–1.27 during transition (2017–2019), and further to 1.09–0.81 in the mature model (2020–2025). These improvements occurred despite increasing patient acuity, including management of NSTEMI, sepsis, and acute stroke. Practice emphasized early diagnostic clarity, proactive disposition planning, and individualized escalation decisions based on physiological reserve and goals of care. A comparator tertiary site did not demonstrate a comparable sustained reduction in ALOS/ELOS.

CONCLUSIONS
An integrated Acute Geriatric Medicine model was associated with sustained improvements in LOS despite increasing patient complexity. Findings suggest that aligning acute care delivery with frailty-informed, patient-centered decision-making may improve hospital flow by better matching care to patient capacity. Further evaluation of downstream outcomes, including readmissions and patient-centered outcomes, is warranted.

ALOS/ELOS Trends (2012–2025): Royal Alexandra Hospital vs Comparator Site

Figure 1: Royal Alexandra Hospital Acute Care Geriatric Medicine ALOS/ELOS

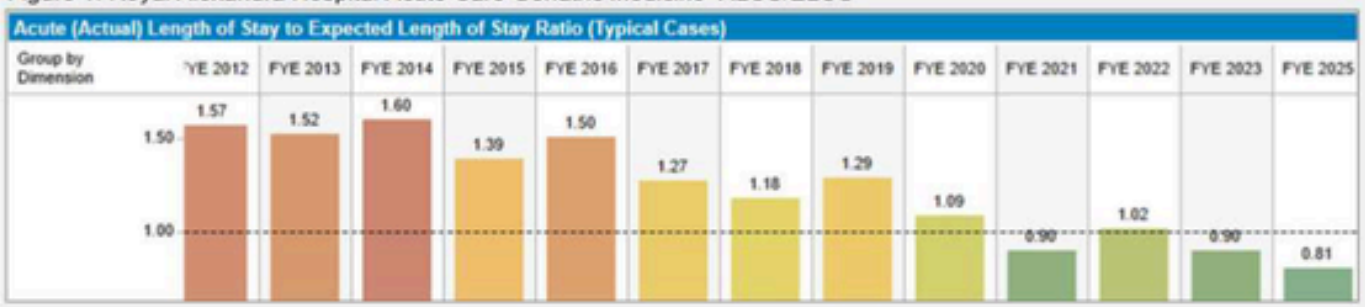


Figure 2: University of Alberta Acute Care Geriatric Medicine ALOS/ELOS (Comparator site)

Source: Alberta Health Services Tableau (Provincial ALOS/ELOS Dashboard). 2024 data for RAH not available in current dataset (Tableau extraction)

- Pre-integration (2012–2016) | Transition (2017–2019) | Mature Model (2020–2025)
- RAH demonstrates a sustained reduction in ALOS/ELOS over time
- Comparator site does not demonstrate a comparable sustained trend

Ketone-Based Therapies in Adults Heart Failure: A Systematic Review and Quantitative Analysis

Aanchel Gupta, Yuliia Smereka, Robert Margaryan, Nariman Sepehrvand, Shubham Soni, Wendimagegn Alemayehu, Justin Ezekowitz
Supervisor: Dr. Justin Ezekowitz

INTRODUCTION
Ketone bodies have shown potential to improve cardiac metabolism and function in patients with heart failure (HF). The objective of this analysis was to evaluate the effects of exogenous ketone-based interventions on cardiac function in patients with HF or related cardiometabolic risk factors.

METHODS
We conducted a systematic review based on a search of MEDLINE, EMBASE, CINAHL, Cochrane Library, and Scopus from inception to January 2025. Eligible studies included randomized controlled trials evaluating exogenous ketones (oral ketones or ketone infusions) compared to placebo in adults with HF or patients with risk factors for HF including type 2 diabetes mellitus, hypertension, or coronary artery disease. Paired reviewers independently screened and identified hits at title-and-abstract and full-text levels to determine eligibility and extracted data from eligible studies. Random-effects meta-analysis was performed. Effects of interventions were summarized as mean differences (MD). Risk of bias was assessed using Cochrane RoB 2.0 tool. Certainty of evidence was evaluated using the GRADE (grading of recommendations assessment, development and evaluation) approach.

RESULTS
Out of 565 unique records, 22 full-text articles were reviewed, and 8 studies met inclusion criteria. Exogenous ketone administration increased left ventricular ejection fraction (LVEF: MD= 3.94, 95% CI 2.18-5.70, p = 0.001), cardiac output (CO L/min: MD= 1.11 L/min, 95% CI 0.55-1.67, p = 0.002), heart rate (HR: 4.85 bpm, 95% CI 2.24-7.46, p = 0.003), and stroke volume (SV: MD 10.21 mL, 95% CI 4.06-16.35, p = 0.005). Pulmonary capillary wedge pressure (PCWP) decreased (MD -0.93 mmHg, 95% CI -1.44 to -0.43, p = 0.003), while mean arterial pressure (MAP) showed no change (MD -1.37 mmHg, 95% CI -3.53 to 0.79, p = 0.18).

CONCLUSIONS
Exogenous ketone-based therapies are associated with improvements in hemodynamic markers of cardiac function, including increases in LVEF, cardiac output, and stroke volume, along with a reduction in pulmonary capillary wedge pressure. These findings suggest that ketone supplementation may offer clinical benefits for patients with HF or vascular disease.

Ketone-Based Therapies in Adults Heart Failure: A Systematic Review & Quantitative Analysis

8 randomized controlled trials • 7 pooled in meta-analysis • crossover design • short-term hemodynamic outcomes

STUDY SELECTION

565
Unique records identified

23
Full-text articles reviewed

8
Studies meeting inclusion criteria

7
Studies in pooled meta-analysis
n = 152 patients

STUDY DESIGN

All crossover RCTs • HFrEF, HFpEF, & cardiometabolic populations • IV & oral ketone formulations • Acute to 14-day follow-up

KEY OUTCOMES - EXOGENOUS KETONES VS. PLACEBO

LVEF
↑ +3.94%
absolute increse
95% CI: 2.18-5.70 •
P = 0.001
Moderate

CARDIAC OUTPUT
↑ +1.11
L/min
95% CI: 0.55-1.67 •
P = 0.002
Moderate

STROKE VOLUME
↑ +10.21
mL
95% CI: 4.06-16.35 •
P = 0.005
Moderate

PCWP
↓ −0.93
mmHg
95% CI: -1.44--0.43 •
P = 0.003
High · I^2=0%

HEART RATE
↑ +4.85
bpm
95% CI: 2.24-7.46 •
P = 0.003
Moderate

MEAN ART. PRESSURE
↔ NS
no significant change
MD -1.37 mmHg • *P* = 0.18
Moderate

PROPOSED MECHANISMS OF BENEFIT

- Alternative metabolic substrate for heart failure
- Vasodilation & improved organ perfusion
- Anti-inflammatory non-metabolic effects
- Improved cardiac function
- Favorable hemodynamic profile vs. inotropes

- Exogenous ketone therapy is associated with consistent short-term improvements in hemodynamic markers across diverse HF populations.
- **↑ CO, ↑ LVEF, ↑ SV, ↓ PCWP** - *without significantly affecting MAP* - distinguishes ketones from traditional inotropes.
- Long-term RCTs powered for patient-important outcomes (mortality, hospitalizations, QoL) are warranted.

From Simulation to Rehabilitation: A Real-Time Digital Twin for Personalized Exoskeleton Therapy

Sina Kazemi
Supervisor: Dr. Vivian Mushahwar

INTRODUCTION

Stroke survivors frequently experience asymmetrical gait deficits that require personalized robotic rehabilitation. However, tuning powered lower-limb exoskeletons still relies heavily on manual trial-and-error procedures in the clinic. This process creates a "tuning bottleneck" that is inefficient and physically demanding for persons living with stroke. To address this limitation, we propose a real-time Digital Twin framework that computationally predicts optimal, patient-specific control parameters before physical intervention (See Figure 1).

METHODS

A novel co-simulation architecture is currently under development to bridge robotic physics and neuromuscular biomechanics. The framework couples MuJoCo, a high-performance physics engine responsible for exoskeleton electromechanics and contact dynamics, with OpenSim, a musculoskeletal solver that calculates muscle activation and metabolic cost. Data exchange occurs through a custom User Datagram Protocol (UDP) socket bridge. The lower-limb musculoskeletal model is currently being parameterized within this environment by adjusting physiological and biomechanical parameters to represent stroke-related impairments, such as drop foot and spasticity, thereby creating a patient-specific "Virtual Patient.

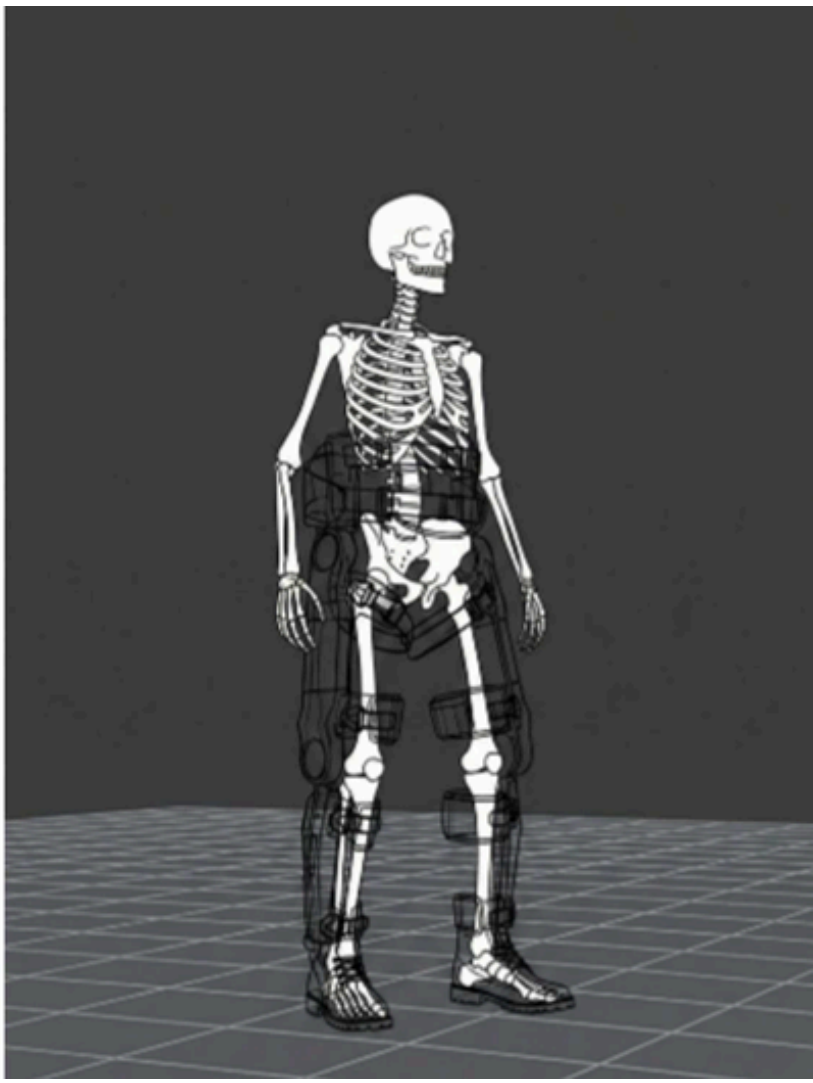
RESULTS

As the project is currently in its foundational phase, the preliminary results mainly include the successful structural development of the simulation architecture. The high-fidelity kinematic modeling of the human–robot system has been completed within the MuJoCo engine, and the baseline musculoskeletal model has been configured in OpenSim. Initial testing of the communication bridge is now underway to validate the stable, real-time exchange of kinematic states and physiological muscle torques. After completion of the benchmarking phase, this framework is expected to demonstrate a significant reduction in computation time compared with traditional biomechanical simulators, while maintaining gold-standard physiological accuracy.

CONCLUSIONS

The initial development of this real-time Digital Twin establishes an important functional bridge between engineering control theory and clinical biomechanics. Ultimately, this framework will enable rapid in-silico optimization of robotic assistance to minimize the metabolic cost of a person with stroke using a rehabilitation robot. In addition, it provides the foundational modular testbed required for evaluating future wearable technologies, including smart garments.


smlp/cosmos



Urban vs Rural Disparities in the Treatment and Outcomes of Metastatic Melanoma

Kyra Lee, Matthew Anaka
Supervisor: Dr. Matthew Anaka

INTRODUCTION

Melanoma is an aggressive skin cancer with rising incidence in Canada . While untreated metastatic melanoma carries a median survival of approximately six months, systemic therapy advances such as checkpoint inhibitor immunotherapy have significantly improved outcomes in clinical trials. However, real world outcomes may be impacted by social determinants of health, including rurality, which can impact access and treatment patterns. Canadian data on the impact of rurality on melanoma outcomes remain limited. Objectives are to evaluate differences in treatment patterns and outcomes between rural and urban patients with metastatic melanoma, and to explore potential mediators of disparities.

METHODS

This retrospective cohort study included metastatic melanoma patients from Northern Alberta, with care coordinated by a CCI oncologist between 2015 - 2025. Data was obtained from the Alberta Cancer Registry and supplemented by chart review. Urban vs rural residency was defined based on postal codes. Information on treatment in tertiary vs regional/community cancer centres was also recorded. Outcomes included first line treatment type, number of therapy lines, overall survival, and adverse events. Statistical analyses used chi-square testing for categorical variables, and Kaplan–Meier curves with log-rank testing for survival.

RESULTS

A total of 236 patients initiating first-line systemic therapy between were analyzed. 196 resided in urban regions, and 40 in rural regions. Most patients (200/236) were treated exclusively at tertiary centres, while 36 received some care in regional or community settings. Rural patients were significantly more likely to receive treatment outside tertiary centres. There were no significant differences in treatment patterns or overall survival by residence or treatment setting. Exploratory analyses showed patients aged >70 years were more likely to receive less intensive therapy and had shorter overall survival.

CONCLUSIONS

Melanoma care and outcomes appear consistent across rural and urban regions, highlighting consistent quality of care in regional and community centres. Age-related differences in treatment and survival warrant further study.

Local patterns and clinical characteristics of carbapenemase-producing organisms from 2017 to 2024

Sunghoon Lee, Stephanie W. Smith
Supervisor: Dr. Stephanie Smith

INTRODUCTION

Carbapenemase-producing organisms (CPO) are associated with increased mortality and treatment remains difficult. Furthermore, the presence of the carbapenemase enzymes on mobile genetic elements leads to the transfer of resistance mechanisms between bacteria. These bacteria are primarily found colonizing the human body and the hospital environment, lending to healthcare-associated outbreaks. Across Canada we have seen increasing rates of colonization and infection. A better understanding of the national and local landscapes of CPO is required to adequately identify cases and prevent spread.

METHODS

We performed a retrospective cohort study at a large tertiary care center in Western Canada of patients who were colonized or infected with CPO between 2017-2024. Cases were obtained through the Infection Prevention and Control database and case characteristics gathered through chart review. CPO genes were confirmed by the National Microbiology Laboratory.

RESULTS

We identified 87 cases of CPO at our site over the 8 year period. There was an increasing number of cases per year, with a quarter of these cases acquired in hospital. 15% of our cases were found in solid organ transplant recipients, a higher rate compared to the national average. NDM was the most common carbapenemase enzyme identified, whereas nationally KPC was the predominant resistance mechanism. Over half of the cases in our cohort did not have any preceding travel exposure. A third of all cases were infected with CPO, with a subsequent 30-day mortality of 14%. The antibiotic with the highest susceptibility rates in our series was Cefiderocol (88% of isolates with known susceptibilities).

CONCLUSIONS

With increasing rates of CPO, we require improved methods of surveillance and detection, particularly as the proportion of travel-related cases decreases. Furthermore, despite increasing availability of newer antimicrobials, isolates remain resistant to many of these, highlighting the ongoing need for infection prevention measures and antibiotic development.

Small Peptide Activator, C43-4, Restores APC Function In Aging and Cancer

Mathew Lubachowski, Troy Harkness
Supervisor: Troy Harkness

INTRODUCTION

Our lab has identified a small peptide, termed C43-4, that is capable of activating the Annaphase Promoting Complex (APC), and restoring its function in aging and disease. Previous work in our lab has shown that APC dysfunction, and substrate accumulation, occurs with age and in aging associated diseases like cancer and progeria. While commercially available APC activators can restore APC function, we predict our C43-4 peptide possesses benefits. We have already characterized the effectiveness of the peptide under plasmid mediated expression, and I am now utilizing exogenous treatment with synthetic C43-4.

METHODS

To identify concentrations of C43-4 capable of sensitizing cancer cells to chemotherapeutics, I performed MTT cell survival assays on drug sensitive and resistant MCF7 and MDA-MB-231 human breast cancer cells treated with varying concentrations of C43-4 in the presence and absence of doxorubicin. Next to confirm that C43-4 is taken up by cancer cells, and localizes to the nucleus I performed fluorescent microscopy on cells treated with FITC tagged C43-4.

RESULTS

I demonstrated that concentrations of C43-4 between 50 µg/mL to 100 µg/mL are capable of synergizing with doxorubicin to increase killing of drug sensitive and resistant MCF7, as well as MDA-MB-231, breast cancer cells. Furthermore, I was able to show that after 2 hours C43-4 can be found localized within the nucleus of treated cells.

CONCLUSIONS

I have demonstrated that our synthetic C43-4 peptide is not only taken up by human breast cancer cells in vitro, but also subsequently localized to the cell nucleus. I have also shown that C43-4 is capable of synergizing with the chemotherapeutic doxorubicin to enhance the killing of both drug sensitive and resistant human breast cancer cell lines. These results suggest that the C43-4 peptide could function as an effective APC activator and potential cancer treatment.

Freedom and Flexibility After Islet Cell Transplantation: Experiences of People Living with Type 1 Diabetes

Robin Lucciantonio, Renee Crossman, Peter Senior
Supervisor: Dr. Peter Senior

INTRODUCTION

Type 1 diabetes (T1D) requires constant self-management and carries substantial psychological and lifestyle burdens. Cell-based therapies such as islet transplantation (ITx) may reduce reliance on exogenous insulin and meaningfully alter lived experience. Our objective is to explore perceptions of freedom, flexibility and risk among ITx recipients and health-care providers (HCPs). Secondly, to increase awareness of ITx benefits and challenges for individuals with T1D, HCPs, and policymakers.

METHODS

Using focused ethnography, semi-structured interviews were conducted with adult ITx recipients, family members, and transplant-HCPs. Thematic analysis was used to systematically identify and interpret patterns across participant narratives.

RESULTS

Identified themes reflected increased autonomy, quality of life, and re-engagement in restricted activities. Participants described freedom from constant T1D vigilance, leading to greater daily flexibility, psychological relief, and renewed social and professional participation. Additionally, HCP–patient relationships were central to care trajectories, with trust, advocacy, and shared decision-making shaping T1D care, transplantation experiences, and sustained outcomes.

CONCLUSIONS

ITx offers both biomedical and psychosocial benefits for people living with T1D. Findings underscore the importance of patient-reported outcomes (PROs) that capture daily experiences, psychosocial well-being, and relational aspects of care. Developing novel tools for measuring perceived freedom, flexibility, quality of life, and care relationships beyond glycemic metrics will be essential to fully assess the impact of emerging cell treatments and possible curative therapies.

Double-balloon ERCP in patients with altered anatomy: experience and outcomes in a single Canadian Centre

Rachel Mackay, John Soleas, Sergio Zepeda-Gomez, Dr. Brendan Halloran, Dr. Shawn Wasilenko
Supervisor: Dr Sergio Zepeda-Gomez

INTRODUCTION

Double-balloon endoscopic retrograde cholangiopancreatography (DBE-ERCP) is a complex endoscopic procedure indicated for the evaluation and treatment of biliary and pancreatic pathology in patients with altered anatomy. There is limited data regarding the experience and outcomes for patients undergoing this procedure in Canada.

METHODS

Retrospective analysis from a prospectively collected database of patients that underwent DBE-ERCP at the University of Alberta Hospital between 2013 and 2024.

RESULTS

In total, 115 patients (47% female; 53% male) were identified and included in the analysis. All the procedures were performed by a single endoscopist. Of these patients, 85 (74%) had a Roux en Y hepaticojejunostomy anatomy. Other surgeries included Roux en Y gastrojejunostomy (n=15, 13%), gastric bypass (n=8, 7%), Whipple's (n=5, 4.3%) and Billroth II (n=2, 1.7%). Obstructive jaundice (n=84, 73%) was the most common indication for DB-ERCP, with 40 patients (35%) presenting with signs of cholangitis. Success in reaching the anastomosis (hepatico-jejunostomy or pancreatico-jejunostomy) was feasible in 99 patients (86%) and therapeutic interventions were performed in 88 cases (76%). Factors that prevented success included a long-surgical limb (n=6), presence of adhesions (n=5) and an angulated Roux en Y anastomosis (n=5). Therapeutic interventions included dilation of anastomosis in 50% of cases, followed by stone extraction and placement of plastic stents. Patients with unsuccessful interventions went for PTC placement (n=3), or re-attempt at DBE-ERCP (n=4). A subset of patients did not require any interventions, as the findings at the anastomosis and biliary tree were normal. Only one major complication was observed (perforation after anastomotic dilation) which was managed conservatively and did not require surgery.

CONCLUSIONS

The use of DBE-ERCP has been shown to be an effective and safe endoscopic strategy for patients with altered anatomy for the treatment of biliary and pancreatic pathology.

A Novel Founder Mutation in Hemojuvelin Identified in an Indigenous Northern Albertan Population leading to Type 2A Juvenile Hemochromatosis

Scott MacKay, Jeffrey Patterson, Alison Eaton, Juan G. Abraldes, Sherry A.M. Taylor, Anna Serebrin, & Malcolm Wells
Supervisor: Dr. Malcolm Wells

INTRODUCTION

Juvenile hemochromatosis most commonly occurs due to mutations in the hemojuvelin (HJV) gene. Rare HJV mutations have been previously reported with varying pathogenesis ranging from asymptomatic disease to cirrhosis, cardiomyopathy, and hypogonadism. A novel mutation in HJV, c.442T>A, was first identified by our team in 2022 in patients in a Northern Albertan Cree community. Patients have since been followed in a joint clinical genetics, hematology and hepatology clinic to provide comprehensive care. This study aims to summarize laboratory, imaging, and FibroScan findings to describe the pathogenesis of a novel HJV mutation causing juvenile hemochromatosis.

METHODS

This prospective cohort study aims to collect serial ferritin and transferrin saturation (TSAT) levels, FibroScan results, abdominal ultrasounds, and cardiac and abdominal MRIs of all individuals identified to be HJV c.442T>A homozygous. Standardized intervals for collection have been difficult to achieve due to scarce healthcare access to tertiary centres for study participants. Genetic analysis and interpretation included single nucleotide variant analysis by Sanger sequencing of exons 2-4 of the HJV gene and assessment of pathogenicity per ACMG criteria.

RESULTS

Four families with 9 confirmed HJV c.442T>A homozygous and 3 heterozygous individuals have been identified. An autosomal recessive pattern of inheritance has been identified and the presence of disease within geographically-linked non-kindred patients suggests a founder mutation. HJV c.442T>A homozygous individuals experience elevated ferritin and TSAT levels, hepatic iron deposition and have developed decompensated cirrhosis and HCC. Heterozygous individuals show no laboratory or clinical abnormalities.

CONCLUSIONS

The c.442T>A mutation in HJV appears to lead to varying levels of disease severity ranging from decompensated cirrhosis complicated by hepatocellular carcinoma to largely benign, asymptomatic disease within our small patient population. The high likelihood of a founder mutation necessitates an ongoing effort for both advocacy and increased healthcare accessibility for this Cree community to identify and treat further cases of juvenile hemochromatosis.

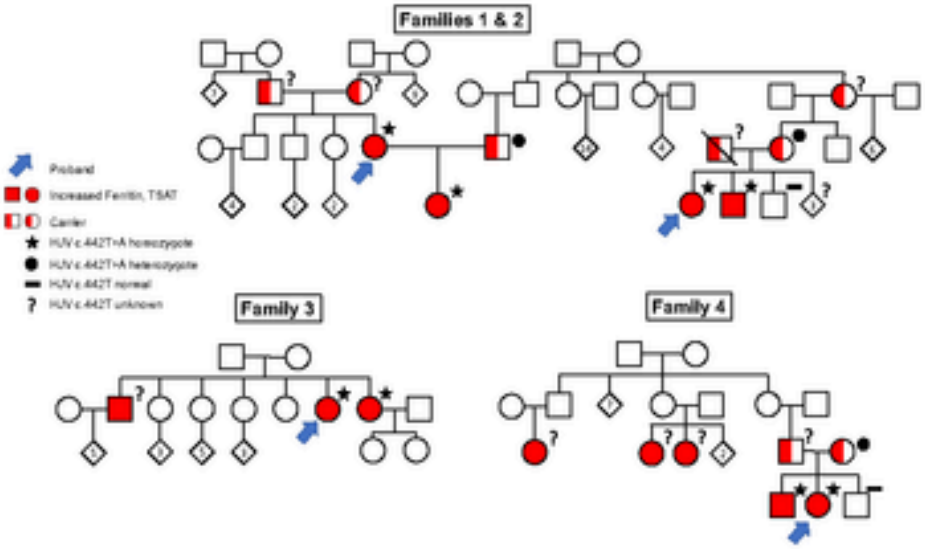


Figure 1. Family pedigrees summarizing the inheritance of c.442T>A homozygous juvenile hemochromatosis in an Indigenous population in Northern Alberta.

Table 1. Summary of pertinent investigations for juvenile hemochromatosis in confirmed c.442T>A homozygous individuals (n = 7).

Demographics				
Age Range (yr)	17 – 57			
Age At Diagnosis (Mean ± SD; yr)	21.6 ± 10.7			
Sex (*n*, %)	Male: 2 (28.6%), Female: 5 (71.4%)			
Disease Characteristics	**# Abnormal**	**Rate Abnormal**	**Range**	**Details**
Ferritin at Diagnosis (µmol/L)	7	100%	378 – 6679	
TSAT at Diagnosis (%)	7	100%	92 – >96	
Phlebotomy Response	2	28.5%	n/a	Partial response (*n* = 1), Refractory (*n* = 1)
Cirrhosis Complications	1	14.2%	n/a	HCC (*n* = 1)
Investigations				
FibroScan (*n* = 7) (kPa)	4	57.1%	3.5 – 30.6	Abnormal = >7 kPa.
Abdominal Ultrasound (*n* = 6)	3	50.0%	n/a	Nodularity and splenomegaly (*n* = 1), moderate steatosis (*n* = 1), mild steatosis (*n* = 1)
EGD (*n* = 3)	2	66.7%	n/a	Large varices (*n* = 1) PHG (*n* = 2)
MRI Cardiac (*n* = 6)	0	0%	n/a	n/a
MRI Abdomen (*n* = 5)	4	80.0%	n/a	Mild Fe deposition (*n* = 3) Moderate Fe deposition (*n* = 2)

Note. HCC = hepatocellular carcinoma, PHG = portal hypertensive gastropathy, Fe = iron.

Pegloticase With Concomitant Immunomodulation in Patients With Gout and Chronic Kidney Disease: A Systematic Review

Aubrey Maltz, Eric Asgari, Ayub Akbari, Priyanka Chandratre
Supervisor: Dr. Priyanka Chandratre, Rheumatologist, The Ottawa Hospital

INTRODUCTION

Gout commonly co-occurs with chronic kidney disease (CKD), and management focuses on lowering serum uric acid (sUA) to target. Pegloticase is effective in refractory gout but limited by anti-drug antibody formation and infusion reactions. Concomitant immunomodulation may improve response to pegloticase, though some immunomodulators require caution in CKD, creating interest in outcomes across renal function. This study aims to evaluate the efficacy and safety of pegloticase with varying immunomodulation, including in the context of CKD.

METHODS

We searched MEDLINE, Embase, and Scopus in January 2025 for English-language studies of pegloticase with immunomodulation in gout which reported renal function. Duplicate datasets were grouped, longest follow-up prioritized for extraction, and studies without original data or non-stratified pooled immunomodulator data were excluded from analysis.

RESULTS

260 patients from 8 unique studies were analyzed. Response rates to pegloticase were highest early and declined over time, with methotrexate-treated patients showing 78.9% response at 6 weeks–3 months and 61.2% at 12 months. Methotrexate was the most commonly used immunomodulator. sUA reductions ranged from 6.0 mg/dL in the mycophenolate cohort to 8.5 mg/dL in transplant immunosuppression patients. Renal function remained stable, with mean eGFR changes of +5.0 mL/min/1.73 m^2 in methotrexate-treated patients and −2.5 mL/min/1.73 m^2 in transplant cohorts. Infusion reactions were uncommon and occurred most often with methotrexate (6/196 patients), while serious adverse events were most frequent in the transplant immunosuppression patients (9/27 patients).

CONCLUSIONS

Pegloticase with immunomodulation maintains high response rates with preserved kidney function and has been most studied with methotrexate. Available data are limited by small sample sizes, heterogeneous designs, and limited renal outcome reporting. Larger prospective studies with standardized renal endpoints and longer follow-up are needed to define safety and efficacy in gout and CKD.

Immunomodulation	n	Included studies	Baseline eGFR (mL/min/1.73m²)	Baseline sUA (mg/dL)	Response rate (6 weeks–3 months)	Response rate (3- 6 months)	Response rate (6-9 months)	Response rate (9-12 months)	Mean sUA decrease (mg/dL)	eGFR change during follow up (mL/min/1.73m²)	Infusion reactions, n	SAE, n
Methotrexate (newly initiated)	196	5	71.1	8.93	78.9	78.3	69.2	61.2	7.33	5.0	6	14
Leflunomide (newly initiated)†	10	1	NR	7.07	NR	70.0	NR	NR	6.2	NR	NR	2
Mycophenolate (newly initiated)	25	2	81.3	8.9	87.7	68.0	NR	NR	6.0	NR	0	2
Azathioprine (newly initiated)†	2	1	NR	NR	50.0	NR	NR	NR	7.6	NR	NR	NR
Chronic transplant immunosuppression*	27	2	45.8	9.4	90.0	80.0	NR	NR	8.5	**-2.5**	0	9

Table 1: Clinical outcomes of pegloticase with concomitant immunomodulation in patients with gout

Response rate: Percent of patients with serum uric acid <6 mg/dL at the specified time point or <6 mg/dL for ≥80% of the time within the specified interval, as reported in the original study.
Included studies: Number of studies reporting original data included in the analysis for respective immunomodulation strategy
sUA: Serum uric acid, mg/dL.
eGFR: Estimated glomerular filtration rate, mL/min/1.73 m².
Infusion reactions, n: Number of patients with infusion reactions.
SAE, n: Number of patients with serious adverse events.
NR: Data not reported.

† There was a paucity of data describing long-term response rates especially for azathioprine and leflunomide, in part related to small sample sizes and limited structured real-world data involving usage of these immunomodulations with pegloticase.
*Chronic transplant immunosuppression: 63% of cohort were exposed to mycophenolate, 48.1% were exposed to tacrolimus, 37% were exposed to cyclosporine, 18.5% were exposed to azathioprine, and 3.7% were exposed to sirolimus

Chronic airway inflammation is associated with sex-specific changes in behaviour, neuroinflammation and gut microbiota

Shivani Mandal, Marie Armbruster, Ritu Mann-nuttel, Paul Forsythe
Supervisor: Paul Forsythe

INTRODUCTION
Asthma is a chronic inflammatory lung disease linked to a higher prevalence of comorbid depression, though the underlying pathophysiology and the influence of biological sex remain poorly understood. To investigate this complex relationship, we employed a chronic airway inflammation mouse model, examining the sex-dependent effects of allergic airway inflammation across systemic, neuroimmune, behavioural, and gut microbiome axes.

METHODS
Male and female C57BL/6 mice received house-dust-mite (HDM) extract or PBS intranasally for 8-weeks (n=14/group). Airway inflammation was evaluated by lung histopathology, and systemic inflammation by serum cytokine profiling. Neuroinflammatory changes were assessed by RNA-sequencing, immunofluorescence and qPCR targeting mast cells, microglia, and astrocytes—regulators of neuroinflammation. Depression-like behaviors were assessed by splash test (grooming) and tail suspension test (behavioural despair) and microbiota composition of small and large intestines by 16S rRNA sequencing. Data were analyzed using two-way ANOVA (mean ± SEM).

RESULTS
HDM induced hallmark features of airway inflammation in both sexes. While females exhibited elevated levels of most measured airway and systemic inflammatory cytokines compared to males, the neuroinflammatory and behavioural changes were more pronounced in males. HDM-exposed males showed increased hippocampal microglial activation($p<0.01$), enhanced mast cell presence($p<0.01$), and widespread hypothalamic transcriptional alterations. Females, however, exhibited increased astrocytic activation($p<0.01$) and enrichment of the estrogen response pathway (FDR=0.044) suggesting a differential, potentially protective, glial responses. Behaviorally, males displayed reduced grooming($p<0.01$) and greater behavioural despair($p<0.01$), consistent with depressive-like phenotypes, whereas females showed reduced grooming only($p=0.04$). Parallel analyses revealed that males experienced more extensive gut microbial disruption, particularly in the small intestine, including reductions in taxa previously associated with depressive behaviors (Romboutsia, Turicibacter) and broader shifts in microbial metabolic pathways.

CONCLUSIONS
The observation that males, despite lower systemic inflammation, exhibit greater neuroinflammatory signatures, hypothalamic changes, and behavioural deficits underscores the necessity of a sex-informed approach to understanding and mitigating the neuropsychiatric sequelae of chronic allergic asthma.

Untargeted Metabolomics of Human Airway Epithelium Reveals Neuroactive Signatures Linked to Pulmonary Neuroendocrine Cell Enrichment and Allergen Exposure

Ritu Mann-Nüttel, Ayshna Diya and Paul Forsythe
Supervisor: Paul Forsythe

INTRODUCTION

Pulmonary neuroendocrine cells (PNECs) are rare airway sensory cells implicated in amplifying allergic inflammation, yet due to their scarcity the contribution of PNECs to metabolic programs and responses of the airway epithelium remain poorly defined. Using a newly developed PNEC-enriched human airway epithelial model (ePNEC), we investigated the influence of PNECs on neuroendocrine and immune-modulatory metabolite production in response to the common aeroallergen, House dust mite (HDM).

METHODS

Human bronchial epithelial cells (HBECs) and ePNEC cultures were differentiated at air–liquid interface. Global untargeted metabolomics was performed to quantify metabolite abundance at baseline and following stimulation with HDM. Differential expression, overlap significance, metabolite class enrichment, and pathway analyses were used to define PNEC-specific metabolic programs.

RESULTS

PCA demonstrated strong baseline separation between ePNECs and HBECs, with HDM inducing additional within-cell-type shifts. ePNECs displayed broader and more pronounced metabolite changes than HBECs. Baseline differences were largely preserved following allergen exposure, with significant overlap in both up- and down-regulated metabolites. ePNECs exhibited enriched neurotransmitter-linked metabolites—including serotonin, L-noradrenaline, dopamine, and histamine—at baseline and after HDM. Amino acid–centered metabolism dominated the dataset, with enhanced histidine and tryptophan pathway activity in ePNECs. Pathway analysis revealed significant enrichment of phenylalanine, tyrosine, tryptophan, glutathione, and arginine–proline metabolism in ePNECs, whereas HBECs showed no significant pathway-level enrichment after HDM.

CONCLUSIONS

Human ePNECs engage a distinct, neuroactive metabolic program that is amplified upon HDM exposure. These findings provide a metabolic framework for how PNECs shape epithelial and neuroimmune responses to inhaled allergens.

Sacubitril suppresses allograft vasculopathy in aged-donor heart allografts by expanding reparative endothelial progenitor cells

Andrew G. Masoud 1,2, Kesheng Tao 2,3, Lori West 2,3, Gavin Y. Oudit 1,4, Allan G. Murray 1,2. 1.Department of Medicine, University of Alberta, Canada. 2.Alberta Transplantation Institute 3. Pediatrics Dep 4. Mazankowski Health Institute, AB, Canada
Supervisor: Dr. Allan Murray

INTRODUCTION
Chronic allograft vasculopathy (CAV) remains the primary barrier to long-term graft and recipient survival following heart transplantation. Aged-donor organs exhibit increased vulnerability to this maladaptive remodeling versus young-donor grafts. The proangiogenic peptide, apelin, protects against CAV and is degraded by neprilysin. We investigated the therapeutic potential of sacubitril, a neprilysin inhibitor, to mitigate CAV following aged-donor transplantation.

METHODS
HY-antigen-mismatched, apelin-knockout or 1-year-old (aged)-donor hearts were transplanted into recipient mice. Pilot studies established that untreated aged grafts develop advanced luminal obliteration by 3 weeks post-transplantation. Experimental groups received daily oral sacubitril, or vehicle control, from post-operative week 1. At week 3, the grafts were harvested and analyzed for luminal occlusion, markers of endothelial regeneration, and fibrosis.

RESULTS
Sacubitril treatment blunted the progression of coronary arterial occlusion (75.89 ± 1.2 vs. 16.82 ± 2.6 %; $P<0.01$) and reduced overall myocardial fibrosis compared to vehicle-treated aged controls. Young donor grafts display increased endothelial progenitor cell (EPC) marker expression in arterial profiles vs. non-transplanted donor hearts. Apelin-deficient grafts show accelerated CAV and failed EPC expression. Aged donor grafts also fail to induce EPC marker expression; however, sacubitril treatment rescues EPC abundance.

CONCLUSIONS
Sacubitril limits maladaptive vascular repair and CAV progression in aged heart allografts. Protection is associated with increased EPC abundance, and is linked to the apelin signaling axis. These results suggest that sacubitril may be a viable therapeutic strategy to improve outcomes for recipients of marginal, aged-donor hearts.

An exploratory analysis of Glycome, Microbiome, and Immune Changes in Patients with Recurrent Clostridioides Difficile Infection (rCDI) Treated with Donor Stool-Based Therapies

Ali Nabavi Rad, Christopher Cheng, Chelsea McDougall, Rose Franz, Karen Wong, Lara Mahal, Dina Kao
Supervisor: Dr. Dina Kao

INTRODUCTION

Although fecal microbiota transplantation (FMT) is highly effective in preventing recurrent Clostridioides difficile infection (rCDI), the mechanisms of action remain incompletely understood. Glycome profiling analyzes the complex carbohydrates (glycans) found on the surface of bacteria and within the human gut, which can be used to study the dynamic interaction between host immune system and microbiota. We aimed to compare the changes in stool glycomics between successful (ie. with no CDI recurrenc) versus failure (ie. with recurrence) outcomes in rCDI patients following microbiome-based interventions, and correlated these results with stool cytokine profile and microbial composition.

METHODS

We completed a randomized clinical trial comparing the efficacy of 2 donor stool based formulations for rCDI: lyophilized FMT (LFMT) contains live bacteria while lyophilized sterile fecal filtrate (LSFF) does not. A successful outcome was defined as no CDI recurrence 8 weeks after intervention. Stool samples from 39 patients in the LFMT group (34/39 without CDI recurrence) and 39 patients in the LSFF group (24/39 without CDI recurrence) at baseline (W0) and 1 weeks (W1) after treatment were chosen for the analysis to characterize early changes during rCDI resolution. The fecal glycome profile was assessed by lectin microarray, fecal cytokine profile by a customized panel of 13 cytokines using ELISA assay, and fecal bacterial community compositions by 16S rRNA gene sequencing. Paired T-test analysis was used to assess the significant changes from W0 to W1 in glycome and cytokine profiles. Variable Importance in Projection (VIP) was utilized to identify the specific bacterial taxa most responsible for differentiating between success and failure outcomes.

RESULTS

In the LFMT group, patients without rCDI had a statistically significant reduction in terminal sialylation and fucose/O-glycans at week 1 compared to those with recurrence (Fig 1A, left panel). In the LSFF group, patients without recurrence had increased terminal N-acetylglucosamine structures compared to those with recurrence (Fig 1A, right panel). Statistically significant changes in cytokine levels from W0 to W1 were observed in those without recurrence and more prominent in the LFMT group. Specifically, IL-1RA and IL-27 were significantly increased in both treatment groups, but IL-17A, IFN-γ, and TNF-α were only significantly elevated in the LFMT group (Fig 2). Regardless of treatment group, predominant microbial changes included increased relative abundance of Butyricicoccaceae, Eggerthellaceae, and Lachnospiraceae, and reduced abundance of Lactobacillaceae in those without CDI recurrence and higher relative abundance of Clostridiaceae in those with recurrence (Figure 1B).

CONCLUSIONS

Prominent glycomic alteration and immune activation are observed in those without CDI recurrence following LFMT compared to LSFF treatment, as well as in those with success compared to failure outcomes. This may suggest that rCDI resolution is achieved through different mechanisms between these 2 treatments, including different mucosal carbohydrate remodeling pathways, and these changes are observed as early as at week 1. These observations need to be validated in a larger cohort.

Targeting Triose Phosphate Isomerase Function to Preserve Ex-Situ Heart Performance, Implications for Cardiac Transplantation

Joseph Nanoa, Sanaz Hatami, Maria Areli Lorenzana-Carrillo, Saymon Tejay, Yuan-Yuan Zhao, Liyan Zhang, Dawn E. Bowles, Evangelos D. Michelakis, John R. Ussher, Seyed Amirhossein Tabatabaei Dakhili, Darren H. Freed and Gopinath Sutendra
Supervisor: Dr Gopinath Sutendra

INTRODUCTION

Cardiac transplantation remains the gold standard therapy for end-stage heart failure; however, many patients die awaiting a transplant, partly due to the limited supply of available useable donor hearts. Normothermic ex-situ heart perfusion (ESHP, i.e., heart in a box) is a novel method to preserve and increase the available time of usable donor hearts (for transplantation) but its function declines after~ 7hrs by a yet unknown mechanism. We hypothesized the decrease in cardiac function from ESHP may be due to a decrease in the metabolic flux from glucose (a prominent metabolic fuel) to pyruvate, the substrate for oxidative phosphorylation in the mitochondria, required for ATP synthesis and optimal cardiac performance.

METHODS

Cardiac -specific ZNF281 overexpression mice were used to assess the role of ZNF281 on cardiomyocyte function. ZNF281 Interfering Molecule (ZIM) was developed to inhibit the interaction of ZNF281 with triose phosphate isomerase (TPI). Explanted human and swine hearts were perfused for both vehicle and ZIM treated groups and cardiac function were assessed at different timepoints.

RESULTS

We found that upon explantation, the integrated stress response pathway is activated, which results in the acute cytoplasmic translation of the stress-response Zn2+ finger protein ZNF281. We found that ZNF281 (in cardiomyocytes from cardiac-specific ZNF281 overexpression transgenic mice) can preferentially bind the glycolytic enzyme triose phosphate isomerase (TPI), decreasing its enzymatic activity and the levels of its glycolytic product glyceraldehyde-3-phosphate (G3P), an intermediate that can eventually increase the levels of pyruvate, and subsequently mitochondrial ATP. At the same time inhibition of TPI increases the levels of a toxic glycolytic byproduct, methylglyoxal (MG) that can promote calcium overload and inefficient contractility. Disruption of ZNF281 and TPI interaction with ZIM (a novel compound that our team generated), promotes complete glucose metabolism (and ATP production) and significantly improves ESHP function at 7hrs and beyond.

CONCLUSIONS

Our findings provide an alternative technology for increasing the donor pool of useable hearts, that is desperately needed.

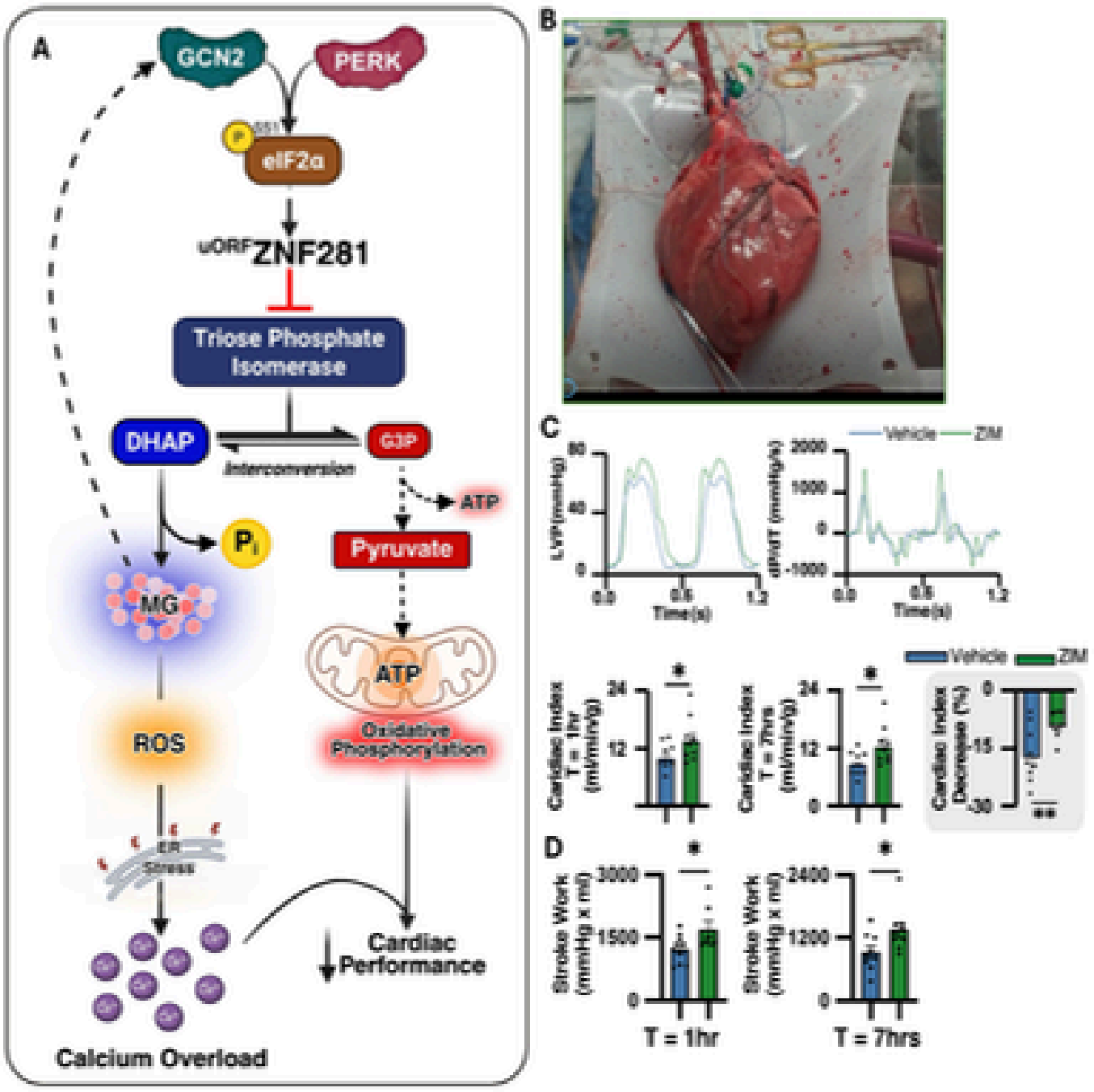


Figure 1

a, Prolonged ESHP activates stress kinases PERK and GCN2, which phosphorylate eIF2α, leading to uORF-selective translation of ZNF281. ^{uORF}ZNF281 represses triose phosphate isomerase (TPI), limiting the interconversion of dihydroxyacetone phosphate (DHAP) and glyceraldehyde-3-phosphate (G3P). As a result, DHAP accumulates and is diverted toward methylglyoxal (MG) production, generating reactive oxygen species (ROS) and calcium overload. Reduced pyruvate entry into oxidative phosphorylation further impairs ATP generation, ultimately leading to diminished cardiac performance during ESHP. **b,** Picture of the ex-situ heart perfusion setup where the aorta and pulmonary artery are cannulated and ex-situ cardiac function is measured by electrical probes. **c,** Ex-situ heart performance (ESHP) in swine hearts treated with vehicle or ZIM. Representative tracings of left ventricular pressure (LVP, left) and dP/dt (right) are shown, along with quantification of cardiac index at 1 hour and 7 hours, and percent decrease in cardiac index over time. Quantification values are represented as mean ± SEM from n = 9 per group. *P <0.05, **P<0.01 compared to vehicle and based on Mann Whitney U test. **d,** Explanted swine hearts perfused with ZIM were compared to control at different times (1hour and 7hours) to assess stroke work (a parameter for cardiac function). Quantification values are represented as mean ± SEM from n = 9 per group. *P <0.05 compared to vehicle and based on Mann-Whitney U test.

Analysis of Long Term Outcomes in Crohn's Patients Post-Balloon Assisted Endoscopic Stricture Dilation: Factors Associated with Surgery and a New Predictive Model

Kunihiko Oguro, Joel C Bowron, Qiming Tan, Muhammad Anas Fazal, Denise Parsons, Farhad Peerani, Michal Gozdzik, Karen Wong, Karen Kroeker, Frank Hoentjen, Shawn Wasilenko, Sergio Zepeda-Gomez, and Brendan Halloran
Supervisor: Dr. Brendan Halloran

INTRODUCTION
Crohn's disease (CD) has a hallmark of the formation of intestinal strictures that may require surgical resection. In patients undergoing successful balloon dilation, factors predicting the need for surgery are poorly understood. This study aims to identify predictors and develop a predictive model for the need for surgery after endoscopic balloon dilation (EBD) in CD patients with small bowel strictures.

METHODS
A retrospective review of CD patients ≥ 18 years of age who underwent one or more BAE with small bowel stricture dilations between January 2012 and January 2024 was conducted at the University of Alberta Hospital. Univariate and stepwise multivariate logistic regression analyses were performed to identify factors predicting need for surgery.

RESULTS
Outcomes for 134 patients who underwent a total of 353 BAEs with stricture dilations were analyzed. Of the 134 patients, 45 (33.6 %) underwent surgery. The mean number of BAEs performed per patient was 2.6. Univariate logistic regression analysis showed active inflammation (OR = 1.36, p = 0.045), non-traversable stricture(s) (OR = 3.55, p = 0.005), and minimum dilation diameter (OR = 0.75, p = 0.0003) were significantly associated with the need for surgery. In stepwise multivariate logistic regression modelling, the variables of significance were age, biologics use, active inflammation, minimum dilation diameter, number of BAEs performed, number of dilations performed for de novo strictures, and presence of a non-traversable stricture. This model demonstrated a bootstrap-corrected area under the curve (AUC) of 0.72. A minimum achieved dilation diameter of 13.5 mm was the optimal cutoff value distinguishing patients who required surgery from those who do not.

CONCLUSIONS
This analysis identifies potentially useful predictors of the need for surgery in CD patients with small bowel strictures. A minimum dilation diameter of 13.5 mm may represent an important therapeutic target to avoid surgery.

Prioritizing Modifiable Risk Factors for Self-Management of Urinary Incontinence in Older Men: Integrating Expert Consensus with Patient Readiness

Olawunmi Olagundoye, Thomas F. Monaghan, William Gibson, Adrian Wagg
Supervisor: Dr. Adrian Wagg

INTRODUCTION
Urinary incontinence (UI) affects up to one-third of men aged ≥65 years, yet tailored self-management strategies remain limited. Interventions targeting modifiable risk factors may improve outcomes, but little is known about which are both clinically relevant and behaviorally feasible. This study combined expert consensus with older men's perspectives to prioritize modifiable UI risk factors previously synthesized through a scoping review.
Objectives:
Identify UI risk factors amenable to self-management in older men.
Assess older men's self-efficacy in managing UI.
Determine which modifiable factors older men feel capable and willing to change.

METHODS
We conducted a sequential multi-methods study: a Delphi survey with continence care experts followed by a cross-sectional survey of community-dwelling men aged ≥65 with UI. Reporting adhered to the Guidance on Conducting and Reporting Delphi Studies (CREDES) and the Checklist for Reporting Of Survey Studies (CROSS) checklists Experts rated the importance and modifiability of evidence-informed risk factors, with consensus defined as ≥75% agreement. Older men reported willingness and capability to modify expert-identified factors and completed the Geriatric Self-Efficacy Index for Urinary Incontinence (GSE-UI).

RESULTS
Experts (n=32 in round 1; n=20 in final round) reached consensus on 19 clinically important and modifiable risk factors, spanning medical (obesity, constipation, diabetes) and behavioral (smoking, alcohol, caffeine) domains. Older men (mean age 77.6 years) reported moderate self-efficacy (overall GSE-UI - 51.0 ± 35.9), with lower confidence in socially or physically challenging situations. No single risk factor met all criteria of high prevalence, willingness, and capability. Anxiety and obesity approached thresholds for both prevalence and readiness, suggesting broad-reach targets, while less prevalent but actionable factors (e.g., constipation, diabetes, voiding symptoms) may suit individualized interventions.

CONCLUSIONS
A mismatch exists between clinically modifiable UI risk factors and patient-reported readiness to change. Integrating expert and patient perspectives provides a patient-centered framework to guide prioritization of self-management interventions for older men with UI.

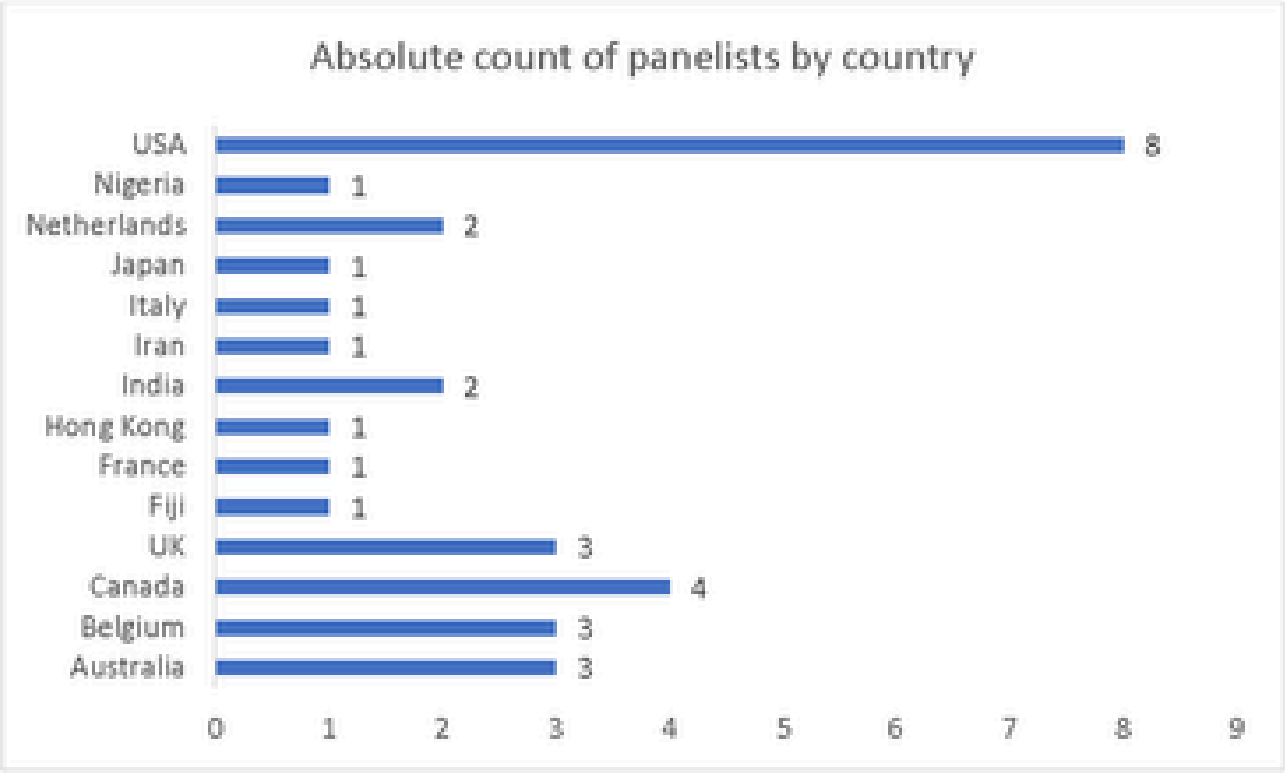


Figure 2: Geographical distribution of Delphi panelists

Behaviour change techniques in eHealth interventions for older, frail, or sarcopenic adults: A systematic review and meta-analysis

Ayushi Omkar, Jennifer Bertrand, Chikku Sadasivan, Emma Osness, Ben Vandermeer, Liz Dennett, Xiaoxu Ding, Julian Mansour, Victor Ezeugwu, Ashley Hyde, Puneeta Tandon
Supervisor: Dr. Puneeta Tandon

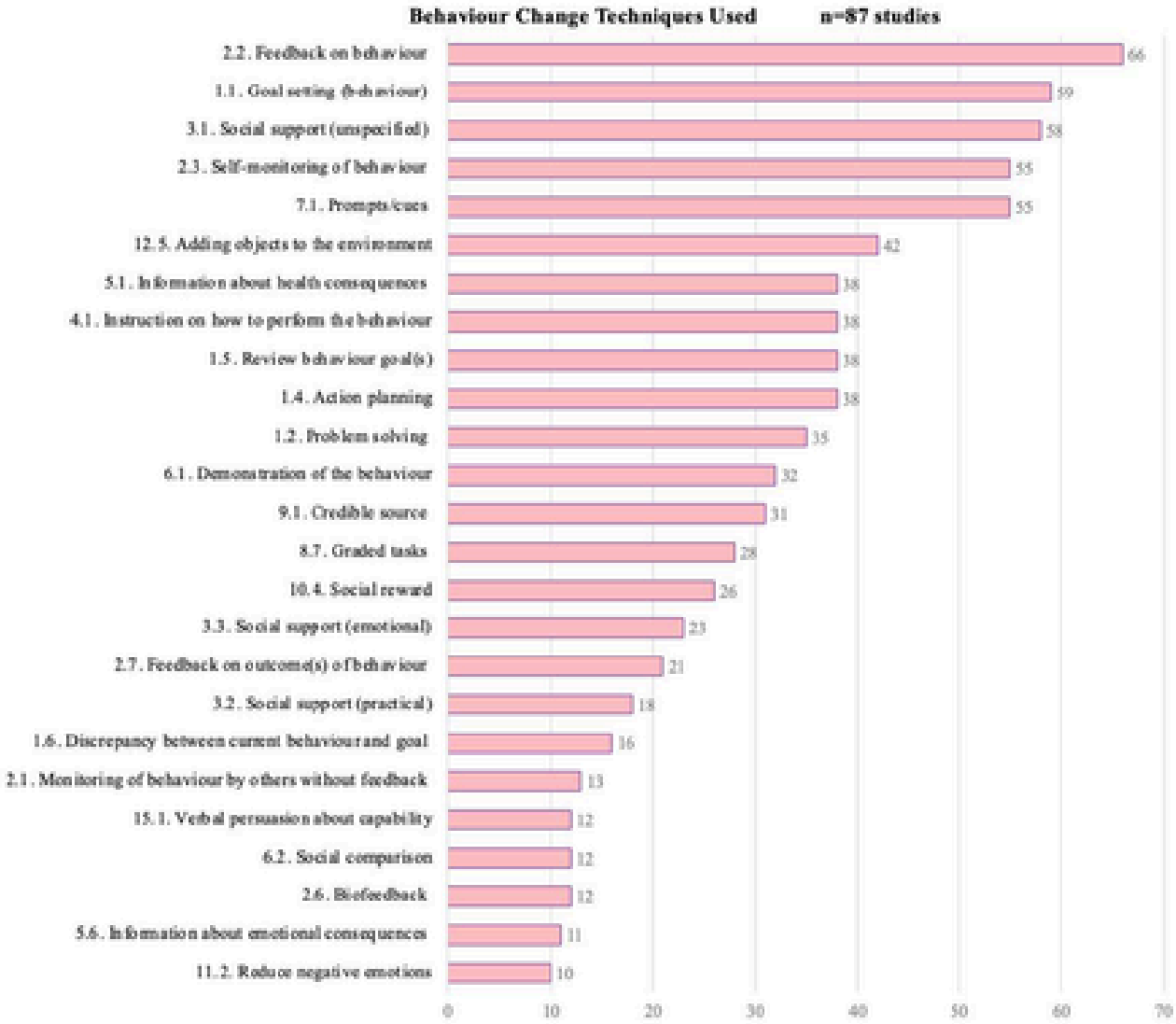
INTRODUCTION
Behaviour change techniques (BCTs) are key components of eHealth physical activity interventions. They may be especially important for older adults and individuals with frailty or sarcopenia, who often face additional barriers to sustaining physical activity. This review aimed to identify BCTs used in eHealth physical activity trials and examine which techniques are associated with greater effectiveness.

METHODS
Six databases (MEDLINE, Embase, CINAHL, CENTRAL, PsycINFO, and Scopus) were searched for randomized controlled trials (RCTs) published up to 2024. Eligible studies evaluated eHealth physical activity interventions delivered to older adults (mean age ≥60 years) or adults with frailty or sarcopenia. Trials delivered exclusively through virtual reality, wearable devices, or telephone-based modalities were excluded. Random-effects meta-analysis estimated pooled effects on physical activity, with subgroup analyses examining differences by BCTs and behavioural theory use. Completion, adherence, and adverse events were summarized descriptively.

RESULTS
Eighty-seven studies met inclusion criteria, and 53 contributed to the meta-analysis. eHealth interventions produced a small positive effect on physical activity (standardized mean difference = 0.20, 95% confidence interval: 0.05–0.34). Completion was generally high and adherence moderate, with few reported adverse events. The most frequently used BCTs were feedback on behaviour, goal setting, social support, prompts/cues, and self-monitoring. Subgroup analyses suggested larger effects for interventions incorporating feedback on behaviour and social support.

CONCLUSIONS
eHealth interventions yield modest improvements in physical activity among older adults, including those with frailty or sarcopenia. Feedback and social support appear promising for optimizing digital intervention design.

Figure 2. Most commonly used BCTs across interventions (n=87).



Advanced therapy experienced patients admitted for UC flare have a two-fold risk of colectomy compared to their advanced therapy naïve counterparts

Andrew Panteluk MD, Kaitlyn Chappell MSc, Michal Gozdzik MD, Karen Kroeker MD
Supervisor: Dr. Karen Kroeker

INTRODUCTION
Acute severe ulcerative colitis (ASUC) remains a significant source of morbidity and mortality for UC patients. Currently, infliximab (IFX) remains the mainstay guideline directed therapy for steroid non-responders with colectomy being reserved for patients with refractory disease and those with complications. With increasing numbers of advanced therapy (AT) options, and many patients now exposed to infliximab or other advanced therapies prior to flares, we wondered how this would impact a patient's risk of colectomy.

METHODS
We conducted a retrospective cohort study for patients admitted to University of Alberta Hospital for UC flare from Nov 2019 to Apr 2024 to assess the risk of colectomy between advanced therapy naïve (having never been exposed) and advanced therapy experienced (having been exposed to one or more advanced therapies prior to admission).

RESULTS
In total, we examined 213 admissions, 127 who were AT-naïve and 87 who were AT-experienced. AT-experienced patients were over two-fold more likely to undergo colectomy compared to AT-naïve with 17.2% compared to 7.9% respectively (RR 2.17, 95% CI 1.02-4.61). Strikingly, all of the AT-experienced patients who underwent colectomy had been exposed to infliximab prior to admission. Furthermore, we found that patients who had been exposed to infliximab + 2 or more therapies, had a much higher risk of colectomy compared to those trialed on fewer therapies.

CONCLUSIONS
Combined, these data show that patients with UC flare have an increased risk of colectomy if they have a history of infliximab use, especially when they have been treated with infliximab + 2 or more advanced therapies prior to admission. This information informs clinicians and patients when making treatment decisions for UC flare as well as numerous questions. Further studies about the role of Jak inhibitors in this patient population are needed, as very few patients (6%) in this study were exposed to these.

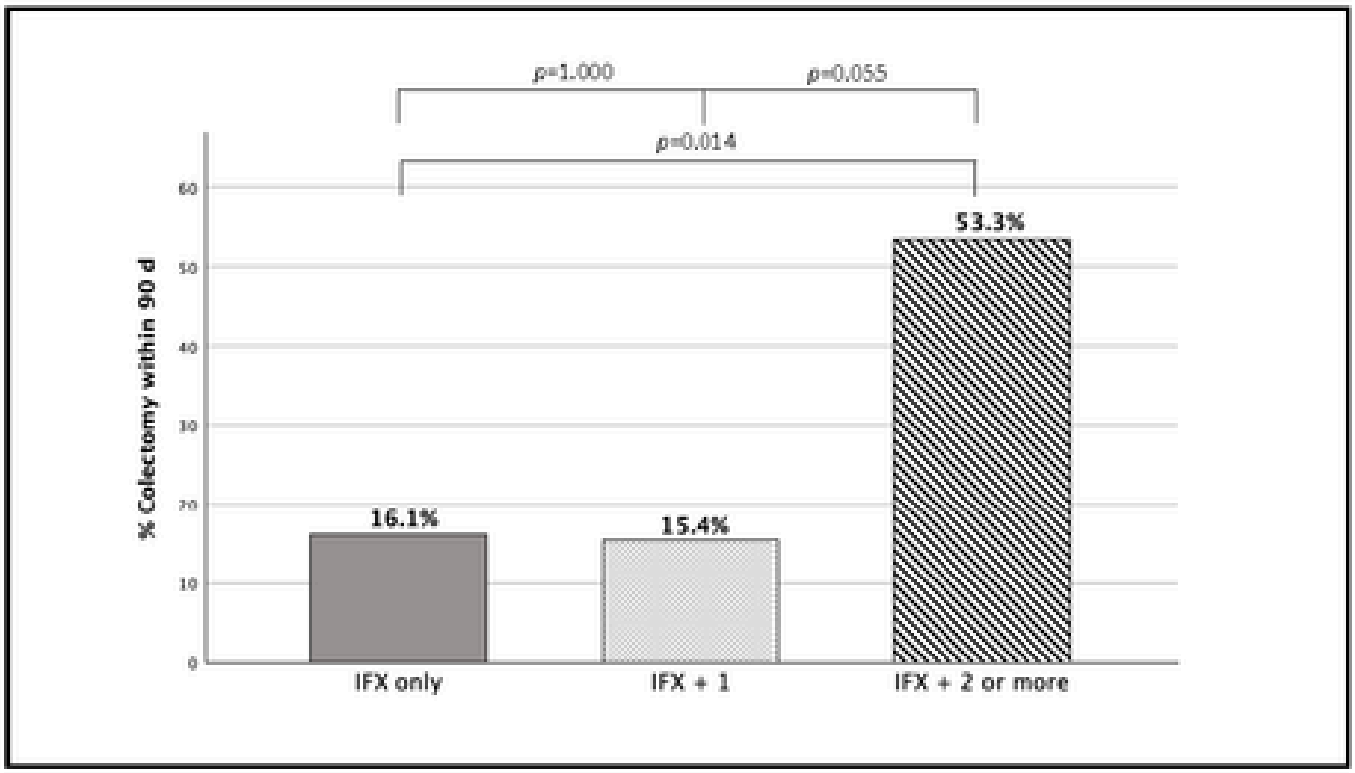


Figure 1. Comparison of colectomy percentages in patients who were infliximab (IFX)-exposed prior to admission. This includes patients who had only been exposed to IFX prior, IFX + 1 other advanced therapy (of any drug class), and IFX + 2 or more other advanced therapies prior to admission. *p*-values calculated using Fisher's Exact Test.

FROM SNAILS TO MAMMALS: A NOVEL INDUCER OF SNAIL HIBERNATION PROMOTES QUIESCENCE IN FIBROBLASTS AND CARDIOPROTECTION IN MOUSE HEARTS UNDER ISCHEMIA REPERFUSION STRESS

Jiyuan Piao, Yongneng Zhang, Yuan-Yuan Zhao, Patrick Hanington, Jacob Hambrook, Yongsheng Liu, John Ussher, Seyed Amirhossein Tabatabaei-Dakhili, Gopinath Sutendra, Evangelos D. Michelakis
Supervisor: Dr. Evangelos Michelakis

INTRODUCTION

A challenge in transplantation is the vulnerability of donor organs to ischemia-reperfusion (IR) injury during procurement and transport to recipients. We studied the molecular rewiring that allows hibernating animals to enter dormancy under stress, characterized by metabolic remodelling, autophagy, and resistance to IR injury. With unbiased metabolomics in a hibernating snail model, we identified a circulating small molecule dormancy-inducing factor, absent in human/mouse metabolomes. In silico modelling showed that it binds the phosphatase PHLPP1 (a regulator of the AKT and mTORC1/S6K1 fuel-sensing networks), inducing its activation. We chemically synthesized it and named it Snail Activator of PHLPP1 (SNAP). Multiple biochemical assays and mutagenesis of its binding sites revealed SNAP specifically activates PHLPP1 and no other phosphatases. In an in vitro model of IR stress, SNAP induced quiescence in mouse fibroblasts, with G0/G1 cell-cycle arrest, enhanced autophagy, suppressed proteo-synthesis and apoptosis; in contrast to the vehicle, which allowed death or senescence. During IR stress, plasma membrane PHLPP1 and p-AKT translocated to the cytoplasm and mitochondria, where SNAP dephosphorylated the PHLPP1 targets p-AKT and p-S6K1. In vitro cardiomyocyte and ex vivo heart IR models (mimicking the stress of hearts offered for transplantation en-route to a recipient), SNAP was cardioprotective, inducing a hibernation-like state. SNAP preserved Pyruvate Dehydrogenase (PDH) activity, prevented mitochondrial depolarization and apoptosis, and suppressed ROS-induced endoplasmic reticulum stress. These effects were absent in cells or hearts lacking PDH. By pharmacologically inducing a stress-tolerance state found only in hibernating animals, SNAP (the first known PHLPP1 activator) provides a novel strategy for organ preservation and new insights in stress biology, since, although mice/humans lost the ability to hibernate in evolution, PHLPP1 is widely conserved.

METHODS

Please see above.

RESULTS

Please see above.

CONCLUSIONS

Please see above.

RESTORATION OF OXIDIZED PHLPP1 ACTIVITY BY A SNAIL HIBERNATION INDUCING FACTOR REVERSES AGE-RELATED METABOLIC REWIRING IN MAMMALIAN CELLS

Jiyuan Piao, Yuan-Yuan Zhao, Yuxin Chen, Gopinath Sutendra, Evangelos D. Michelakis
Supervisor: Dr. Evangelos Michelakis

INTRODUCTION

A hallmark of aging is a progressive metabolic dysregulation of metabolism and stress response, in part due to oxidation-induced enzymatic dysfunction. The recently discovered phosphatase PHLPP1 is critical for metabolism and senescence as its targets include p-AKT, p-S6K and p-STAT1. Here, we report a novel mechanism driving cellular senescence through the oxidation of PHLPP1 which inhibits its function, failing to suppress the stress-induced pro-survival activation of these factors. We recently synthesized a first-in-class specific PHLPP1 activator, based on a hibernation-inducing factor we discovered in a snail hibernation model. SNAP (Snail Activator of PHLPP1) induced hibernation in snails (a state associated with decreased ageing rates), protected mice hearts from ischemia reperfusion injury (IRI) and induced quiescence (the cellular equivalent of hibernation) in IRI-stressed fibroblasts.

The phosphatase activity of human recombinant PHLPP1 was inhibited by H_2O_2. In silico GROMACS-simulation pinpointed two cysteine residues (C1082 and C1312) whose oxidation predicts conformational changes reducing catalytic activity. HPLC/MS/MS confirmed the oxidation (sulfonylation) of these two cysteines. Mutagenesis to amino acids that mimic sulfonylated cysteine confirmed the inhibition of normal PHLPP1 function. The binding site of SNAP did not include oxidation-prone cysteines (neighbouring Arginines), and as a result, SNAP was able to increase the activity of oxidized PHLPP1, re-establishing the oxidation-induced functional inhibition. In cellular models of H_2O_2-induced stress, SNAP prevented the onset of cellular senescence via elevating PHLPP1 activity and inhibition of its targets. SNAP- replenished the intracellular NAD^+/NADH and $NADP^+$/NADPH pools, elevating the GSH/GSSG ratio (all measured with mass spec), neutralizing the accumulation of ROS and significantly mitigating downstream DNA damage, confirmed by the Comet assay. SNAP decreased senescence markers in ROS-promoting IRI models of mouse fibroblasts in vitro.

By pharmacologically rescuing oxidized PHLPP1, SNAP may be a novel anti-aging intervention and suggests that the oxidation-prone PHLPP1 may be important in ageing biology and the promotion of quiescence, which characterizes stem cells central to rejuvenation strategies.

METHODS

Please see above

RESULTS

Please see above

CONCLUSIONS

Please see above

Dietary patterns and diet quality in adults with cirrhosis: a scoping review of clinical and nutritional outcomes

Danielle R. Picard, Tahira Shaikh, Christofer Cruz, Jack Bates, Puneeta Tandon
Supervisor: Dr. Puneeta Tandon

INTRODUCTION
Cirrhosis is frequently accompanied by malnutrition and poor clinical outcomes. Nutrition intervention is an important aspect of cirrhosis management, but the role of specific dietary patterns and diet quality on clinical outcomes remains unclear in this population. This scoping review aimed to map the existing literature on dietary patterns and diet quality in adults with cirrhosis, including methods of dietary assessment, use of diet quality indices, and associations with clinical and nutritional outcomes.

METHODS
This scoping review was conducted in accordance with PRISMA-ScR guidelines. A comprehensive search of MEDLINE, Embase, Scopus, and CINAHL identified studies published from 1946 to February 18, 2025. Eligible studies included adults with cirrhosis and assessed dietary intake in relation to clinical or nutritional outcomes. Data were extracted on study design, dietary assessment methods, diet quality indices, and reported outcomes.

RESULTS
The scoping review findings are preliminary and analysis is still underway. 48 studies across 20 countries were included, with 90% published since 2020. Most studies were observational (75%), including cohort (n=21) and cross-sectional designs (n=14). Dietary exposures were heterogeneous, and food-frequency questionnaires were the most commonly used assessment tool (48%). 21% of studies assessed diet quality or dietary patterns using established diet indices. Approximately two-thirds of studies assessed habitual dietary intake, while one-third evaluated dietary intake within intervention contexts.

Hepatic encephalopathy, mortality, and hospitalization were the most frequently reported outcomes. Across the studies included in this scoping review, plant-based and DASH-style dietary patterns and higher total antioxidant capacity tended to be associated with more favorable survival-related outcomes, whereas higher dietary inflammatory potential, greater dietary acid load, and higher intake of less healthy plant-based foods tended to be associated with less favorable outcomes. Across studies, baseline energy and protein intake were inconsistently reported.

CONCLUSIONS
This scoping review highlights substantial heterogeneity in dietary assessment and a limited use of validated diet quality indices in cirrhosis research. Overall, poor diet quality was associated with adverse clinical and nutritional outcomes. These findings underscore the need for standardized dietary assessment approaches and the development of cirrhosis-specific dietary pattern frameworks to inform clinical care and future interventions.

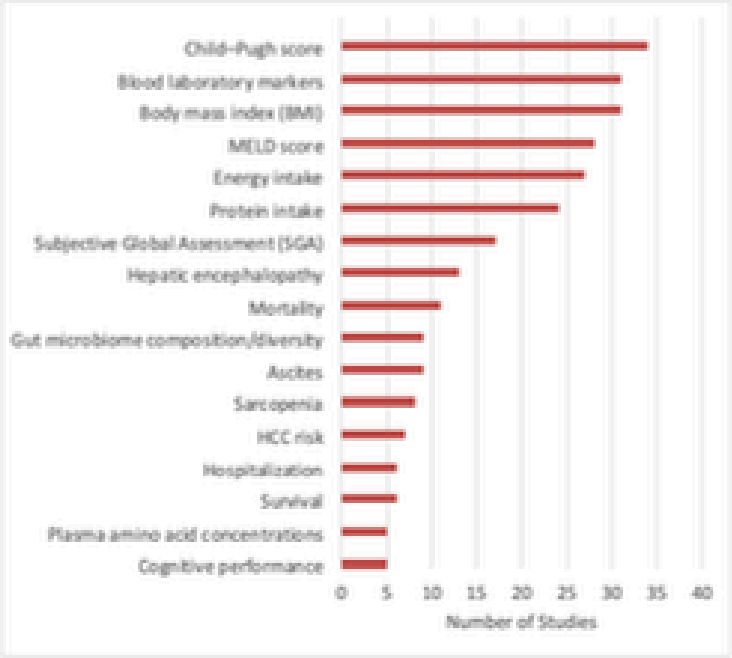


Figure 1. Frequency of clinical, nutritional, and mechanistic outcomes assessed across included studies. Bars represent the number of studies reporting each outcome.

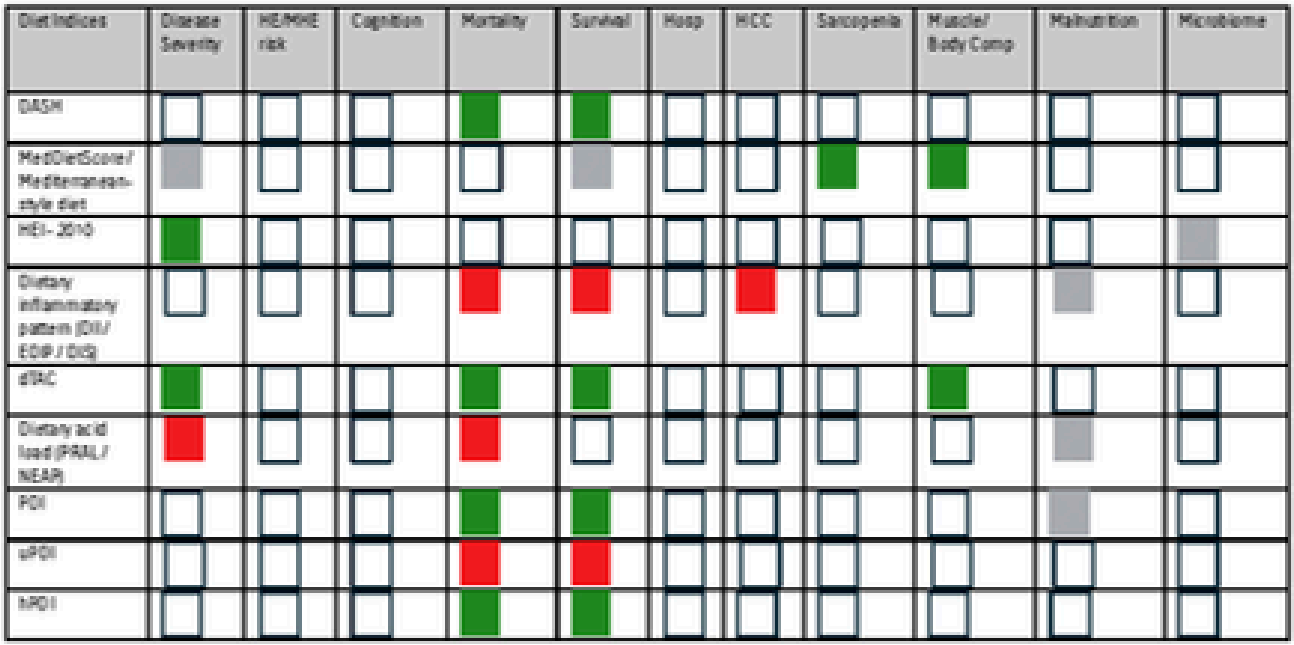


Figure 2: Evidence map of associations between dietary indices and clinical outcomes in adults with cirrhosis

Green squares indicate statistically significant associations with favourable clinical outcomes, while red squares indicate significant associations with adverse outcomes. Grey squares represent non-significant findings, and white squares indicate outcomes not assessed in the included studies. Associations reflect reported relationships and do not imply causality. Abbreviations: Body Comp = Body composition; DASH = Dietary Approaches to Stop Hypertension; DIS = Dietary Inflammatory Score; dTAC = Dietary Total Antioxidant Capacity; DII = Dietary Inflammatory Index; EDIP = Empirical Dietary Inflammatory Pattern; HCC = Hepatocellular carcinoma; HE = Hepatic encephalopathy; HEI-2010 = Healthy Eating Index-2010; Hosp = Hospitalization; hPDI = Healthy Plant-Based Diet Index; MedDietScore = Mediterranean Diet Score; MELD = Model for End-Stage Liver Disease; MHE = Minimal hepatic encephalopathy; NEAP = Net endogenous acid production; PRAL = Potential renal acid load; uPDI = Unhealthy Plant-Based Diet Index.

Accuracy of Dietitian-Estimated Dietary Intake in Patients with Cirrhosis Undergoing Liver Transplant Assessment

Danielle Picard, Poshika Dhingra, Tahira Shaikh, Jack Bates, Karen Attia, Christofer Cruz, Adedamola Bello, Puneeta Tandon
Supervisor: Dr. Puneeta Tandon

INTRODUCTION
Malnutrition is highly prevalent in cirrhosis and is associated with adverse clinical outcomes. Accurate assessment of energy and protein intake is essential for optimizing nutritional status prior to liver transplantation (LT). In clinical practice, dietitians often estimate intake from recalls or food records without validated analysis software, which may introduce systematic error. The objective was to evaluate the agreement between dietitian-estimated energy and protein intake and computerized nutrient analysis in patients with cirrhosis undergoing LT assessment.

METHODS
We conducted a retrospective chart review of adults with cirrhosis evaluated for LT (2019–2024). Dietitian-estimated energy and protein intakes were extracted from clinical documentation. Corresponding dietary recalls were analyzed using Food Processor® (v11.7). Agreement between methods was assessed using two-way mixed-effects intraclass correlation coefficients (ICC, absolute agreement) with 95% confidence intervals (CI). Analyses were conducted using complete paired observations for each nutrient.

RESULTS
A total of 494 records were available; ICC analyses included 205 energy and 287 protein paired observations. Mean (SD) age was 56 (10) years, and 63% were male. Most patients were classified as SGA A (40%) or SGA B (49%), and 94% had a documented nutrition diagnosis. Dietitian-estimated intake was lower than computerized analysis for both energy (1619 vs 1767 kcal/day; 8% underestimation) and protein (69 vs 88 g/day; 22% underestimation). Agreement between methods was poor for both energy (ICC 0.32, 95% CI 0.19–0.44) and protein (ICC 0.35, 95% CI 0.18–0.49).

CONCLUSIONS
Dietitian-estimated dietary intake consistently underestimated energy and protein intake compared with computerized analysis, with poor agreement between methods. Improving access to validated nutrient analysis tools may enhance accuracy in dietary assessment, support individualized nutrition interventions, and enable more comprehensive evaluation of dietary quality in patients awaiting LT.

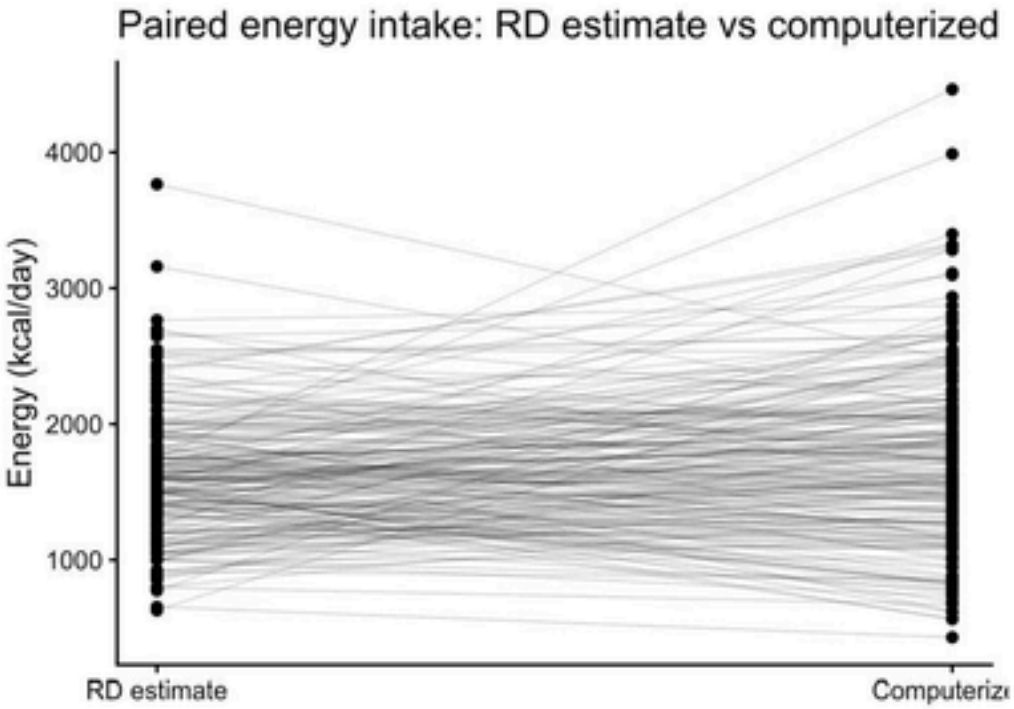


Figure 1. Dietitian-estimated vs computerized energy intake: paired participant-level comparison.
Dietitian estimates were lower than computerized analysis in most participants.

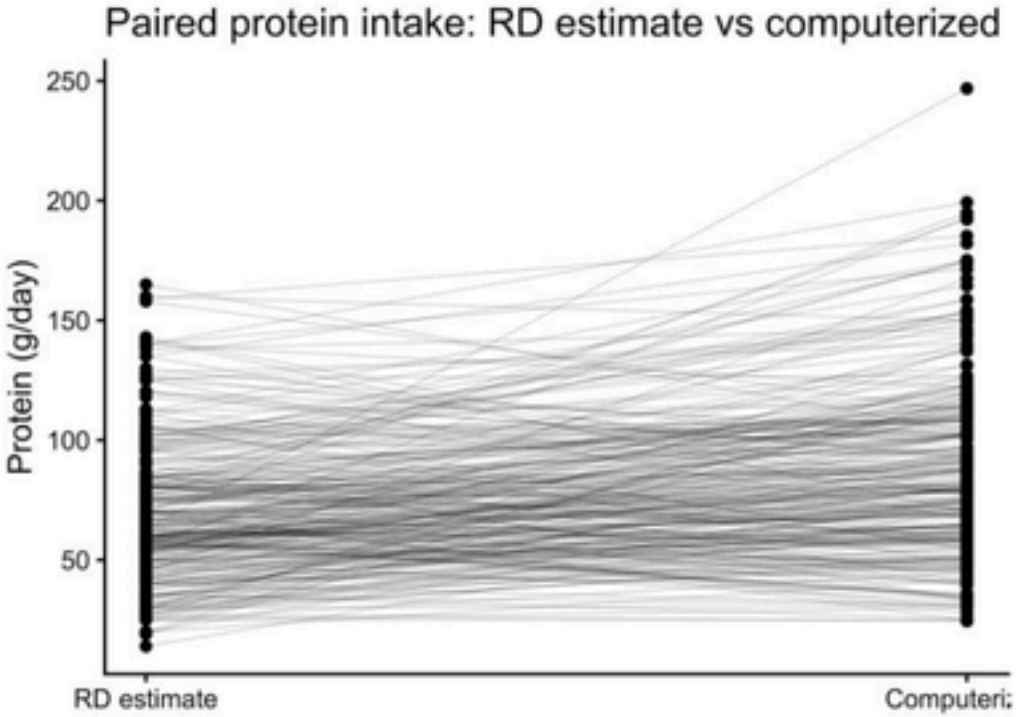


Figure 2. Dietitian-estimated vs computerized protein intake: paired participant-level comparison.
Dietitian estimates were lower than computerized analysis in most participants.

Heightened Vulnerability: Frailty and Aging Effects on the Ulcerative Colitis Mucosal Gut Microbiome

Cassandra Popoff, Dr. Guanmin Meng, Christopher Cheng, Dr. Karen Madsen and Dr. Farhad Peerani
Supervisor: Dr. Farhad Peerani

INTRODUCTION

Gut microbial composition plays a significant role in the pathogenesis of Ulcerative Colitis (UC). However, despite the rising prevalence of UC in individuals over 60, age-related differences in the gut microbiome remain underexplored. In addition, aging itself is associated with a pro-inflammatory state, which may be worsened by concomitant frailty.

METHODS

In this pilot study, we investigated the impact of aging and frailty on the gut microbiome of UC patients using colonic mucosal biopsies collected from adult (aged 18-40) UC patients with active (n=18) and inactive disease (n= 13), elderly (aged >60) UC patients with active (n=17) and inactive disease (n= 17) and healthy age and sex-matched controls (n=29). To minimize medication-related effects on the microbiota compositions, we ensured all participants were not receiving any immunosuppressive therapeutics. Frailty was characterized using the Clinical Frailty Scale. Microbial composition was characterized using 16S rRNA sequencing. Alpha diversity (Shannon, Simpson indices), beta diversity (Bray-Curtis) and differential abundance (DA) (ANCOM-BC, Lefse) analyses were performed.

RESULTS

DA analysis revealed a decrease in short chain fatty acid producing taxas and an increase of facultative anaerobes in the gut microbiome in elderly UC cohorts compared to adults. These pro-inflammatory microbiota shifts correlated further with the Clinical Frailty Scale, leading to more prominent changes as frailty increased. Specifically, along the increasing Clinical Frailty Scale, beneficial taxa (Bacillota, Clostridia, Faecalibacterium) decreased, and facultative anaerobes (Pseudomonadota, Enterobacteriaceae, Escherichia-Shigella) increased.

CONCLUSIONS

These findings indicate that frailty is associated with microbiome alterations that may further promote a pro-inflammatory environment in elderly UC patients. This study provides preliminary evidence supporting a role for age- and frailty-associated microbial changes in UC pathogenesis. Results highlight the need for larger studies to validate these associations with increased statistical power and ability to correct for possible confounders, in order to inform targeted therapeutic strategies.

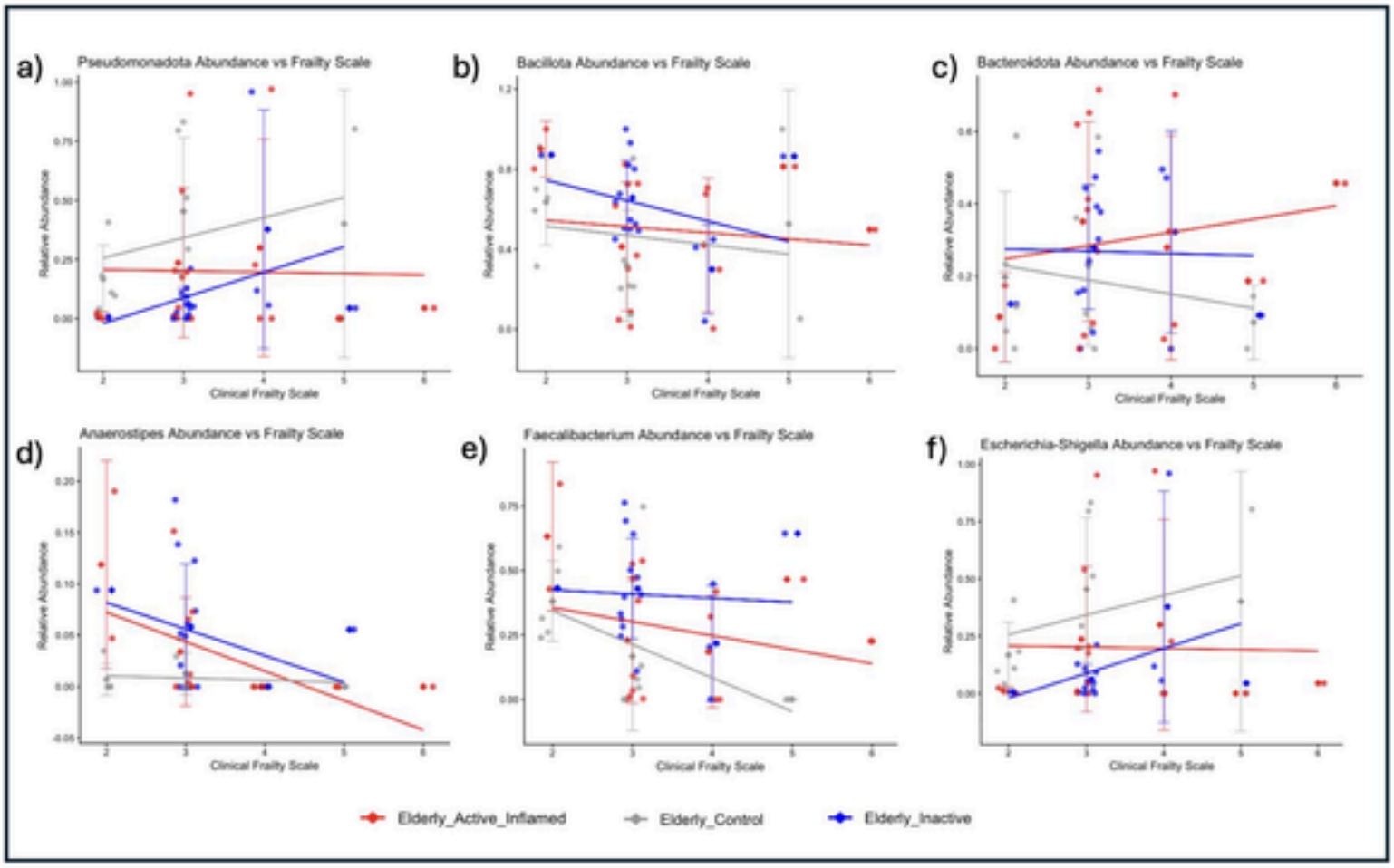


Figure 1. Frailty associated microbiota shifts occurring in the elderly ulcerative colitis gut microbiome.

Cell cortex proteins CLICs and taperin interact directly, but not at the cortex

Md Mizanur Rahman, Kevin Mac, Laiji Li, Barbara Ballermann, Richard Schulz, and Peter Hwang
Supervisor: Dr. Peter Hwang

INTRODUCTION

Taperin and CLIC5 are two proteins implicated in human deafness, co-localizing to the tapered stalk at the base of stereocilia in inner ear hair cells. According to Alphafold3, taperin is almost entirely intrinsically disordered, but it forms a structured helix-strand-helix-strand motif in residues 280-338 that is predicted with high confidence to extend the central β-sheet of the N-terminal thioredoxin domain of CLIC proteins. Our goal was to focus on the interaction between human CLIC4 and CLIC5A proteins with human taperin isoforms and to explore whether their interaction is important for their subcellular abundance.

METHODS

We conducted a yeast two-hybrid assay to demonstrate the direct interaction of CLIC4 or CLIC5A with taperin, and used confocal microscopy to study their subcellular colocalization.

RESULTS

We demonstrate that in HeLa cells, full-length taperin (1-711) localizes predominantly to the nucleus and to a lesser extent to the cell cortex. In contrast, GFP-CLIC5A appears predominantly at the cell cortex, as does GFP-CLIC4, though GFP-CLIC4 shows more general distribution throughout the cell. Heterologous co-expression of CLIC4/CLIC5A causes taperin (1-711) to disappear from the nucleus, and this appears to be due to increased degradation of taperin rather than a shift to the cytoplasm and cortex. Paradoxically, cortical RFP-CLIC4/5A does not co-localize GFP-taperin (307-711) or GFP-taperin (272-385), even though both truncated constructs are predicted to bind directly, as was confirmed by yeast two-hybrid assay. Taperin is targeted to the cortex not through direct interaction with CLICs, but rather through a sequence contained within taperin (1-306), which does not bind to CLICs.

CONCLUSIONS

Thus, taperin and CLICs do co-localize, but they are targeted to the cell cortex independently of each other.

The role of mutant p53R175H in de novo activation of von Willebrand factor expression in tumor cells

Noorossadat Seyyedi, Chu Shiun Lo, Parnian Alavi, Manijeh Pasdar, Nadia Jahroudi
Supervisor: Dr. Nadia Jahroudi

INTRODUCTION

The glycoprotein von Willebrand Factor (VWF) is essential for primary hemostasis and is normally expressed strictly in endothelial cells (ECs) and megakaryocytes. However, VWF is aberrantly expressed in some non-endothelial/megakaryocytic cancer cells. A cohort of transacting factors, including GATA6 (activator) and NF-1B (repressor), regulates VWF transcription. We previously showed de novo VWF expression in osteosarcoma cells linked to increased GATA6 and reduced NF-IB binding to the VWF promoter. NF-IB is a downstream target of transcription factor and tumor suppressor p53, which is frequently mutated in cancer. We have also shown that plakoglobin restores the tumor suppressive function of some p53 mutants, including p53R175H. Here we aimed to explore the role of p53 in de novo activation of VWF expression in cancer cells of non-endothelial/megakaryocytic origin.

METHODS

The analyses of 100 VWF-positive cancer cell lines revealed NF-IB downregulation and/or p53 mutation. Using p53-null and plakoglobin-deficient H1299 non-small cell lung carcinoma cell lines, we determined the effect of wild type and mutant p53 expression on VWF expression, and the molecular component contributing to this process.

RESULTS

Expression of p53R175H induced de novo VWF expression. Mechanistically, p53R175H interacted with NF-IB and GATA6, preventing NF-IB repressive and promoting GATA6 activating functions, leading to VWF transcriptional activation. Functionally, p53R175H markedly enhanced cancer cell-platelet heteroaggregates formation. Co-expression of plakoglobin reversed VWF upregulation and reduced platelet adhesion.

CONCLUSIONS

These findings identify a novel mechanism of VWF expression involving mutant p53 in cancer cells and reveal plakoglobin as a potent antagonist of this pathway.

Assessing the Southend GCA Probability Score in patients referred to a University Rheumatology practice for suspected giant cell arteritis (GCA)

Hae-Won Son, Vanessa Kissner, Steven Katz, Alison Clifford
Supervisor: Dr. Alison Clifford

INTRODUCTION
The Southend GCA Probability Score (GCAPS) is tool developed to assess the pre-test probability of giant cell arteritis (GCA) to guide decisions for testing and/or prednisone initiation. We aimed to retrospectively assess its validity in patients referred to the University of Alberta for suspected GCA.

METHODS
Records of patients referred to University of Alberta Rheumatology for query GCA between January 2022 to 2024 were retrospectively reviewed and scored using the Southend GCAPS Calculator. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of a High, Intermediate or Low risk GCAPS score was calculated using either 1) the clinical diagnosis at 3 months, and 2) confirmed diagnosis by testing as gold standard. Receiver operator characteristic (ROC) curves were plotted using numerical GCAPS scores.

RESULTS
81 referrals for suspected GCA were identified, of which 62 contained all data to calculate a GCAPS score. GCA was diagnosed in 39 patients and excluded in 23. See Table 1 for distribution of results.
Using clinical diagnosis at 3 months as gold standard, the sensitivity of either Intermediate/or High risk GCAPS was very high at 97.4%, with specificity of 30%, PPV of 70.4% and NPV 87.5%. The sensitivity of High risk GCAPS alone was lower at 66.7%, but with higher specificity of 78.3%, PPV=83.9%, NPV=58.1%.
Using only confirmed diagnosis of GCA as gold standard, the sensitivity of Intermediate/or High risk GCAPs was 100%, with specificity of 30%, PPV of 62.8% and NPV 100%.
The GCAPS ROC AUC was good at 0.805 (95% CI 0.697-0.913). At the previously determined optimal cut-point of 9.5, the sensitivity was 97.4% but specificity was low at 34.8%.

CONCLUSIONS
In our population, an Intermediate or High risk GCAPS score was highly sensitive for the final diagnosis of GCA, suggesting that for those with Low risk scores, alternative diagnoses be strongly considered.

Table 1. Distribution of GCA diagnosis and risk level

	High Risk	Intermediate Risk	Low Risk	Sum
Diagnosis of GCA confirmed by test	20	7	0	27
Diagnosis of GCA made clinically	6	5	1	12
Diagnosis of GCA excluded	5	11	7	23
Sum	31	23	8	62

Magnitude of hepatic venous pressure gradient reduction predicts clinical events in portal hypertension: Meta-regression analysis of randomized-controlled trials

Matthew Tam, Irene Pascual, Daniel van Zanten, Shuen Sung, Jarell Jie- Rae Tan, Yu Jun Wong, Juan G Abraldes
Supervisor: Dr. Juan Gonzalez Abraldes

INTRODUCTION
Portal hypertension is a primary driver of mortality and complications in cirrhosis. While observational studies demonstrate that reductions in hepatic venous pressure gradient (HVPG) correlate with improved outcomes, the magnitude of risk reduction per unit decrease in HVPG has not been quantified across randomized controlled trials (RCTs).
We performed a meta-regression to quantify the relationship between HVPG reduction and clinical outcomes in RCTs.

METHODS
We systematically searched databases for RCTs in portal hypertension testing a drug intervention over placebo or no therapy, and reporting HVPG measurements and clinical outcomes. The predictor was the between-group difference in HVPG reduction (treatment minus control in mmHg). The endpoints were mortality and “variceal event” defined hierarchically: progression (when reported); otherwise variceal bleeding. This aimed to maximize usable RCTs while capturing clinically meaningful portal hypertension progression. We performed random-effects meta-regression, examining the association between HVPG reduction and log odds ratios for these clinical outcomes. Sensitivity analyses tested different weighting schemes to account for measurement error in HVPG.

RESULTS
Twenty-two RCTs including a total of 2,844 patients were included. Within the trials, HVPG was measured in 2,048 individuals.Each 1 mmHg reduction in HVPG was associated with reduced mortality (OR 0.850, 95% confidence interval 0.768 to 0.941, p=0.005) and variceal progression or bleeding (OR 0.854, 95% confidence interval 0.747 to 0.975, p=0.031), with low heterogeneity (I 2 0% and 18.5% respectively). Results were robust across multiple weighting schemes accounting for HVPG variability.

CONCLUSIONS
Using a meta-analytic approach, we demonstrate a dose-dependent relationship between HVPG reduction and clinical outcomes in RCTs of portal hypertension, with approximately 15% lower odds of mortality and variceal events per 1-mmHg reduction.
These findings may inform the design and powering of Phase III trials based on HVPG responses in Phase II studies.

Figures and/or Tables (up to 2)

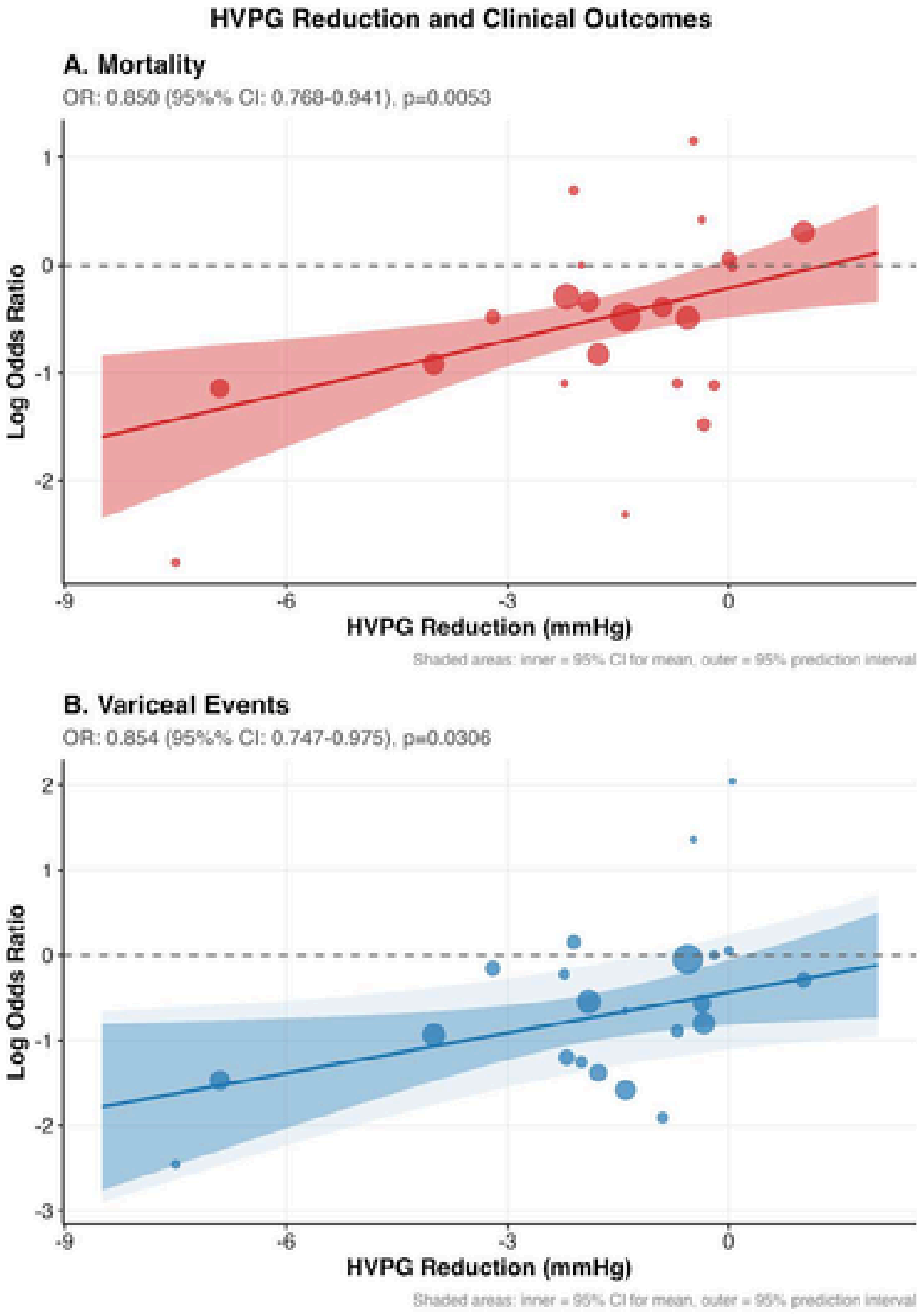


Figure 1: Meta-regression of the odds ratio of mortality (A) and variceal events (B) per mmHg change in HVPG. The shaded area reflects the 95% confidence interval of the regression line. The slope of the mortality regression line is 0.133 (95% CI: -0.036, 0.301), with an intercept of -0.301 (95% CI: -0.820, 0.218). The slope of the variceal events regression line is 0.162 (95% CI: 0.054, 0.271), with an intercept of -0.214 (95% CI: -0.487, 0.0599).

Validation of diabetes-dependent differences in FIB-4 predictions of fibrosis in patients with MASLD referred from primary care

Matthew Tam, Dr. Juan Gonzalez Abraldes, Dr. Mang M Ma, Chris Lauber, Shuen Sung, Saumya Jayakumar
Supervisor: Dr. Juan Gonzalez Abraldes

INTRODUCTION

Previous observations have shown that the Fibrosis-4 (FIB-4) score considerably underestimates the risk of fibrosis in patients with both metabolic-dysfunction associated liver disease (MASLD), suggesting inadequacy of the current primary care pathway. In this study, we aimed to explore in our previous data (from 2016-2021) the FIB-4-VCTE association in patients with and without diabetes, and to validate these findings in a prospectively collected new sample of paired FIB-4-VCTE observations (from 2025).

METHODS

This is a cross-sectional diagnostic validation study. Data was collected from the MASLD triage clinic at the Zeidler Ledcor clinic, where VCTE examinations are performed. Our previous cohort (n=985) was used to create an ordinal regression model of the effect of diabetes on the association between FIB-4 and VCTE. We prospectively collected data from 200 patients (aiming for 400 patients total) to validate this model. We also explored the adequacy of using lower FIB-4 values to triage patients with diabetes and MASLD.

RESULTS

The derivation and validation cohorts overall had different proportions of patients with liver stiffness measurements (LSM) ≥8 kPa (13.6% vs 31.0%) and ≥10 kPa (9.6% vs 22.8%). Among patients with diabetes, these cohorts also had different proportions of LSM ≥8 kPa (31.2% vs 41.5%) and ≥10 kPa (25.2% vs 33.8%). When modeling the FIB-4-VCTE association (adjusting by diabetes), lowering the cut-off of FIB4 was still inadequate to triage patients with diabetes (Figure 1). We tested the regression in this validation set, and confirmed adequate calibration.

CONCLUSIONS

Our model accurately captures the effect of diabetes on the FIB-4-VCTE relationship despite the differences between the two cohorts. This is shown by the similarity in the predicted and observed probabilities of LSM ≥ 8 kPa and LSM ≥ 10 kPa. The MASLD referral pathway needs to be modified for patients with diabetes.

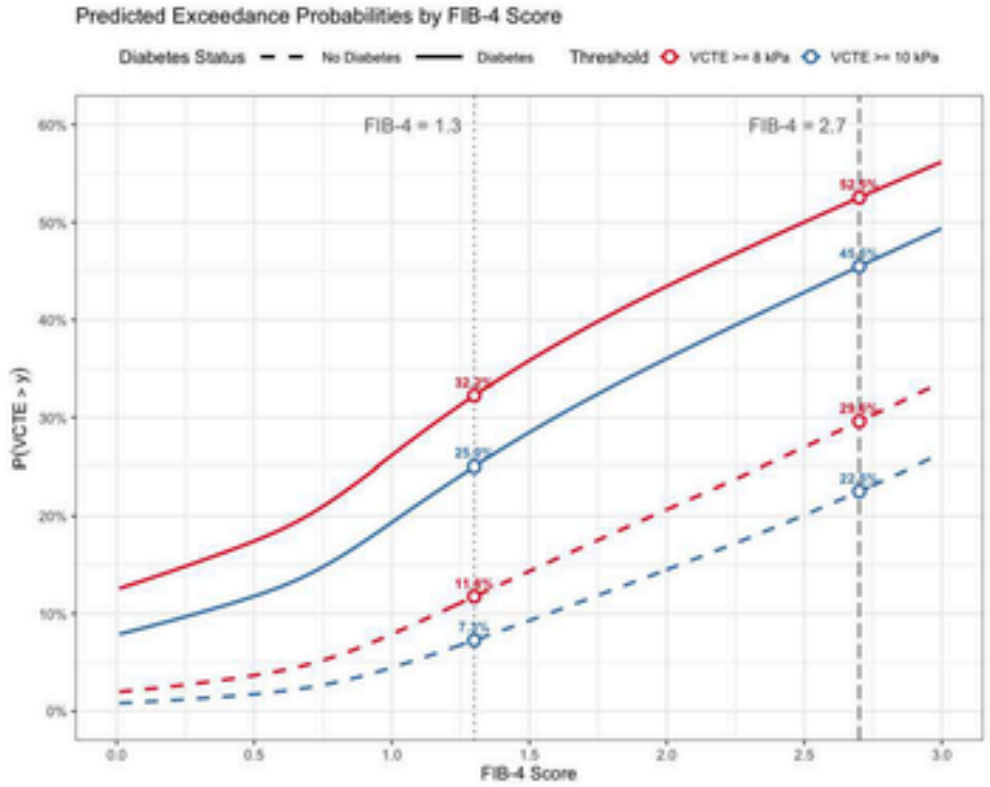


Figure 1: Predicted exceedance probabilities of VCTE ≥8 kPa and ≥10 kPa for patients with diabetes and without diabetes, based on our previous sample of 985 patients with MASLD.

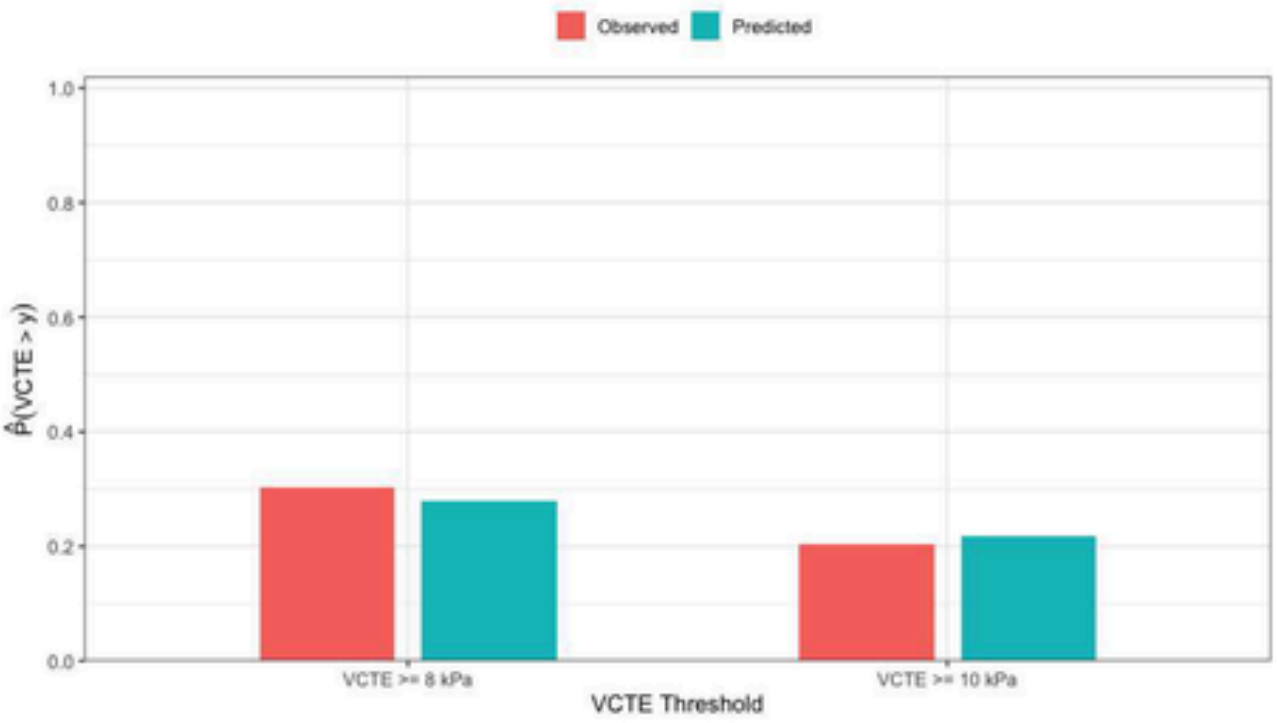


Figure 2: Observed and predicted probabilities of exceeding VCTE ≥ 8 kPa and VCTE ≥ 10 kPa in the validation set. Predicted exceedance probabilities were determined using the formula from the model from our previous sample of patients.

The Representation Gap: Demographic Disparities in Contemporary Systemic Sclerosis Clinical Trials

Shabnum Teja MD, Matthew A. Turk MD, Janet E. Pope MD
Supervisor: Dr. Janet E Pope

INTRODUCTION
Systemic sclerosis (SSc) is a rare, progressive autoimmune disease with high morbidity and mortality, characterized by fibrosis and multi-organ involvement. Randomized controlled trials (RCTs) are essential to evaluating therapeutic interventions. However, their clinical applicability depends on the representativeness of enrolled populations. SSc disproportionately affects certain racial and ethnic groups with documented differences in disease severity and outcomes. However, the extent to which RCTs reflect these populations who are most affected by this disease is unclear.

METHODS
Published SSc RCTs were systematically searched from 2004 onwards with population demographics including age, sex, race and ethnicity extracted for analysis. Eligible studies include RCTs evaluating treatment or outcomes in SSc. Revman 5.4 was used to calculate pooled proportions, with a random-effects model applied due to high heterogeneity. Reporting practises and methods of race and ethnicity were also assessed.

RESULTS
Of 1,682 identified studies, 24 RCTs (n = 2,925 participants) met inclusion criteria. Race and ethnicity were reported in 87.5% of studies; however, 37.5% reported only “White” versus “non-White” categories. The majority of participants identified as White (77–88%), while representation of other groups was limited: Asian (11%, 95% CI: 5–18), Black or African American (5%, 95% CI: 4–6), and Indigenous (1%, 95% CI: 0–2). Only 25% of studies specified how race and ethnicity were determined, all via self-report. Females comprised 77% (95% CI: 75–79) of participants, consistent with known disease epidemiology. No studies reported additional sociodemographic variables such as socioeconomic status, geographic ancestry, or access to care.

CONCLUSIONS
The racial and ethnic composition of SSc RCTs does not reflect populations affected by SSc. This can affect the generalizability of results and equity of trials. Future clinical research needs to incorporate broader sociodemographic measures to improve equity in research.

Do Follow-Up 18F-FDG PET/CT Findings Reflect Clinical Improvement in Large-Vessel GCA? A Systematic Review and Meta-analysis

JoAnn Thai, MD, Ashley Yip, MD, Joanne Homik, MD, MSc, Ben Vandermeer, Janice Y. Kung, Jan Willem Cohen Tervaert, MD, PhD, Alison H. Clifford, MD MSc
Supervisor: Dr. Alison Clifford

INTRODUCTION
Imaging biomarkers for disease activity are urgently needed in giant cell arteritis (GCA). Whether 18F-fluorodeoxyglucose positron emission tomography (PET) can be used to follow disease activity in those with large vessel vasculitis (LV-GCA) is still unclear. We aimed to determine how often large vessel inflammation improves or becomes radiographically-quiescent on follow up PET in patients with LV-GCA who clinically improve on treatment.

METHODS
MEDLINE, EMBASE, CINAHL, Scopus, and Cochrane Library were searched from inception through February 29, 2024. Studies describing patients with active LV-GCA on baseline PET, with a follow up PET scan repeated after escalating immunosuppression, and an assessment of clinical disease activity were included. Meta-analysis of the pooled sensitivity of 1) improved PET for clinical improvement and, 2) normalized PET for clinical remission in treated GCA patients was performed, with subgroup analysis of tocilizumab (TCZ)-treated patients.

RESULTS
Of 3131 unique references, 25 studies were included. The pooled sensitivity of improved vascular FDG uptake on follow up PET for clinical improvement of GCA was 0.95 (95% CI 0.82- 1.00), and the pooled sensitivity of normalized vascular FDG uptake on follow up PET for clinical remission was 0.53 (95% CI 0.34-0.72). In TCZ-treated patients, the pooled sensitivity of improvement and normalization of follow up PET was 1.00 (95% CI 0.99-1.00) and 0.78 (95% CI 0.50-0.97), respectively.

CONCLUSIONS
Follow up PET images improved in most (81.9%) patients with LV-GCA who clinically improved on treatment, but LVV became radiographically quiescent in only 46.9%. Better responses were seen in those receiving TCZ.

Do Follow-Up 18F-FDG PET/CT Findings Reflect Clinical Improvement in Large-Vessel GCA? A Systematic Review and Meta-analysis

JoAnn Thai[1], MD, Ashley Yip, MD[2], Joanne Homik, MD, MSc[1], Ben Vandermeer[3], Janice Y. Kung[4], Jan Willem Cohen Tervaert, MD, PhD[1], Alison H. Clifford, MD MSc[1]

[1]University of Alberta, Edmonton, [2]University of British Columbia, Vancouver, [3]EPICORE Centre, University of Alberta, [4]Geoffrey & Robyn Sperber Health Sciences Library, University of Alberta

INTRODUCTION

- Large vessel involvement (LVV) is common in giant cell arteritis (GCA)[1]
- There is no gold standard test for disease activity.
- ESR and CRP are unreliable — especially in patients treated with tocilizumab (TCZ)[2].
- 18F-FDG PET (PET) has high diagnostic accuracy in untreated GCA[3].
- The role of FDG PET in monitoring treated patients remains unclear.

Fig 1. The spectrum of vessel involvement in GCA[3]

OBJECTIVES

To determine:

1. How often does vascular FDG uptake improve on follow-up PET in LV-GCA patients who clinically improve?
2. How often does FDG uptake normalize on follow-up PET in patients who enter clinical remission?
3. What about in patients treated with tocilizumab?

METHODS

- Systematic search: MEDLINE, EMBASE, CINAHL, Scopus, Cochrane (through Feb 29, 2024)
- Inclusion criteria: GCA patients with
  - Baseline PET positive for LVV
  - Repeat PET ≥ 3 months after treatment initiation/ escalation
  - Clinical disease activity assessment at follow up
- Meta-analysis of pooled sensitivity
- Subgroup analysis: Tocilizumab-treated patients

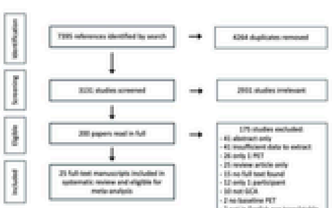


Fig 2. Flow diagram of included studies

RESULTS

PET Improvement in Clinical Improvement

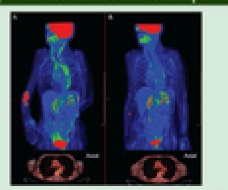


Fig 2. An example from Banerjee et al. showing decreased FDG uptake on repeat PET in a patient treated with tocilizumab[4]

PET Normalization in Clinical Remission

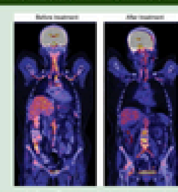


Fig 3. An example from Beyer et al. showing complete resolution of FDG uptake on repeat PET in a patient treated with tocilizumab[5]

All Studies

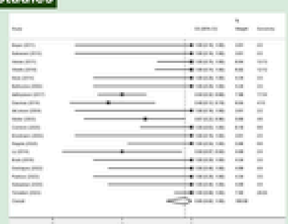


Fig 4. Pooled sensitivity of improved LVV on follow up PET for clinical improvement in treated GCA patients

- 19 studies contributed data
- 15/19 studies showed improvement in all cases
- Improvement of follow up PET occurred in 122/149 (81.9%) cases of patients who clinically improved
- Pooled sensitivity: **0.95**
- Heterogeneity: I^2 = 68.6%

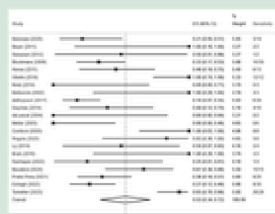


Fig 5. Pooled sensitivity of normalized LVV on follow up PET for clinical remission in treated GCA patients

- 21 studies contributed data
- Normalization of follow up PET occurred in 119/254 (46.9%) cases of patients in clinical remission
- Pooled sensitivity: **0.53**
- Heterogeneity: I^2 = 83.8%

Tocilizumab Subgroup

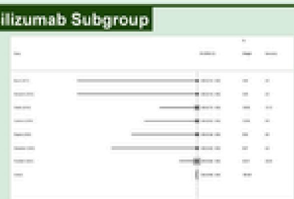


Fig 6: Subgroup analysis of improved LVV on follow up PET for clinical improvement in TCZ-treated patients

- 7 studies contributed data
- **All studies showed PET improvement in all cases (62/62)**
- Pooled sensitivity: 1.00
- Heterogeneity: I^2 = 0%

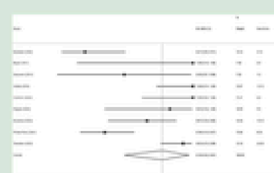


Fig 7. Subgroup analysis of normalized LVV on follow up PET for clinical remission in TCZ-treated patients

- 9 studies contributed data
- Normalization of PET occurred in 76/112 (67.9%) cases of patients in clinical remission
- Pooled sensitivity: 0.78
- Heterogeneity: I^2 = 86.2%

CONCLUSION

Clinical Interpretation

- Radiographic improvement is seen in 95% of patients who clinically respond to treatment.
- Normalization of follow up PET occurs in only ~50%.
- TCZ-treated patients demonstrated more frequent radiographic normalization.
- Persistent uptake does not necessarily indicate active disease.

Why this matters

- Persistent vascular FDG uptake is common despite clinical remission.
- PET must always be interpreted in clinical context and compared with prior imaging.
- TCZ may be associated with greater radiographic response.
- Follow-up PET may help establish an individual patient's "radiographic baseline" in remission.
- Key unanswered questions:
  1. What does persistent update indicate?
  2. Does PET normalization predict sustained remission?

TAKE AWAYS

1. Follow-up PET improves in most LV-GCA patients who clinically improve, but radiographic quiescence with clinical remission occurs infrequently.
2. Serial PET can provide useful adjunctive information but does not replace clinical assessment.
3. Further prospective studies are needed to clarify the significance of persistent uptake.

ACKNOWLEDGEMENTS

Funding:
This work was supported by the Anthony S. Russell Scholarship.

Methodologic & Statistical Support:
We thank Ben Vandermeer (Epicore Centre, University of Alberta) for statistical guidance.

Literature Search Support:
We acknowledge Janice Y. Kung (Geoffrey & Robyn Sperber Health Sciences Library, University of Alberta) for developing and executing the systematic search strategy.

REFERENCES CITED:

(1) Narváez J, Estrada P, Vidal-Montal P, et al. Usefulness of 18F-FDG PET-CT for assessing large-vessel involvement in patients with suspected giant cell arteritis and negative temporal artery biopsy. Arthritis Res Ther. 2024 (26(1):13.
(2) Stone JH, Tuckwell K, Dimonaco S, et al. Glucocorticoid Dosages and Acute-Phase Reactant Levels at Giant Cell Arteritis Flare in a Randomized Trial of Tocilizumab. Arthritis Rheumatol. 2019;71(8):1329-38.
(3) van der Geest KS, Sandovici M, Bley TA, Stone JH, Slart RH, Brouwer E. Large vessel giant cell arteritis. The Lancet Rheumatology. 2024 Jun 1;6(6):e397-408.
(4) Banerjee S, Quinn KA, Gribbons KB, et al. Effect of treatment on imaging, clinical, and serologic assessments of disease activity in large-vessel vasculitis. The Journal of rheumatology. 2020 Jan 1;47(1):99-107.
(5) Beyer C, Axmann R, Sahinbegovic E, et al. Anti-interleukin 6 receptor therapy as rescue treatment for giant cell arteritis. Annals of the Rheumatic Diseases. 2011 Oct 1;70(10):1874-5.

Impact of MASLD on treatment response, clinical outcomes and prognosis in PBC: findings from a multicenter longitudinal GLOBAL PBC registry

Shagani Thisairajah, Ellina Lytvyak, Yu Jun Wong, Bettina Hansen, Sara Lemoinne, Gideon Hirschfield, Aliya Gulamhusein, Albert Pares, Ignasi Olivas, Maria-Carlota Londono, Sergio Rogriguez-Tajes, Aldo J. Montano-Loza, Christophe Corpechot
Supervisor: Dr. Ellina Lytvyak & Dr. Aldo Montano-Loza

INTRODUCTION
Metabolic dysfunction-associated steatotic liver disease (MASLD) becomes increasingly common, and its concomitance with primary biliary cholangitis (PBC) is not fully explored. We aimed to evaluate the impact of MASLD on treatment response, clinical outcomes, and their prediction in people with PBC.

METHODS
We analyzed data of 1209 PBC patients from 21 centers across North America, Europe, and Asia, with ≥1 reliable controlled attenuation parameter (CAP) by vibration-controlled transient elastography (VCTE), measured before the occurrence of any events, and ≥6 months of follow-up. MASLD was defined as CAP≥270 dB/m or histologically confirmed steatosis, plus ≥1 cardiometabolic risk factor and no history of heavy alcohol use. Treatment response was evaluated using conventional criteria. Clinical outcomes included liver decompensation, hepatocellular carcinoma, liver transplantation
(LT), or death.

RESULTS
Over 90% were females, with mean age 62.9±11.7 years, and MASLD was diagnosed in 26.6%. Proportion of females (89.3% vs. 91.3%), age at diagnosis (53.3±11.9 vs. 52.4±12.2 y.o.), and time from VCTE to follow-up (2.6±1.6 vs. 2.7±1.7) did not differ between PBC-MASLD and PBC. Liver stiffness measurement (LSM) by VCTE was higher among PBC-MASLD (10.9±11.3 vs. 9.1±8.3 kPa; p=0.014).

Treatment response achievement was more pronounced in PBC-MASLD, as per Paris-2 (30.7% vs. 20.7%, p=0.007), Toronto (31.4% vs. 19.7%, p=0.002) criteria, ALP normalization (34.8% vs. 22.2%, p=0.001), and deep biochemical response (38.7% vs. 21.9%, p<0.001), with same tendency observed for GLOBE score (28.5% vs. 20.0%, p=0.075).

MASLD was not associated with higher risk of poor outcomes (HR 0.68, 95%CI 0.38-1.22, p=0.192) overall, and in high-risk group (LSM≥15.0 kPa, HR 0.89 [0.43-1.83], p=0.747).

Predictive value of LSM, GLOBE, UK-PBC, APRI, and FIB-4 scores did not change when adjusted for MASLD (HR 1.05 [1.04-1.06], p<0.001; HR 3.15 [2.30-4.33], p<0.001; HR 2.27 [1.69-3.06], p<0.001; HR 1.68 [1.44-1.95, p<0.001; HR 1.38 [1.28-1.49], p<0.001), respectively. Probability of LT and liver-related death (as per UK-PBC risk score) was similar between PBC-MASLD and PBC (5-year: 2.5±4.7% vs. 3.1±5.6%, p=0.280; 10-year: 7.4±11.7% vs. 9.1±12.7%, p=0.213; 15-year: 12.3±16.3% vs. 14.8±17.4%, p=0.150).

CONCLUSIONS
Prevalence of MASLD in PBC is comparable to the general population, and does not negatively impact either treatment response, clinical outcomes, or predictive value of LSM and established prognostic scores.

Figure 1: Comparison of biochemical treatment response between patients with PBC and those with concomitant MASLD, assessed using ALP normalization, Paris-2, Toronto criteria, and GLOBE score. Patients with MASLD demonstrated higher rates of treatment response across multiple criteria.

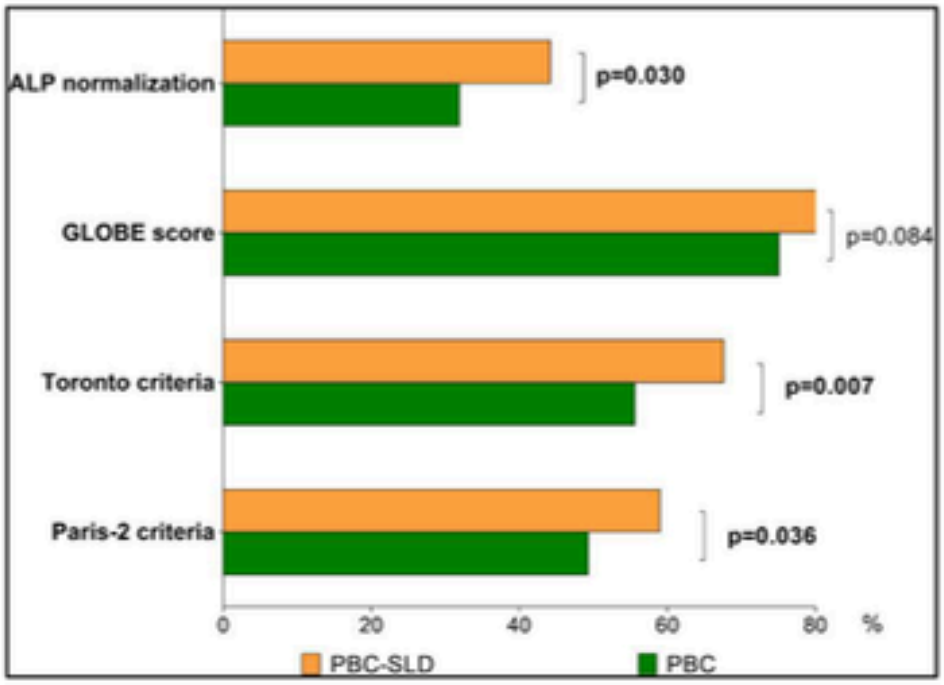
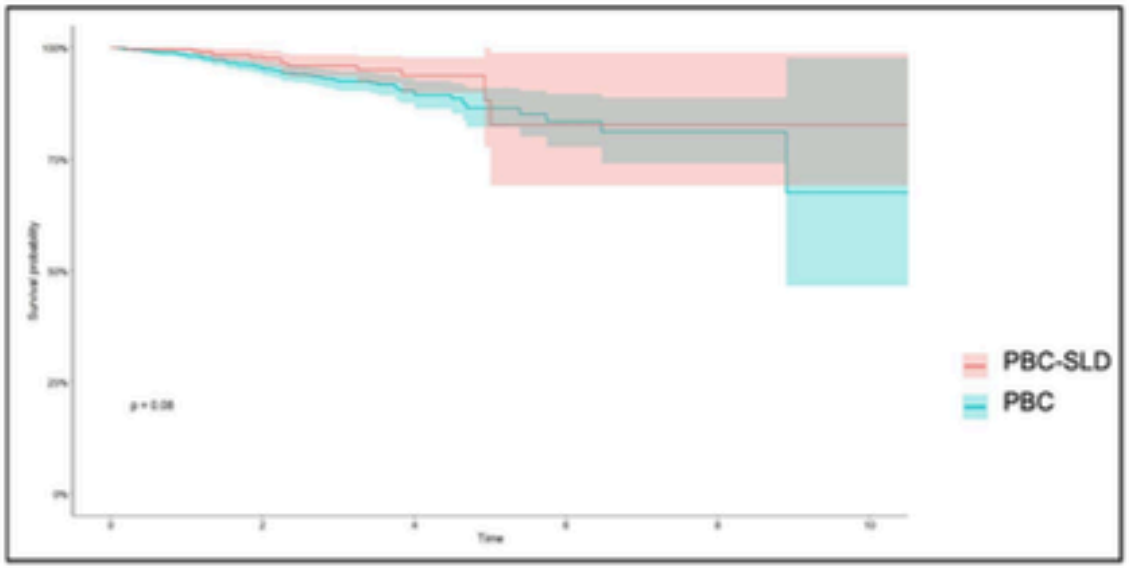


Figure 2: Time-to-event analysis of composite adverse clinical outcomes (liver decompensation, hepatocellular carcinoma, liver transplantation, or death) in patients with PBC with and without MASLD. No significant difference in event-free survival was observed between groups.



Prognostic value of dynamic liver stiffness measurement in autoimmune hepatitis

Shagani Thisairajah, Yu Jun Wong, Ellina Lytvyak, Aliya F Gulamhusein, Christina G Plagiannakos, Hin Hin Ko, Nabiha Faisal, Kristel Leung, Jean-Philippe Wallach, Devika Shreekumar, Narmeen Umar, Karim M Qumosani, Mina Niazi, Julian Hercun
Supervisor: Dr. Ellina Lytvyak & Dr. Aldo Montano-Loza

INTRODUCTION
Although liver stiffness measurement (LSM) is widely used for monitoring and prognostication in chronic liver disease, its dynamic prognostic role in autoimmune hepatitis (AIH) remains uncertain. We evaluated whether longitudinal changes in LSM improve prediction of hepatic decompensation (HD) in treated AIH.

METHODS
We analyzed data from the nationwide multicentre registry, including patients diagnosed with AIH who underwent ≥1 LSM after treatment initiation. Patients with prior decompensation, unreliable LSM, liver transplantation, or follow-up <6 months were excluded. Using a landmark approach, we compared baseline LSM (LSM1; ≥6 months after diagnosis) and most recent LSM (LSMc) for prediction of HD using Cox regression and discrimination analyses.

RESULTS
Among 832 patients (median follow-up 137 months), 65 (8.4%) developed HD, 2.7% underwent liver transplantation, and 5.8% died.
Both LSM1 (HR 1.07 per kPa, p<0.001) and LSMc (HR 1.07 per kPa, p<0.001) independently predicted HD, with superior discrimination for LSMc (AUROC 0.81 vs 0.79). LSM trajectories reclassified risk among patients in biochemical remission. Among patients with compensated advanced chronic liver disease (LSM1 ≥15 kPa), ≥20% LSM reduction was associated with significantly lower HD risk (HR 0.19, 95%CI: 0.06-0.55). Conversely, in patients with LSMc ≥15 kPa, LSM increase conferred markedly higher HD risk (HR 9.36, 95% CI 3.31–26.45), while ≥20% LSM reduction was protective (HR 0.20, 95% CI 0.07–0.56).

CONCLUSIONS
Dynamic LSM trajectories provide clinically meaningful prognostic information in AIH independent of biochemical response. Serial LSM complements biochemical monitoring and enables dynamic risk stratification, identifying patients at persistent risk despite apparent remission.

Figure 1: Baseline liver stiffness measurement beyond 15 (LSM ≥15kPa) predicts index hepatic decompensation in autoimmune hepatitis. Time-to-event analysis showing event-free survival probability of hepatic decompensation according to LSM1, with liver transplantation and death as competing events. Shaded areas represent 95% confidence intervals. Numbers at risk are shown below the plot. LSM: Liver stiffness measurements; HR: hazard ratio

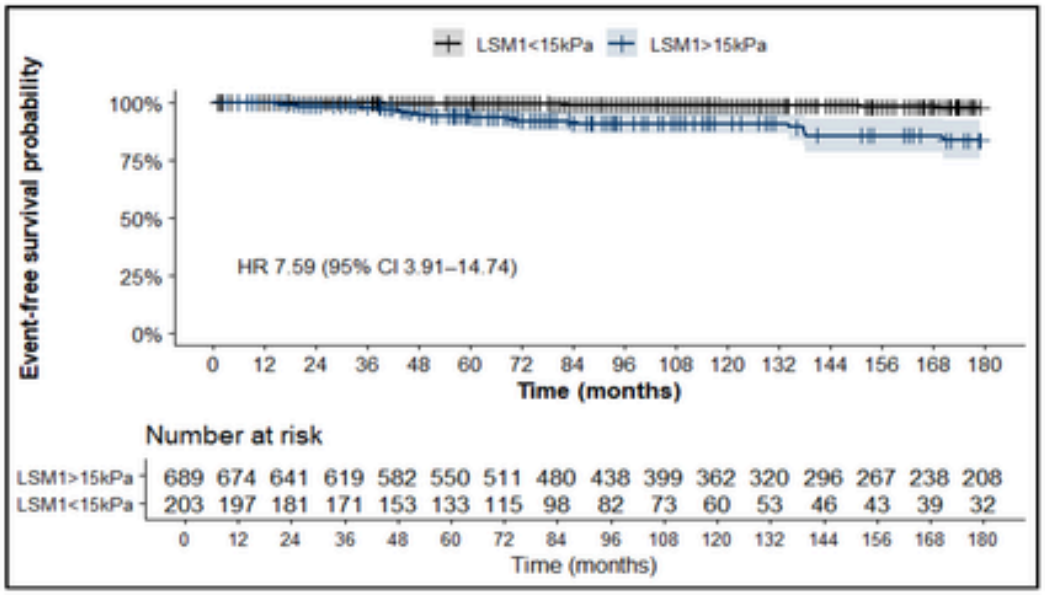
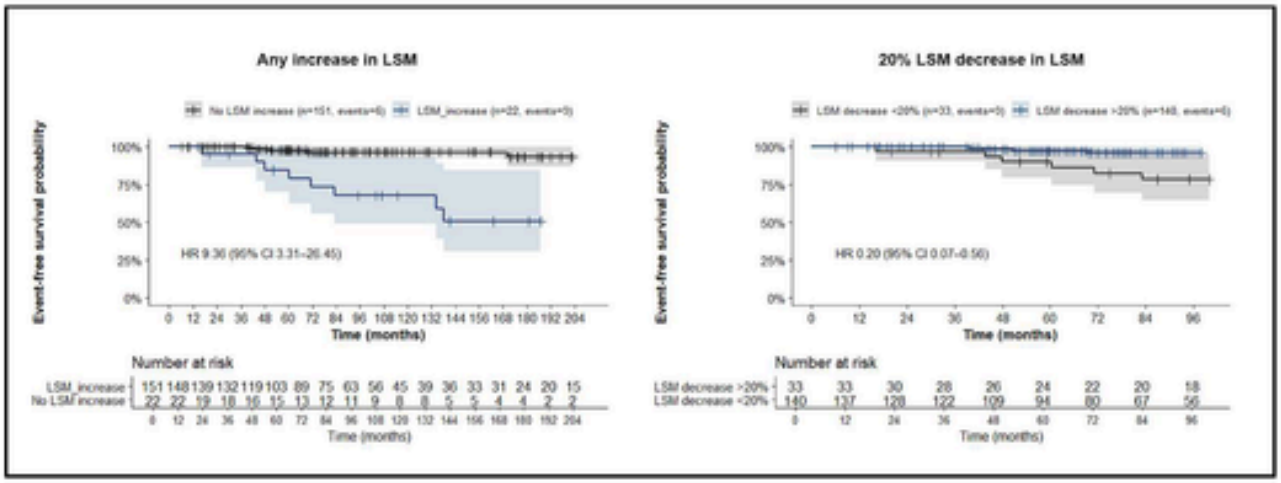


Figure 2: Among high-risk AIH patients (LSMc ≥ 15kPa), the risk of index hepatic decompensation was significantly higher in patients with increase in LSM, but significantly lower in patients achieving 20% decrease in LSM. Time-to-event analysis showing event-free survival probability of hepatic decompensation between patients with and without dynamic changes in LSM, with liver transplantation and death as competing events. Shaded areas represent 95% confidence intervals. Numbers at risk are shown below the plot. LSM: Liver stiffness measurements; HR: hazard ratio



The coexistence of sarcopenia and myosteatosis is associated with adverse clinical outcomes following liver transplantation

Shagani Thisairajah, Ellina Lytvyak, Yu Jun Wong, Glenda Meeberg, Devika Shreekumar, Maryam Motamedrad, Alessandro Parente, Norman M. Kneteman, Khaled Dajani, Blaire Anderson, David Bigam, A M James Shapiro, Aldo J. Montano-Loza
Supervisor: Dr. Ellina Lytvyak & Dr. Aldo Montano-Loza

INTRODUCTION

Sarcopenia and myosteatosis are individually associated with adverse outcomes in chronic liver disease, however their combined impact of this “double-muscle defect” on post-liver transplantation (LT) survival remains unclear. We hypothesized that the co-existence of sarcopenia and myosteatosis defines a distinct, high-risk muscle phenotype associated with poorer post-LT outcomes beyond conventional risk markers.

METHODS

We conducted a prospective cohort study that included 400 adult patients undergoing LT. Skeletal muscle index and radiodensity were measured from pre-LT computed tomography (CT) scans three months before their LT to define sarcopenia and myosteatosis, using established cut-offs. The primary outcome was post-LT mortality; secondary outcomes were ICU and total hospital length of stay (LOS). Multivariable Cox-regression adjusted for age, sex, and MELD score at LT.

RESULTS

The cohort was 70% male Caucasians (76.5 %), with median age 53.5 years [IQR 44.2 - 60.5] and median BMI 25.9 kg/m2 [IQR 23 - 30.2]. Sarcopenia was present in 54.5 %, myosteatosis in 47.3 %, and both in 29.8 % patients.

LT recipients with simultaneous sarcopenia and myosteatosis had longer post-LT ICU stay (4 [2 - 11] vs. 3 [2 - 6] days, $p = 0.01$), and longer post-LT hospital LOS (27 [16 - 50] vs. 21 [14 - 34] days, $p = 0.004$).

Importantly, simultaneous sarcopenia and myosteatosis was independently associated with a higher risk of mortality (adjusted HR 1.57 [1.05 - 1.91], $p = 0.029$), after adjustment by sex, age at transplant, cirrhosis etiology, presence of acute-on-chronic liver failure, and pre-LT MELD score.

The 5-year post-LT survival (72 % vs. 82 %, $p = 0.015$) was significantly worse for patients with simultaneous sarcopenia and myosteatosis. This effect was magnified in patients > 60 year-old (62 % vs. 72 %, $p = 0.015$), and those requiring ICU admission pre-LT (66 % vs. 87 %, $p = 0.014$).

CONCLUSIONS

Simultaneous sarcopenia and myosteatosis is a clinically meaningful, independent predictor of post-LT mortality and morbidity, especially in older and critically ill patients. Incorporation of dual muscle assessment into pre-LT evaluation may provide a more objective means to enhance risk stratification, guide candidate selection, and reduce futile transplantation—particularly in older and critically ill patients.

Point-of-care liver stiffness measurement predicts liver-related events in autoimmune hepatitis: results from a large nationwide multicenter longitudinal CaNAL study

Lytvyak E, Hirschfield GM, Wong YJ, Thisairajah S, Ko HH, Hercun J, Niazi M, Vincent C, Qumosani KM, Chen T, Cheung A, Flemming J, Leung K, Wallach JP, Faisal N, Shreekumar D, Umar N, Gulamhusein AF
Supervisor: Dr. Aldo Montano-Loza

INTRODUCTION
Liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE) is a validated noninvasive tool for fibrosis assessment and prognostication in chronic liver diseases. However, its role in predicting clinical outcomes in autoimmune hepatitis (AIH) remains incompletely defined. We aimed to evaluate the prognostic utility of point-of-care LSM for liver-related events (LRE) in a large, nationwide, multicenter AIH cohort.

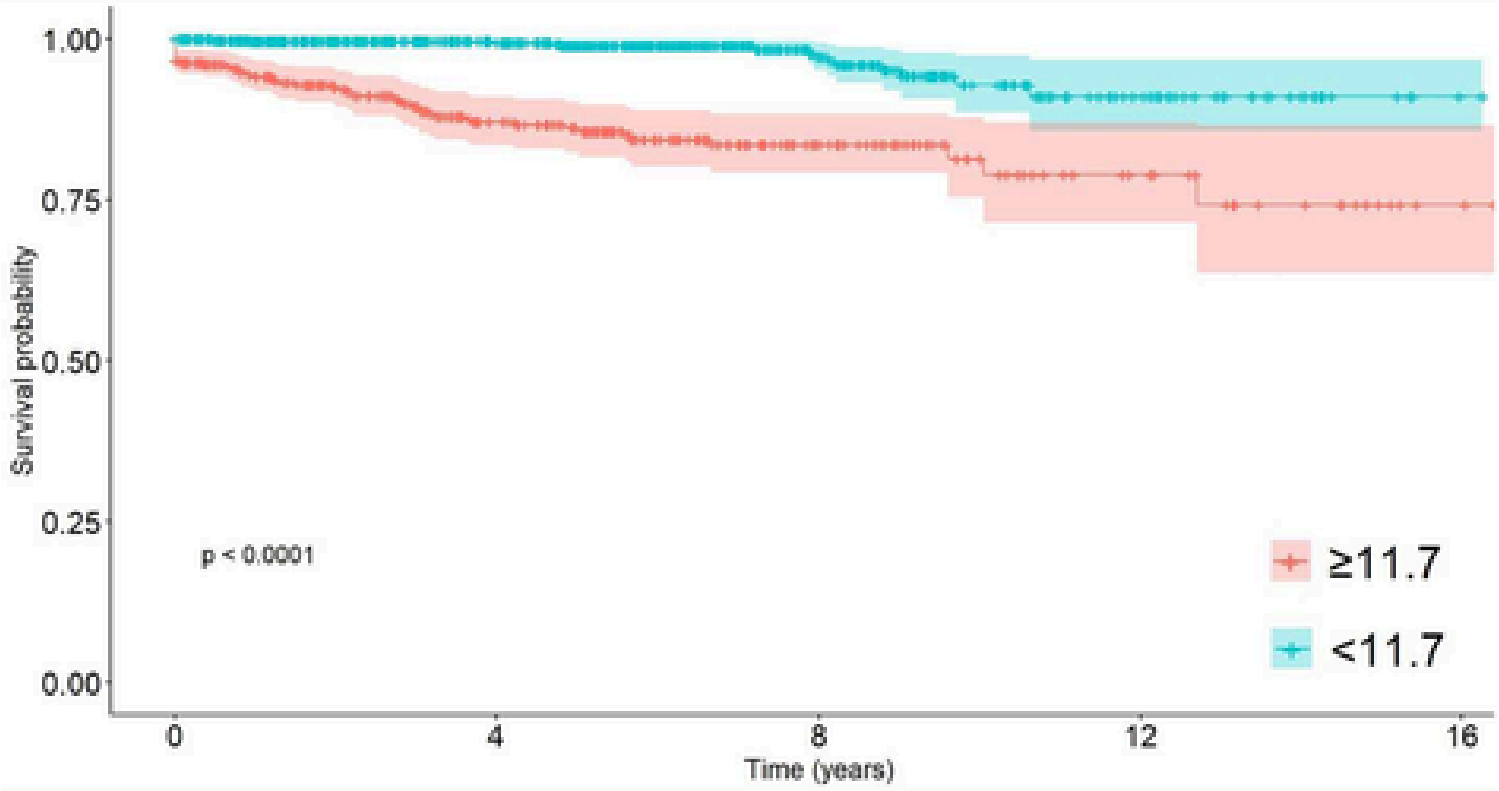
METHODS
We conducted a Canada-wide multicenter cohort study using the Canadian Network for Autoimmune Liver Diseases (CaNAL) registry. Adults with AIH (simplified score ≥6) and ≥1 reliable LSM (IQR/median ≤0.30) performed at or after diagnosis and prior to any adverse events were included. The primary composite outcome was time to first LRE (hepatic decompensation, hepatocellular carcinoma, liver transplantation, or liver-related death). Multivariable Cox regression and landmark analyses were performed adjusting for demographic, clinical, and biochemical factors. Predictive performance was assessed using Harrell's C-index with bootstrap validation.

RESULTS
A total of 1147 patients were included (74.3% female, median age 48.6 years). Median LSM was 8.1 kPa, and 19.0% had cirrhosis at diagnosis. Over follow-up, 5.5% developed LRE. LSM demonstrated a monotonic association with risk of adverse outcomes. In multivariable analysis, higher LSM independently predicted LRE (HR ~1.03-1.06 per kPa, p≤0.007), alongside cirrhosis at diagnosis and type 2 diabetes. An optimal LSM cutoff (~11-11.7 kPa) identified a high-risk group with ~3-fold increased risk of LRE. Incorporation of LSM significantly improved model discrimination (C-index increase to ~0.80-0.88). Notably, sex, obesity, inflammatory markers, and lifestyle factors were not independently associated with outcomes.

CONCLUSIONS
Point-of-care LSM is a robust independent predictor of liver-related events in AIH, beyond traditional risk factors and biochemical response. Integration of LSM into routine clinical assessment can enhance risk stratification and inform personalized surveillance and management strategies.

Event-free survival by liver stiffness measurement (LSM) risk categories

Event-Free Survival by High-risk versus Low-risk Categories



Genomic instability in systemic sclerosis is promoted by a PERK/FOXO1-dependent axis

Lamia Khan, Junquin Wang, Charmaine van Eeden, Carmanah Hunter, Lisa Willis, Caylib Durand, Jan Storek, Ben Korman, Janet Pope, Jan Willem Cohen Tervaert, Robert Gniadecki and Mohammed Osman*
Supervisor: Robert Gniadecki

INTRODUCTION

Diffuse cutaneous Systemic Sclerosis (dcSSc) is a life-limiting autoimmune disease with minimal treatment options. Autologous hematopoietic stem cell transplantation (ASCT) is a potent disease-modifying therapy in dcSSc; however, its effects on fibroblasts are unknown. We recently showed that dermal fibroblasts (DFs in patients with dcSSc develop a cancer-like phenotype characterized by genomic instability and increased double-stranded DNA breaks (DSBs). However, little is known about the mechanisms promoting DF survival following the accumulation of genomic mutations.

We hypothesized that in dcSSc DF genomic instability results in the accumulation of genomic mutations; and that this results in the activation of Protein Kinase R-like ER Kinase (PERK) and transcription of forkhead box1 (FOXO1) promoting resistance-to-apoptosis and fibrosis (Fig. 1).

METHODS

We used whole exome sequencing (WES) to characterize the mutational frequencies and their associated signatures in dcSSc patients who did not undergo ASCT (dcSSc, N=35) and those who did (post-ASCT, N=9). We also generated DFs from dcSSc, post-AHSCT (or age/sex matched healthy controls (HC), (N=8-10 patients/group), and quantified the frequency of DSBs via γ-H2AX levels (immunoblot (IB)), and DSB nuclear foci (confocal microscopy). We measured the relative ROS levels, mitochondrial membrane potential, and phospho-PERK (active) in DFs to mechanistically link DSB with PERK activation using flow cytometry and/or IB, respectively. We also determined the downstream effects of PERK activation on mitochondria (e.g. mitochondrial dynamics and biogenesis). Then, we measured FOXO1 activation via nuclear translocation, IB, and expression of its downstream mRNA target SOD2. Finally, mitochondrial-dependent resistance-to-apoptosis was determined at baseline, and following treatment with cyclophosphamide, a PERK or a FOXO1-inhibitor using TUNEL and cleaved caspase 9/3 levels (IB).

RESULTS

dcSSc patients' DFs had increased genomic instability and DSBs compared to patients treated with ASCT. dcSSc DFs had increased indicators associated with PERK activation (phospho-PERK, ROS, and mitochondrial membrane potential). This was associated with increased mitochondrial remodelling, mitochondrial biogenesis, and mitochondrial fusion. Importantly, FOXO1 was exclusively activated in dcSSc, but not HC or post-ASCT DFs. Inhibition of PERK or FOXO1 resulted in increased mitochondrial-dependent apoptosis.

CONCLUSIONS

Our study highlights a novel mechanism whereby genotoxic signals in dcSSc promote cell survival via a PERK/FOXO1-dependent axis and associated metabolic remodeling (Fig. 1). It also provides mechanistic insights related to how changes to the mutational landscape reduce pro-fibrotic signals in DF after ASCT. Future studies targeting this dysregulated pathway may provide an additional rationale for exploring it therapeutically in patients with dcSSc.

Evaluating the Feasibility and Impact of a Tailored, Multidisciplinary Preoperative Assessment with Multiple Risk Stratifications in Complex Surgical and Pre-Transplant Patients

Su Jin Yim, MD, Farah Upoma, MD, Victor E. Ezeugwu, PT, PhD, Naheed Rajabali, MD
Supervisor: Dr. Naheed Rajabali

INTRODUCTION
Complex surgical and transplant candidates often present with multimorbidity, frailty, and cognitive vulnerability, making risk estimation and perioperative decision-making challenging. Traditional internal medicine consultations may not fully capture this multidimensional complexity or support coordinated interdisciplinary care. The Complex Perioperative Assessment Clinic (CPAC) was developed to provide an integrated, risk-informed, and collaborative approach to perioperative assessment.

METHODS
We conducted a retrospective descriptive study of 20 randomly selected CPAC consultations from a cohort of 106 patients. Data included surgical outcomes, care plan modifications, and optimization strategies. A clinician survey assessed perceived impact on decision-making and collaboration (n=15). Preliminary patient experience surveys were also analyzed (pending ethics approval).

RESULTS
Surgery proceeded in 12/20 (60%), while 8/20 (40%) did not proceed following reassessment of candidacy. Overall care plans were changed or refined in 12/20 (60%), including procedural modifications (6/20). Previously unrecognized or under-addressed clinical issues were identified in 8/20 (40%), and medical optimization was initiated in 19/20 (95%). Risk mitigation strategies were incorporated in all patients proceeding to surgery.

All clinicians reported improved decision-making and added clinical value; 100% of surgeons/interventionalists (n=10) reported increased confidence and would refer similar patients again. Hematology (n=3) and allied health (n=2) respondents reported improved clarity in decision-making and interdisciplinary collaboration.

Patients reported improved understanding of risks, increased confidence, and greater clarity in decision-making, with benefits extending beyond surgical planning.

CONCLUSIONS
CPAC represents an innovative model that integrates multidimensional risk assessment with collaborative decision-making. It influences care planning, supports clinician confidence, and enhances patient understanding, with benefits extending beyond the perioperative period.

Acknowledgements

DR. NARMIN KASSAM	Professor & Chair Department of Medicine
DR. EVANGELOS MICHELAKIS	Co-Associate Chair Research Department of Medicine
DR. GOPINATH SUTENDRA	Associate Professor & Co-Associate Chair, Graduate Programs Department of Medicine
DR. MAEVE SMITH	Associate Professor Department of Medicine
DR. PAMELA MATHURA	Quality Improvement Specialist & Assistance Clinical Professor, Department of Medicine
JENNIFER WOODS	Executive Director, UAH/EZ Medicine Program and UAH/Stollery Emergency
DR. NANCY ZHU	Deputy Zone Clinical Department Head, Medicine
DR. NADIA JAHROUDI	Associate Professor and Associate Chair, Graduate Programs Department of Medicine
ELENI KARAGEORGOS	Team Lead - Research Department of Medicine
ERIN PEARASE	Internal Engagement & Events Team Department of Medicine