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RESEARCH SHOWCASE

**Abstracts
& Posters**

2026



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Anatomy, Physiology & Pharmacology





Erica Andres (Dr. Robert Laprairie)

Pharmacodynamics of Nine Synthetic Cannabinoid Receptor Agonists at CB1R and CB2R

Synthetic cannabinoid receptor agonists (SCRAs) are a novel class of psychoactive substances showing high prevalence in illegal markets. Unlike THC, a partial agonist of the type one and type two cannabinoid receptors (CB1R and CB2R), SCRAs can be full agonists of these receptors. This likely accounts for the increased instances of adverse effects from SCRA usage including tachycardia, vomiting, and psychosis. In order to better inform regulations made by Health Canada regarding these drugs, these compounds and their activity at CB1R and CB2R needs to be characterized. Nine different SCRA compounds are to be tested in vitro for their pharmacodynamics at CB1R and CB2R.

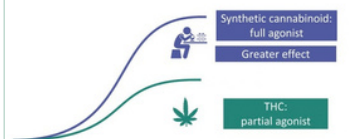
Pharmacodynamics of Nine Synthetic Cannabinoid Receptor Agonists at CB1R and CB2R

Erica Andres¹, Roberta Costi², Davide Lalongo², Valentina Noemi Madia², Robert Laprairie¹

¹College of Pharmacy and Nutrition, University of Saskatchewan
²Department of Chemistry and Technology of Drug Design, Sapienza University of Rome

INTRODUCTION

- Synthetic cannabinoid receptor agonists (SCRAs), also known as “spice” or “K-2” compounds, are one of the fastest growing classes of recreational drugs in Canada.^{1,3}
 - SCRAs were originally intended to aid in drug development but are now used recreationally for their psychoactive effects.¹
- SCRAs may bind type 1 (CB1R) and type 2 (CB2R) cannabinoid receptors.²
 - SCRAs can be full agonists of these receptors as opposed to Δ^9 -tetrahydrocannabinol (THC), which is only a partial agonist.²
- Because SCRAs can be more active at CB receptors, this likely accounts for the increased number of instances of adverse effects and overdoses caused by SCRAs when compared to THC.²

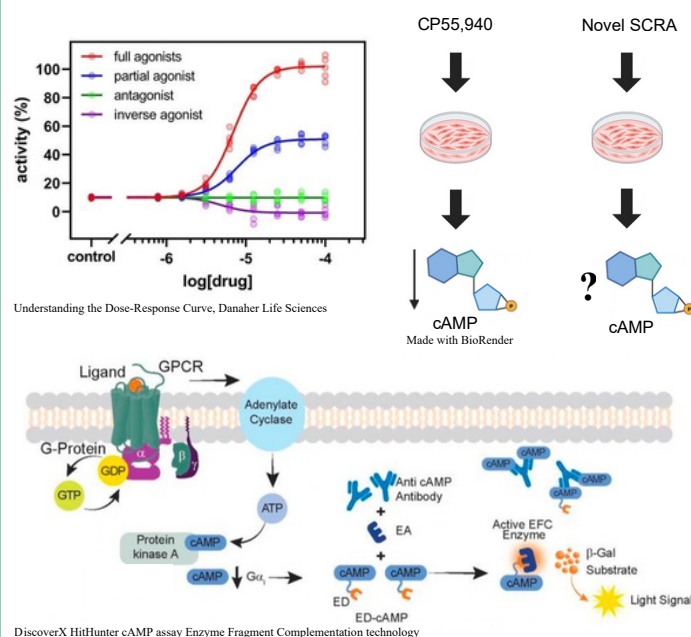


- SCRAs are currently illegal in Canada and the EU but remain accessible through illegal online markets.¹

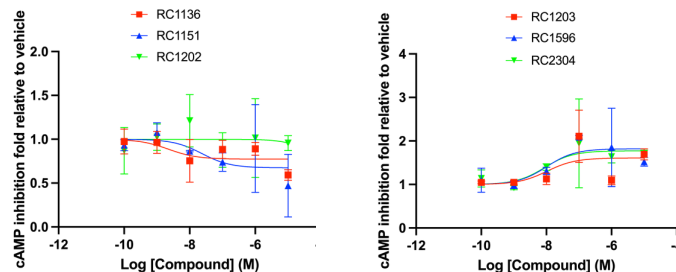
OBJECTIVES

- Characterize the pharmacodynamics of nine novel SCRAs at CB1R and CB2R
- Provide Health Canada with needed information to inform their policies and regulations around these drugs

METHODS



RESULTS



Inhibition of FSK-stimulation cAMP accumulation in CHO-K1 cells stably expressing human CB1R and treated with SCRA compounds, shown as cAMP inhibition fold relative to vehicle.

CONCLUSIONS

- RC1202 appear to be inactive at CB1R.
- RC1136 and RC1151 appear to be CB1R inverse agonists.
- RC1203, RC1596, and RC2304 appear to be CB1R agonists, but additional work comparing against the reference agonist CP55,940 is required to determine whether these compounds are full or partial agonists.

FUTURE WORK

- Test all nine compounds at CB1R and CB2R in vitro for their pharmacodynamics
- Take up to two of the most potent compounds for an in vivo assessment in a mouse model

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ACKNOWLEDGMENTS

Thanks to everyone in the Laprairie lab for their support!



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Ty Deutscher (Dr. Justin Botterill)

Evaluating the Role of Dorsal Mossy Cells in Cognitive and Affective Behaviors Using Optogenetics

The dentate gyrus (DG) is a region in the hippocampus that is critical for cognitive and affective behaviours. Mossy cells (MCs) of the DG remain understudied and are of particular interest because of their proposed role in novelty detection and anxiety-like behaviours. Recent studies suggest that dorsal and ventral MCs differ in gene expression, morphology, and circuitry. However, no study to date has directly compared the contributions of dorsal and ventral MCs to diverse hippocampal functions. To investigate these comparisons, we injected an adeno-associated virus (AAV) encoding the light-sensitive inhibitory protein eOPN3 into the dorsal hilus of dopamine receptor D2 transgenic mice (Drd2-Cre). We then used optogenetics to selectively silence dorsal MCs during a battery of cognitive and affective behaviour tests. Dorsal MC inhibition did not affect anxiety-like behaviour in the open-field test or elevated plus maze and did not alter contextual fear conditioning. However, dorsal MC inhibition significantly reduced novel object discrimination and produced a trend toward impaired novel location discrimination. These preliminary results suggest dorsal MCs play a significant role in novelty detection while having limited contributions to affective behaviours. Future experiments aim to target ventral MCs to compare functional differences between dorsal and ventral MC populations.

Evaluating the Role of Dorsal Mossy Cells in Cognitive and Affective Behaviours Using Optogenetics

Ty Deutscher¹, McKenna Bolger¹, Caleb White¹, Kirk Mulatz¹, Justin Botterill¹
Department of Anatomy, Physiology, and Pharmacology, University of Saskatchewan, Saskatoon, SK, Canada

Introduction

- The **hippocampus** is a brain region in the medial temporal lobes that is critical for learning, memory, and emotional responses¹.
- The hippocampus can be functionally and anatomically divided into dorsal and ventral domains in rodents, which correspond to the posterior and anterior hippocampus in humans^{2,3}.
- In rodents, the dorsal and ventral hippocampus appear to serve distinct functions, whereby the **dorsal hippocampus** is critical for cognitive and spatial functions, while the **ventral hippocampus** supports emotional and stress responses^{4,5}.
- Mossy cells (MCs)** are a unique and understudied excitatory cell population found exclusively in the **dentate gyrus (DG)** subfield of the hippocampus^{4,5}.
- Emerging research has shown that MCs are critical for hippocampal-dependent learning and memory, spatial exploration, novelty detection, and emotional behaviours⁶.
- This study seeks to evaluate the role of dorsal MCs in cognitive and affective behaviours by selectively inhibiting dorsal MC populations using optogenetics.

Methods

Ethics: All procedures were conducted in accordance with the University of Saskatchewan Animal Care Committee guidelines.

Animals: All experiments used dopamine receptor D2 transgenic mice (Drd2-Cre) to selectively target MCs with adeno-associated viruses (AAV). **Stereotaxic surgery:** Adult male and female Drd2-Cre mice (2-3 months old) underwent stereotaxic surgery. Mice were anesthetized with isoflurane and attached to a stereotaxic frame. A bilateral craniotomy was made above the dorsal hippocampus to enable targeting of MCs. An adeno-associated virus (AAV) encoding a light-sensitive neuronal silencer (SlO-eOPN3-mScarlet) or an inert control fluorophore (DIO-mCherry) was injected bilaterally in the hilus of the dorsal hippocampus. Optical probes were inserted bilaterally at the site of injection. Mice recovered for 3 weeks before behaviour testing.

Optogenetics: During behaviour testing, a PlexBright 4 Channel Optogenetic Controller with Radiant v2 and a PlexBright Dual LED Commutator were used for optogenetic stimulation. Mice had their optic fiber probes connected to a Plexon patch cord to deliver a 532nm light at 1 Hz frequency for MC silencing (eOPN3) or control stimulation (mCherry).

Analysis: AnyMaze software was used for mouse tracking and video scoring. GraphPad Prism was used for statistical analysis and generation of graphs.

Open Field Test (OFT): Mice freely explored a square box (Fig. 2) while receiving 532nm light stimulation for 10 minutes.

Elevated Plus Maze (EPM): Mice freely explored elevated maze with two open arms and two closed arms (Fig. 8) while receiving 532nm light stimulation for 10 minutes.

Novel Object Location (NOL): **Training phase:** mice received 532nm light stimulation and explored a square box with two identical objects for 10 minutes (Fig. 14). **Testing phase:** 1 hour after training and without optogenetic stimulation, mice were placed in the same box with one of the objects moved to a new location (Fig. 14) and explored for another 10 minutes.

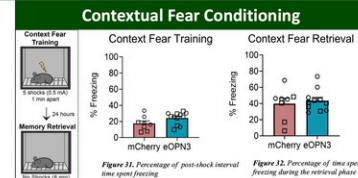
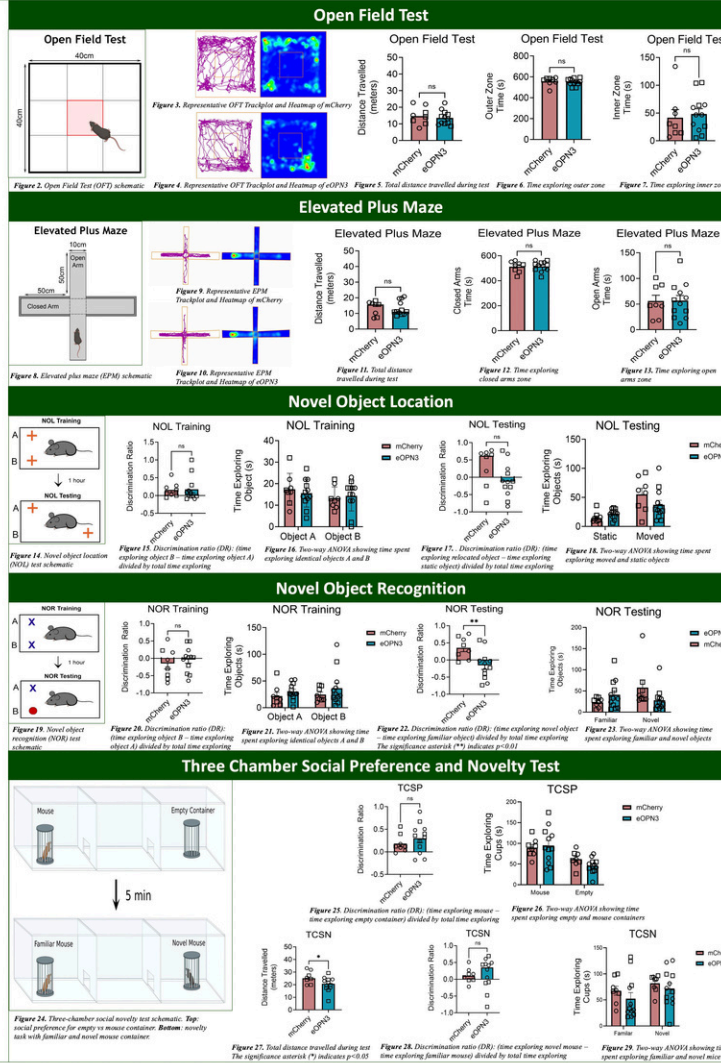
Novel Object Recognition (NOR): **Training phase:** mice received 532nm light stimulation, were placed in a square box with two identical objects different from those used in NOL and explored for 10 minutes (Fig. 19). **Testing phase:** 1 hour after training and without optogenetic stimulation, mice were placed in the same box with one of the objects replaced with a novel object (Fig. 19) and explored for 10 minutes.

Three-Chamber Social Preference and Novelty (TCSP and TCSN): Mice were acclimated to empty three-chamber box twice before testing. **TCSP:** Mice explored the three-chamber box for 10 minutes with an unfamiliar mouse in one container and the other container left empty (Fig. 24). **TCSN:** A novel mouse was placed in the previously empty container, while the familiar mouse remained in the same container. The test mouse was returned to the box (Fig. 24) and allowed to explore for another 10 minutes. Mice received 532nm light stimulation during both tests. Mice in containers were age and sex-matched to test mice.

Contextual Fear Conditioning (CFC): **Training phase:** Without optogenetic stimulation, mice explored the fear box for a 2-minute baseline period with no shocks and subsequently received 5 0.5mA shocks spaced 1 minute apart (Fig. 30). **Retrieval phase:** 24 hours later, mice were placed in the same fear box with optogenetic light stimulation and received no shocks for the entirety of the 8-minute testing period (Fig. 30).

Anatomy: Mice were anesthetized with a high dose of avertin and transcardially perfused with phosphate-buffered solution (PBS) and 4% paraformaldehyde (PFA) 90-minutes post-CFC. 50µm coronal brain sections were cover slipped for imaging using the Zeiss Axio Observer 7 high-throughput fluorescence microscope to verify viral expression.

Figure 1: Experimental timeline. Mice and female Drd2-Cre mice undergo stereotaxic surgery to inject dorsal MCs with Cre-dependent eOPN3. Mice are implanted with optical fibers in the dorsal hippocampus. After 3 weeks, mice undergo a battery of behavioural tests designed to test emotional behaviour (open field test, OFT), elevated plus maze (EPM), novelty (novel object location, NOL), novel object recognition, NOR, three-chamber social preference, TCSP and contextual fear conditioning (CFC) while receiving optogenetic light stimulation. Mice are euthanized after the last behavioural test to validate viral expression.



Results

OFT: Mice generally spent more time in the outer zone than the inner zone (Fig. 6 and 7). No differences were observed between treatment groups.

EPM: Mice generally spent more time in the closed arms than the open arms (Fig. 12 and 13). No differences were observed between treatment groups.

NOL Training: Mice explored both objects similarly and did not discriminate between objects A and B. **Testing:** The DR of the control group was greater than the experimental group (Fig. 17) suggesting the experimental group was less able to discriminate between the moved and static objects than the control group. This difference trended towards significance however potential outliers in both treatment groups may be influencing the results.

NOR Training: Mice explored both objects similarly and did not discriminate between objects A and B (Fig. 21). **Testing:** The DR of the control group was significantly greater than the experimental group (Fig. 22) suggesting the experimental group was less able to discriminate between the novel and familiar objects than the control group. This result is consistent with the hypothesis that silencing dorsal MCs may impair novelty detection.

TCSP: The DR trended towards significance (Fig. 25) however a larger sample size is required to determine whether there is an effect. Mice in both treatment groups generally spent more time exploring the mouse container than the empty container (Fig. 26). **TCSN:** Mice in the experimental group travelled significantly less distance than the control group (Fig. 27). The positive DR in the eOPN3 group relative to the control group indicates the mice spent more time with the novel mouse than the familiar mouse (Fig. 28). While this slightly contradicts our prediction that MC silencing should impair novelty detection, this observation did not reach significance. Both treatment groups spent more time exploring the novel mouse than the familiar mouse (Fig. 29).

CFC: There was no observable difference in fear training or retrieval with MC manipulations (Fig. 31 and 32).

Discussion and Future Directions

- We were able to silence dorsal MCs using optogenetics while simultaneously performing a battery of cognitive and affective behavioural tests.
- Unsurprisingly, dorsal manipulations did not have an effect on anxiety-like behaviours measured in EPM and OFT. However, dorsal MC inhibition significantly reduced novel object discrimination and produced a trend toward impaired novel location discrimination.
- These findings support our prediction that dorsal MCs are preferentially involved in cognition and novelty detection.
- Due to the short nature of the project, we have not confirmed viral targeting in all animals. Confirming viral targeting will allow us to correlate behaviour with viral expression and eliminate potential outliers.
- Future experiments plan to target ventral MCs to determine their contribution to affective behaviours and to compare the effect of silencing dorsal vs ventral MCs.

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Annika Dixon (Dr. Eric Noyes)

*Sebum and Cerumen Analysis for the Identification of Biomarkers in Parkinson's Disease and Related Disorders".
First choice for category is Anatomy, Physiology & Pharmacology. Second choice for category is Biochemistry,
Microbiology & Immunology*

The worldwide prevalence and incidence of Parkinson's disease (PD) are rising, yet diagnostic investigations remain scarce. Clinical diagnosis of PD is approximately 80% accurate at first assessment but increases to >97% when assessed by a movement disorders subspecialist after 5 years of disease duration, particularly due to initial difficulty in differentiating PD from various mimic syndromes. Detection of signature volatile organic compounds (VOCs), metabolic products in biofluids reflecting the body's health status, may aid in differentiating PD and PD-mimic syndromes; These can be isolated from easily accessible biofluids such as cerumen and sebum. Early analysis from our lab has identified seven VOCs of interest which demonstrate segregation of PD from PD-mimic syndromes and healthy controls ($p < 0.0001$). Retrospective chart review was conducted on 222 of these participants with corresponding cerumen and sebum samples, allowing us to further characterize collected clinical and demographic data. This work established foundational data for performing multivariate analysis, with the goal of understanding whether any clinical and demographic variables affect VOCs sample results. Such analysis will provide further insights into the utility of these biofluids as biomarkers and may help develop non-invasive diagnostic tools in PD and related disorders.

Sebum and cerumen analysis for the identification of biomarkers in Parkinson's disease and related disorders

Annika Dixon¹, LeiLei Sun², Paul Jones⁴, Bashir Daud Shah¹, Alex Rajput^{1,3}, Haixia Zhang², Eric Noyes^{1,3}

College of Medicine, University of Saskatchewan¹, Food and Bioproduct Sciences, University of Saskatchewan², Saskatchewan Movement Disorders Clinic³, Toxicology Center, University of Saskatchewan⁴

BACKGROUND

- Parkinson's disease (PD) affects over 110,000 Canadians.¹
- Clinical diagnosis of PD is only 75-80% accurate at the first visit with a neurologist.²⁻³
- Investigations that aid in the clinical diagnosis of PD include specialized imaging, spinal fluid analysis, and genetic testing, all of which are scarce, expensive, or physically invasive.⁴⁻⁷
- Non-invasive approaches for PD biomarker screening are desirable for aiding in PD diagnosis;
- One such approach is the detection of unique volatile organic compounds (VOCs) in earwax (cerumen) and skin oil (sebum) samples in PD patients, those with PD-mimic syndromes, and healthy controls.
- Early analysis from our lab has identified seven VOCs of interest which demonstrate segregation of PD from PD-mimic syndromes and healthy controls ($p < 0.0001$).

OBJECTIVE

Our objective is as follows:

Perform a retrospective chart review of patients with PD, PD-mimic syndromes, and healthy controls who donated sebum and cerumen samples for VOCs analysis, eventually allowing us to perform statistical analysis of collected demographic and clinical data to investigate if any variables affect VOCs sample results.

METHODS

- **Retrospective chart review** of 222 patients (110 female, 112 male)
- Demographic collected data: age, sex, residence, and ethnicity.
- Clinical collected data: age of disease onset, disease duration, disease staging, motor severity scoring, Levodopa equivalent dose, lipid medications and doses, presence of non-motor features of PD such as anosmia and isolated rapid eye movement sleep behaviour disorder (IRBD), mini-mental status exam score, and genetic testing results.

RESULTS

Variables	Controls	PD	PD-mimic syndromes
n	88	106	28
Average age at first assessment	64	71	71
% Female	76	30	39
% Male	23	70	61
% Urban	66	65	71
% Rural	36	35	29
Average age of motor onset	N/A	61	60
Average disease duration (years)	N/A	10	11
Average disease staging (1-5)	N/A	3	N/A
Average motor severity scoring /132	N/A	32	N/A
Average Levodopa equivalent daily dose at first visit (mg)	N/A	809	232
% experiencing anosmia	N/A	47	21
% experiencing IRBD	N/A	50	39
Average MMSE score /30	N/A	27	25
% genetic testing done	N/A	13	14
% on lipid medications	N/A	35	18

CONCLUSIONS

- This work established foundational clinical and demographic data for performing multivariate analysis, with the goal of understanding whether any variables affect VOCs sample results.
- We hypothesize that the unique VOCs in participants of a single category will be affected by demographic and clinical variables.
- We will continue to recruit participants with a goal of ≥ 250 participants overall, including 100 PD subjects, 100 control subjects, and ≥ 35 subjects for the PD-mimic syndromes group.

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Maureen Ekwunife (Dr. Sébastien Gauvrit)

Investigating the role of Elk3 in zebrafish lymphatic development

Lymphatic vessels, lined by lymphatic endothelial cells (LECs), mediate interstitial fluid drainage and immune cell trafficking. Despite their critical physiological functions, the molecular mechanisms regulating LEC development remain poorly understood. ELK3, an ETS family transcription factor, regulates vascular endothelial growth factor (VEGF) receptor signaling during vascular development. Previous studies have shown that ELK3 regulates LEC migration, tube formation, and vascular permeability, suggesting a potential key role in lymphangiogenesis.

Here, we developed new genetic tools to investigate the role of Elk3 in vivo during zebrafish lymphatic vascular development. Using CRISPR/Cas9 genome editing, we generated a knock-in line in which a fluorescent reporter is driven by the endogenous elk3 promoter while simultaneously disrupting Elk3 function. Reporter expression in trunk vessels confirmed both successful genome editing and elk3 expression in the developing vasculature. To further determine loss-of-function phenotypes, we designed and injected multiple guide RNAs targeting elk3 exons and assessed injected embryos for lymphatic defects.

In parallel, we tested a whole-mount Elk3 immunostaining protocol, which will require further optimization. Together, these tools establish zebrafish as a tractable in vivo platform for dissecting the molecular regulation of Elk3 during lymphatic vascular development.



Mahrukh Hassan (Dr. Michelle Collins)

Exploring the Effects of PITX2C Deficiency on Fatty Acid Metabolism

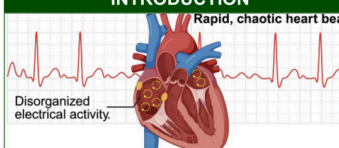
PITX2 (paired-like homeodomain transcription factor 2) is strongly associated with atrial fibrillation. Targeted central carbon metabolomics and RNA sequencing of Pitx2c-deficient cardiomyocytes reveal that fatty acid metabolism is amongst the top dysregulated pathways. However, it is unknown how exactly the pathway is impaired. We hypothesize that PITX2C regulates the handling of fatty acids in cardiomyocytes. The experiment treated control and Pitx2c-deficient neonatal rat cardiomyocytes with BSA or high fatty acid media. The cells were then stained with BODIPY and analyzed using fluorescence microscopy. We found no significant difference in lipid droplet area as a percentage of total cell area but a significant decrease in the number of lipid droplets for both control and knockdown cells when treated with the high fatty acid media. These findings suggest that high fatty acid exposure alters lipid droplet distribution in cardiomyocytes without significantly changing the overall area occupied by lipid droplets.

Exploring the Effects of PITX2C Deficiency on Fatty Acid Metabolism

Mahrukh Hassan, Andy Kim, Michael Norrie, Michelle Collins

INTRODUCTION

Rapid, chaotic heart beat.



Disorganized electrical activity.

Atrial Fibrillation Risk Factors

Modifiable	Non-modifiable
- Excessive alcohol consumption - Sedentary lifestyle - Obesity	- Age - Genetics - Sex

Atrial Fibrillation (AF) is the most common type of supraventricular arrhythmia. The *PITX2* gene is strongly associated with AF. *PITX2C* transcriptionally regulates atrial metabolic processes.

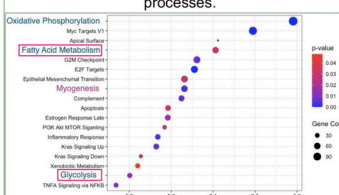


Fig. 1 Bulk RNA-seq analysis of *Pitx2c*-deficient cardiomyocytes. [1]

Loss of *PITX2C* decreases glycolysis.

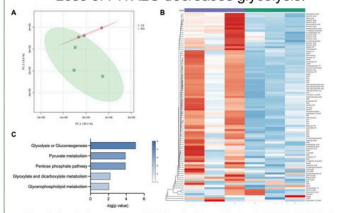


Fig. 2 Central carbon metabolomics in control and *Pitx2c*-deficient cardiomyocytes. Metabolomics data and analysis by Andy Kim.

HYPOTHESIS

We hypothesize that *PITX2* transcriptionally regulates how cardiomyocytes use fatty acids.

MATERIALS AND METHODS

Developing *Pitx2c* knockdown model.

Post-natal day 2 rat pup heart dissection and isolation of atria

Atrial cardiomyocyte primary cell culture and siRNA knockdown of *Pitx2c*.

Western Blots and BODIPY staining

BSA Media

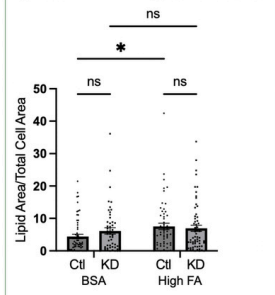
High Fatty Acid Media

8% BSA in DMEM (no glucose)

Palmitate: 100uM
Oleate: 100uM

RESULTS

Lipid Area as a Percentage of Total Cell Area



ns

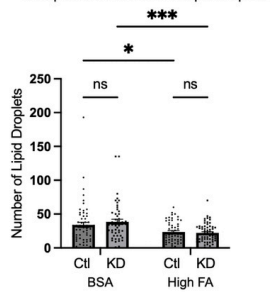
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Ctl BSA KD BSA Ctl FA KD FA

Comparison of Number of Lipid Droplets



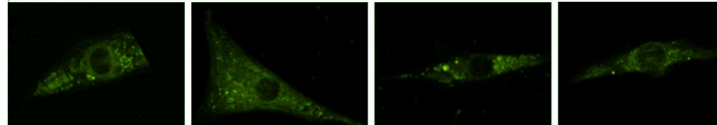
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Ctl BSA KD BSA Ctl FA KD FA



CONCLUSION

- The change in lipid droplet accumulation between control and *PITX2* deficient cells was not statistically significant.
- Thus, lipid droplet accumulation is not a mechanism of fatty acid metabolism dysfunction.

FUTURE DIRECTIONS

- Further work required to understand how *PITX2* regulates fatty acid and glucose metabolism.
- Continue with Western Blots to examine protein levels of key fatty acid metabolism enzymes.

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ACKNOWLEDGEMENTS

Thank you to Andy Kim, Dr. Michelle Collins and everyone in the Collin's Lab for their continuous support.

This project was funded by:




CIHR IRSC
And Biomedical Summer Research Project Award.



Aniela Zyna Hernandez (Dr. Sébastien Gauthier)

Investigating bidirectional heart—brain vascular cross talk in zebrafish models of atrial fibrillation

Atrial fibrillation (AF) is the most common cardiac arrhythmia and a major risk factor for ischemic stroke. Although AF-associated thromboembolism is well established, the effects of cardiac dysfunction on cerebrovascular integrity before stroke remain poorly understood. Furthermore, the brain–heart relationship is bidirectional, and emerging evidence suggests ischemic stroke is also capable of affecting cardiac function.

This project aimed to utilize the zebrafish model, which offer high genetic similarity to humans, rapid development, and optical transparency that enables simultaneous visualization of the heart and brain. Using a *pitx2c* loss-of-function model of AF, we investigated the early effects of cardiac dysfunction on blood–brain barrier (BBB) integrity. Immunofluorescence analysis showed reduced brain vascular structure in *pitx2c* mutants, while transcriptomic analysis indicates reduced expression of junctional markers such as *cldn5a* and *cdh5*, involved in maintaining BBB integrity. Transporter, endothelial, and pericyte markers show no apparent changes, suggesting altered BBB integrity rather than changes in endothelial or pericyte identity. In a complementary approach, a targeted optogenetic stroke model will be developed to examine whether ischemic injury alters cardiac function. Together, these studies will provide insight into the bidirectional mechanisms linking cardiac dysfunction, cerebrovascular integrity, and ischemic injury.

Investigating bidirectional heart—brain vascular crosstalk in zebrafish models of atrial fibrillation (AF)

Aniela Zyna Hernandez¹, Liubov Lobanova¹, Wrynun Munabirul¹, Ana Gabriel¹, Michelle Collins¹, Sébastien Gauvrit¹

¹ Department of Anatomy, Physiology, and Pharmacology, College of Medicine, University of Saskatchewan.

BACKGROUND

- Atrial fibrillation (AF)** is the most common cardiac arrhythmia, characterized by an irregular heart rhythm¹.
- AF increases the risk of **ischemic stroke** that is commonly associated with cardioembolism², while emerging evidence also suggests a role for neuroinflammation^{3,4}.
- The **blood-brain barrier (BBB)** is a specialized vascular barrier that protects the brain by regulating exchange between the bloodstream and brain tissue⁵. Disruption of BBB integrity may increase susceptibility to cerebrovascular injury.
- PITX2C** is a cardiac-specific transcription factor that plays a role in heart development and cardiac rhythm regulation⁶.
- Zebrafish *pitx2c* loss-of-function phenocopies human AF, including **reduced mean blood flow velocity and atrial blood pooling**⁴.

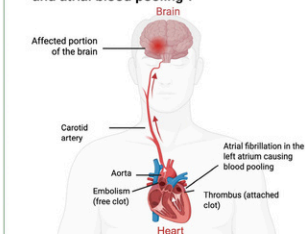


Figure 1. Schematic representation of cardioembolic stroke.

The knowledge gap

- The direct effects of AF on brain blood vessel structure and integrity have not been well characterized, highlighting the need for experimental models to investigate the heart–brain relationship.

Zebrafish model for brain-heart research

- ~70% of human protein-coding genes have zebrafish orthologues⁸.
- Conserved molecular mechanisms result in brain organization that closely parallels that of mammals⁷.
- High fecundity and rapid development enable efficient disease modelling.
- Optically transparent embryos enable real-time and simultaneous imaging of heart and brain vascular development.

OBJECTIVES

- To determine whether *pitx2c* loss of function compromises cerebrovascular barrier.
- To determine the effects of a zebrafish ischemic stroke model on cardiac health including rhythm and output dynamics.

HYPOTHESIS

Atrial fibrillation in the zebrafish loss of function *pitx2c* model promotes neurovascular dysfunction and inflammation may lead to impaired blood-brain barrier integrity, and overall reduced brain health.

MATERIALS AND METHODS

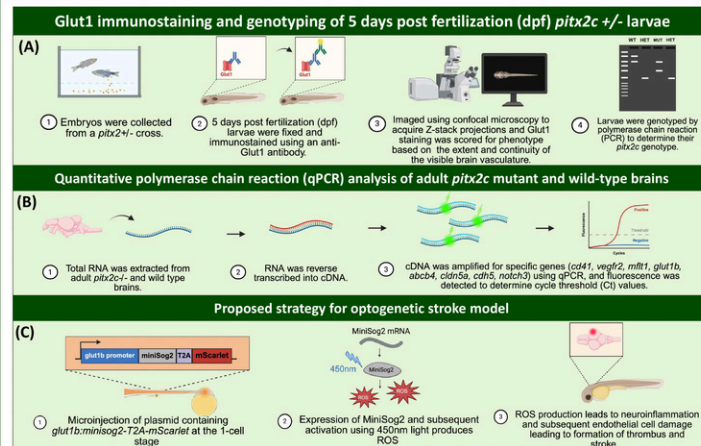


Figure 2. (A) Glut1 immunostaining and genotyping of 5 dpf *pitx2c* +/- heterozygotes were crossed and larvae were fixed, immunostained for Glut1 (glucose transporter enriched in BBB), and imaged by confocal microscopy. Z-stack projections of the head were used to score brain vasculature as **weak**, **moderate**, or **strong** based on staining extent and continuity, followed by genotyping. (B) qPCR analysis of adult *pitx2c* mutant and wild-type brains. Total RNA was extracted from adult *pitx2c* +/- and wild-type brains, reverse transcribed to cDNA and amplified by qPCR for genes associated with vascular and blood-brain barrier function, including *cd41* (thrombocyte marker), *vegfr2* and *mlf1* (endothelial markers), *glut1b* (glucose transporter), *cldn5a* (tight junction protein), *abcb4* (ABC transporter), *cdh5* (adhesion junction protein), and *notch3* (pericyte marker). (C) Proposed strategy for a targeted optogenetic stroke model. A *glut1b*-MiniSOG2-mScarlet construct was designed for brain endothelial-enriched expression. Blue-light activation generates reactive oxygen species, induce endothelial damage and thrombosis, and mScarlet enables identification of construct-positive embryos.

RESULTS

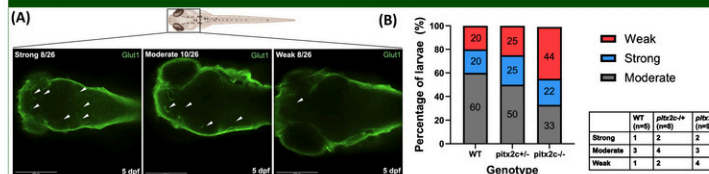


Figure 3. (A) Glut1 vascular phenotype scoring criteria. Strong, moderate, and weak phenotypes were defined by the extent and continuity of Glut1-positive brain vasculature, with strong showing the most continuous vasculature, moderate showing reduced continuity, weak showing minimal or absent vasculature, as shown by arrowheads. Images are snapshots from z-stack acquisitions of the head region, acquired at approximately the same z-step. Representative images were selected from 26 larvae (strong, n=6; moderate, n=10; weak, n=8). (B) Percentage of 5 dpf *pitx2c* larvae with strong, moderate, or weak Glut1 immunostaining by genotype. Bars represent the percentage of larvae within each genotype assigned to each staining category (wild type, n=5; *pitx2c* +/-, n=8; *pitx2c* -, n=9). Four larvae were excluded from genotyping analysis.

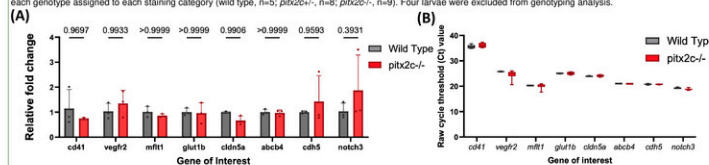


Figure 4. (A) Relative expression of *cd41*, *vegfr2*, *mlf1*, *glut1b*, *cldn5a*, *abcb4*, *cdh5*, and *notch3* in adult wild-type and *pitx2c* mutant brains. Total RNA was extracted from adult brain tissue and analyzed by qPCR. Gene expression was normalized to *ef1a* using the $\Delta\Delta Ct$ method and presented as mean $\pm$ SD (n=3 biological replicates per genotype). Statistical significance was defined as $p < 0.05$. *vegfr2* showed increased mean expression in *pitx2c* mutants, driven by outliers. *mlf1*, *glut1b*, and *abcb4* showed no apparent difference between genotypes. *notch3* showed an apparent increase driven by an outlier, with otherwise comparable expression between genotypes. The junctional markers *cldn5a* and *cdh5* showed a trend toward decreased expression in mutants. *cd41* expression was also influenced by an outlier. (B) Raw cycle threshold values obtained from qPCR. *cd41* showed relatively high Ct values, indicating low transcript abundance and reduced reliability of relative expression measurements. *vegfr2* showed an unusually low Ct value in one sample, which contributed to an apparent increase in relative expression.

CONCLUSIONS

- Immunostaining of *pitx2c* +/- larvae showed a **trend toward weaker Glut1 localization** in brain vasculature, suggesting potential alterations in cerebrovascular integrity.
- pitx2c* +/- mutant brains showed a **trend toward reduced expression of the junctional markers *cldn5a* and *cdh5***. In contrast, endothelial cell markers, transporters, and pericyte markers remain largely unchanged, suggesting altered brain vascular integrity rather than reduced blood vessel density.

Future directions

- Increase the number of brains analyzed for qPCR beyond the current three biological replicates to further assess changes in BBB junctional markers.
- To functionally assess blood-brain barrier integrity, we will perform a permeability assay using Rhodamine B-conjugated dextran of different molecular weights to assess extent of BBB leakage.
- Establish a miniSOG2 optogenetic construct, microinject into one-cell stage embryos, and assess the effects of endothelial damage to cardiac function, including heart rate and stroke volume.

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ACKNOWLEDGEMENTS

I would like to thank the members of the Gauvrit Lab, Dr. Sébastien Gauvrit, Liubov Lobanova, Wrynun Munabirul, Ana Gabriel, and Dmytro Stupak as well as the members of Dr. Michelle Collins' Lab, for their support and guidance throughout this project. This work received summer research funding by NSERC USRA and Office of Vice-Dean Research's BioMed Projects program.



Isabelle Monsman (Dr. Anand Krishnan)

Revealing a new interacting partner for MANF for its neurotrophic actions

Peripheral Nerve Injury affects millions of people, often resulting in irreversible loss of function. Despite this, there are currently no pharmacological treatments available. Mesencephalic Astrocyte-derived Neurotrophic Factor (MANF) is a growth factor we previously showed to promote nerve regeneration in animal models. The mechanism of MANF's growth-promoting actions is currently unknown. Prior to this project, Bio-ID was used to identify major signalling molecules associated with MANF. One hit from the Bio-ID was GDNF Family Receptor $\alpha 1$ (GFR $\alpha 1$), a membrane-bound receptor that partners with GDNF to support axonal regeneration and Schwann Cell (SC) plasticity, the same effects MANF was found to promote. Given this, we hypothesize that MANF interacts with GFR $\alpha 1$ in its growth promoting actions. We used a Co-Immunoprecipitation assay to confirm physical interaction between MANF, GFR $\alpha 1$, and other common partners in GFR $\alpha 1$ signalling in SCs. Next, shRNA knockdown was used to suppress GFR $\alpha 1$ expression in SCs in order to evaluate the role of GFR $\alpha 1$ in MANF-driven proliferation and molecular changes. Cell proliferation (MTT) assays showed that cellular proliferation was suppressed after GFR $\alpha 1$ depletion, further supporting the hypothesis that GFR $\alpha 1$ is critical for MANF's activity. Overall, this project suggests a potential role for GFR $\alpha 1$ as a receptor for MANF.

Revealing a New Interacting Partner for MANF for its Neurotrophic Actions

Isabelle Monsman, Bhadrappriya Sivakumar, Anand Krishnan

Department of Anatomy, Physiology, and Pharmacology, College of Medicine, University of Saskatchewan, Canada

INTRODUCTION

MANF and Peripheral Nerve Regeneration

- Peripheral Nerve Injury affects millions of people, often resulting in irreversible loss of functions.¹
- At present, no effective pharmacological therapies are available for peripheral nerve repair.
- Our recent findings showed that Mesencephalic Astrocyte-Derived Neurotrophic Factor (MANF) promotes nerve regeneration in animal models.^{2,3}
- Although a promising therapeutic candidate for nerve repair, the mechanism of MANF's growth promoting actions is currently unknown.
- To explore the mechanism of action of MANF, our lab recently performed a Bio-ID assay and identified potential interacting partners of MANF.⁴



Fig 1: A cartoon showing Bio-ID workflow.

Potential Interacting Partners of MANF

- Our Bio-ID assay result suggested that six major signaling modules are associated with MANF: *GFRa1*, *Sema/Plexin*, *ECM/Integrin*, *IL-6*, *Protein processing in ER*, and *Protease remodeling modules*.

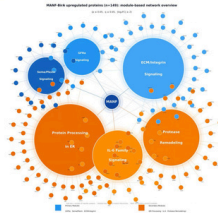


Fig 2: Bio-ID assay result shows 149 potential interacting hit candidates for MANF, distributed into six major signaling modules. Blue modules relate to peripheral nerve regeneration; orange modules relate to MANF's other functions.

- Among the six modules shortlisted, *GFRa1* signaling has been shown to promote axon regeneration and Schwann Cell (SC) plasticity, effects which MANF has also been observed to promote.⁵

- GFRa1* acts through canonical and non-canonical signaling, with GDNF and RET involved in the former and GDNF and N3CAM involved in the latter.

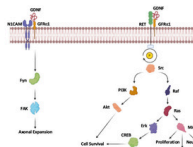


Fig 3: An illustration of GFRa1 canonical (right) and non-canonical (left) signaling.⁶

HYPOTHESIS

Our Bio-ID result suggests that MANF's mechanism of action is linked to *GFRa1* signaling. Based on this and, given that MANF and *GFRa1* have similar effects on axon growth and SC plasticity, we hypothesize that MANF interacts with *GFRa1* in its growth promoting actions.

OBJECTIVES

- Examine the physical interaction of MANF, *GFRa1*, and other partners of the *GFRa1* signaling module using Co-immunoprecipitation assay.
- Investigate the role of *GFRa1* in MANF-driven proliferation and molecular changes in Schwann Cells.

MATERIALS AND METHODS

Co-Immunoprecipitation (Co-IP) Assay

- The Schwann Cell (SC) line S16 was used.
- The cells were transfected with lentivirus carrying Doxycycline (Dox)-inducible MANF (L-Dox MANF) and treated with 1 µg/mL Dox to overexpress MANF.
- 1 mg of total protein collected from L-Dox MANF was incubated on agarose beads precoated with control IgG or *GFRa1* antibody for 24 h.
- After, the bound protein fraction was eluted for analysis with western blot.



Fig. 4: Workflow of Co-IP assay

Knockdown (KD) of *GFRa1*

- Control and *GFRa1* shRNAs were purchased from VectorBuilder.
- S16 cells previously transfected with L-Dox MANF were incubated with either control shRNA or *GFRa1* shRNA (25 MOI) for 24 h.
- The cultures were treated with 30 µg/mL puromycin for 24 h, followed by *GFRa1* knockdown validation using western blot.

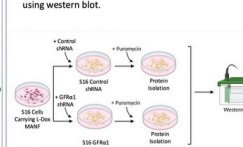


Fig. 5: Workflow of *GFRa1* knockdown experiment

Effects of *GFRa1* KD on MANF's Actions

- Cell Proliferation Assay (MTT Assay)**
 - 500 µg/mL MTT was added 24, 48, and 72 h post-Dox administration to S16-MANF or shRNA S16-MANF cells to evaluate the effect of MANF and *GFRa1* KD on cell proliferation.

Molecular Changes

- Western blot was performed to examine ERK signaling in S16-MANF and shRNA S16-MANF cells after supplementation with Dox.

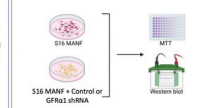


Fig. 6: Workflow of molecular studies

RESULTS

MANF Interacts with *GFRa1* and RET

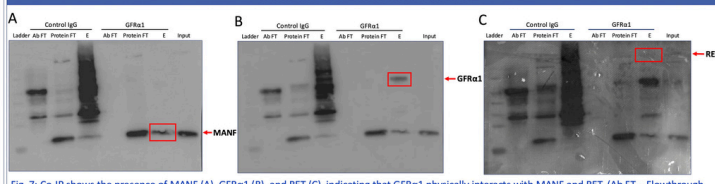


Fig. 7: Co-IP shows the presence of MANF (A), *GFRa1* (B), and RET (C), indicating that *GFRa1* physically interacts with MANF and RET. (Ab FT – Flowthrough of Unbound Antibody, Protein FT – Flowthrough of Unbound S16 MANF Protein, E – Eluate of Antibody-Protein Complex, Input – S16-MANF Protein).

GFRa1 KD in S16 cells pre-Transfected with L-Dox MANF

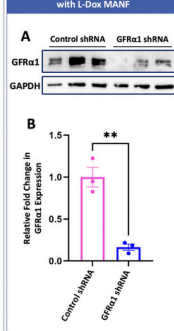


Fig. 8: (A) Western blot image shows knockdown efficiency of *GFRa1* in S16 cells transfected with L-Dox-MANF. (B) Quantification of western blot (mean ± SE; standard t-test; n=3; **p<0.01).

GFRa1 Knockdown Suppresses MANF-Induced Proliferation of S16 Cells

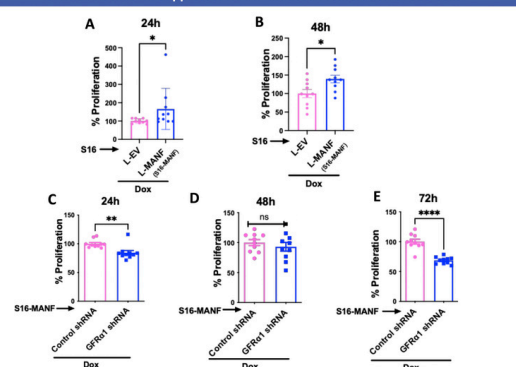


Fig. 9: (A,B) MTT Assay shows significant increase in proliferation of S16 cells overexpressing MANF (S16-MANF) at 24 h and 48 h (mean ± SE; standard t-test; n=10; *p<0.05). (C,D,E) MTT assay shows significant decrease in proliferation of S16 cells overexpressing MANF (S16-MANF) at 24 h and 72 h after *GFRa1* knockdown (mean ± SE; standard t-test; n=10; **p<0.01, ***p<0.0001).

RESULTS

Effect of *GFRa1* KD on ERK Signaling in S16-MANF Cells

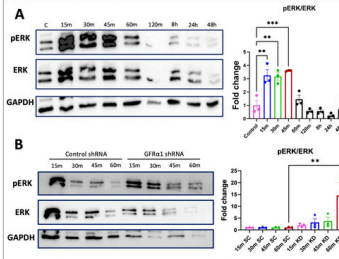


Fig.10: (A) Representative images and quantification of western blot shows pERK upregulation in S16 cells following Dox-induced MANF expression (mean ± SE; One-Way ANOVA; n=3; *p<0.05, **p<0.01, ***p<0.001). (B) Representative images and quantification of western blot shows pERK upregulation in S16 cells treated with *GFRa1* shRNA, compared to control shRNA treatment, following Dox-induced MANF expression (mean ± SE; One-Way ANOVA; n=3; **p<0.01).

CONCLUSION

- Co-IP assay shows that MANF physically interacts with *GFRa1*.
- Co-IP assay also shows the presence of RET, suggesting that MANF activates the canonical signaling pathway of *GFRa1*.
- Proliferation (MTT) assay shows suppression MANF-driven SC proliferation after *GFRa1* depletion, indicating that the function of *GFRa1* is critical for MANF's actions.
- Western blot data shows inconclusive results on the effect of MANF on ERK signaling (*GFRa1* KD and control shRNA treated S16-MANF shows inconsistent results).
- Overall, our observations show that *GFRa1* is a potential receptor for MANF.

FUTURE DIRECTIONS

- Re-examine ERK signaling in S16-MANF cells.
- Investigate whether *GFRa1* is critical for MANF-driven neurite outgrowth in primary neurons.
- Examine the role of MANF in GDNF-*GFRa1* interaction (GDNF is a natural ligand for *GFRa1*).

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ACKNOWLEDGEMENTS

- I would like to acknowledge Bhadrappriya Sivakumar, Dr. Anand Krishnan, and the other lab members for all their support and mentorship over the summer.
- This project was funded by the Biomedical Summer Research Award and NSERC USRA.





Janelle Proctor (Dr. Michael Levin)

The role of RNA binding protein dysfunction in neuronal synaptic pathology

Synapse dysfunction and neurodegeneration drive disability in multiple sclerosis (MS). Dysfunction of heterogenous nuclear ribonucleoprotein A1 (A1), an RNA binding protein, contributes to neurodegeneration in MS and dysregulates synaptic mRNA metabolism. A1 dysfunction alters the expression of synaptotagmin (Syt) genes, calcium sensors that facilitate neurotransmitter release and synapse homeostasis. We hypothesized that A1 dysfunction-induced changes in synaptic mRNA would impact synaptic protein localization, abundance, and function. To examine the effects of A1 dysfunction-induced alterations in synaptic mRNA, we modelled A1 loss-of-function by CRISPR/Cas9 A1 knock-out of mouse primary embryonic cortical neurons, performed RT-qPCR to quantify synaptic mRNA abundance, and western blotting and immunostaining to quantify protein abundance and localization, respectively. I found that Syt2 ($p=0.041$) and Kcnh3 ($p=0.030$) mRNA was increased and Grin1 was alternatively spliced ($p=0.021$) with A1 knock-out. There was a non-significant trend to upregulation of total Syt2 protein ($p=0.087$), and a visible increase of Syt2 within neuronal processes that will be quantified in future studies. These results show that A1 dysfunction alters synaptic mRNA expression and may impact synaptic function by altering the localization of synaptic proteins like Syt2. Changes in synaptic protein expression and localization could disrupt homeostasis, leading to synapse dysfunction and neurodegeneration in MS.

The role of RNA binding protein dysfunction in neuronal synaptic pathology



Janelle E. Proctor¹⁻³, Miranda L. Messmer¹⁻³, Michael C. Levin¹⁻⁴

Office of the Saskatchewan Multiple Sclerosis Clinical Research Chair, University of Saskatchewan¹, Cameo MS Neuroscience Research Centre, Saskatoon City Hospital², Department of Anatomy, Physiology and Pharmacology, University of Saskatchewan³, Department of Medicine (Neurology), College of Medicine, University of Saskatchewan⁴

BACKGROUND

- Neurodegeneration, the death and damage to neurons, axons, and synapses, drives disability in multiple sclerosis (MS)^{1,2}
- Dysfunction of heterogeneous nuclear ribonucleoprotein A1 (hnRNP A1), an RNA binding protein, marked by nuclear depletion and cytoplasmic accumulation leads to neurodegeneration⁴
- hnRNP A1 dysfunction alters stability, splicing, and abundance of synaptic gene mRNA^{3,4}. RNA sequencing data from our lab shows differential expression of synaptic mRNA with hnRNP A1 knock-out (KO), a model of hnRNP A1 loss of function.
- Synapses are crucial to neuronal communication and viability. Synaptic pathology (changes to synaptic structure or function) contributes to neurodegeneration in MS⁵
- As such, there is an opportunity to study how hnRNP A1 dysfunction causes synapse dysfunction and contributes to neurodegeneration in MS

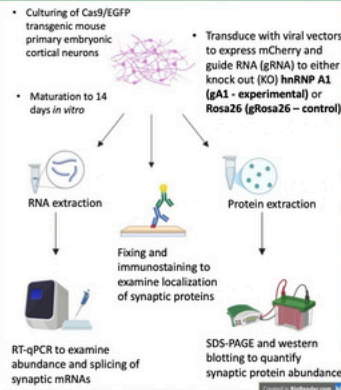
HYPOTHESIS & OBJECTIVES

Hypothesis: I hypothesize that hnRNP A1-dysfunction induced changes in the mRNA of synaptic genes will impact synaptic protein abundance, localization, and function in neurons, resulting in synapse dysfunction

Objectives:

- Validate the hnRNP A1 dysfunction model by measuring hnRNP A1 protein expression
- Quantify mRNA abundance and splicing of synaptic genes using RT-qPCR.
- Quantify abundance of synaptic protein targets in the hnRNP A1 dysfunction model by western blotting and assess protein localization by immunostaining

METHODS



RESULTS

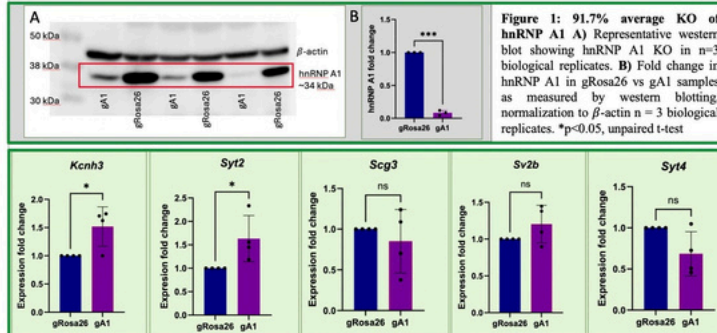


Figure 2: RT-qPCR for presynaptic protein targets shows upregulation of *Kcnh3* and *Syt2*. Reverse transcription (RT) performed with RNA from n=4 biological replicates. qPCR reactions run in triplicate and results normalized to β -actin. *p<0.05, unpaired t-test

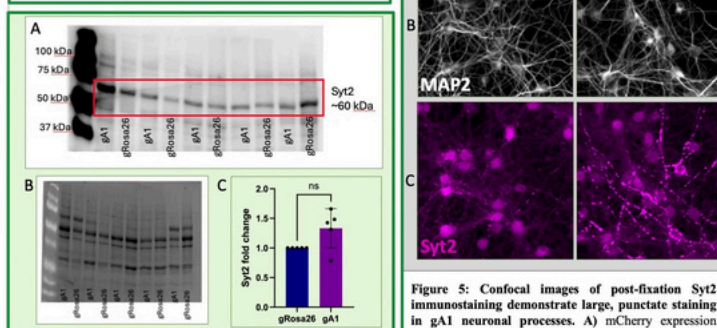
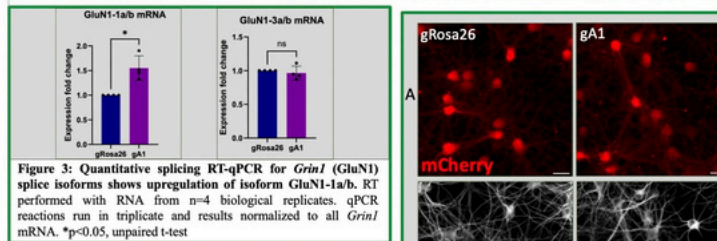


Figure 4: Synaptotagmin 2 (Syt2) western blot shows a non-significant trend towards upregulation. A) Western blot for Syt2, n=5 biological replicates B) Stain-free total protein blot. C) Fold change in Syt2 between gA1 and gRosa26 samples. Normalization to total protein. *p<0.05, unpaired t-test

CONCLUSIONS

- hnRNP A1 loss of function leads to differential expression of *Syt2*, *Kcnh3*, and *GluN1-1a/b* mRNA.
- Preliminary results show a trend of increased Syt2 protein and potential change in Syt2 localization in gA1 neurons compared to gRosa26 neurons, though further analysis is required
- Therefore, preliminary observations indicate that changes in mRNA abundance observed through RT-qPCR may correspond with changes in protein localization
- Syt2 is a calcium sensor that facilitates inhibitory neurotransmitter release in the forebrain^{6,7}. Therefore, increased presynaptic Syt2 could alter neurotransmission
- Synapse homeostasis is crucial to neuron survival⁵. Changes in synaptic protein expression and localization, such as seen with Syt2, could disrupt homeostasis, leading to synapse dysfunction and thus neurodegeneration

FUTURE DIRECTIONS

- Perform Syt2 western blot with new protein samples
- Quantify Syt2 immunostaining to assess changes in Syt2 localization.
- Western blotting and immunostaining for *Kcnh3*, *GluN1*

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ACKNOWLEDGEMENTS





Uday Sandhu (Dr. Changting Xiao)

Uptake of Gut-Derived Extracellular Vesicles into Rat Aortic Endothelial Cells

Extracellular vesicles (EVs) are cell-derived particles responsible for important biological functions, such as communications with distant cells. The uptake of EVs into target cells is crucial for their functions. The small intestine plays significant roles in energy homeostasis and systemic health. We recently described the secretion of EVs from the intestine; however, the functions of EVs originating from the intestine are largely unknown. We hypothesize that gut-derived EVs regulate vascular functions. The objective of this project is to characterize the uptake of gut-derived EVs into cultured rat aortic endothelial cells (RAOEC). EVs were isolated from rat mesenteric lymph (which contains gut secretions) with centrifugation at 20,000g x 20min to remove cell debris and two rounds of ultracentrifugation at 100,000g x 90min to remove lipoproteins and isolate EVs. Isolated EVs were fluorescently labelled by incubating with PKH67 Green Membrane dye and ultracentrifuging twice at 190,000g x 120 min to remove free dye and ensure purity. RAOEC were incubated with Hoechst Blue Nuclear Stain first, followed by incubation with labelled EVs, in the presence and absence of various endocytosis inhibitors (e.g. cold temperature and heparin or chlorpromazine at different concentrations). Cells were imaged with an EVOS 5000 fluorescence microscope, and images were analyzed with ImageJ and GraphPad PRISM. We detected significant uptake of EVs by RAOEC, which was significantly inhibited by cold temperature and heparin. These results support that gut-derived EVs enter aortic endothelial cells through specific endocytosis pathways. Future research will examine the functional roles of gut-derived EVs on endothelial cell function and health.

INTRODUCTION

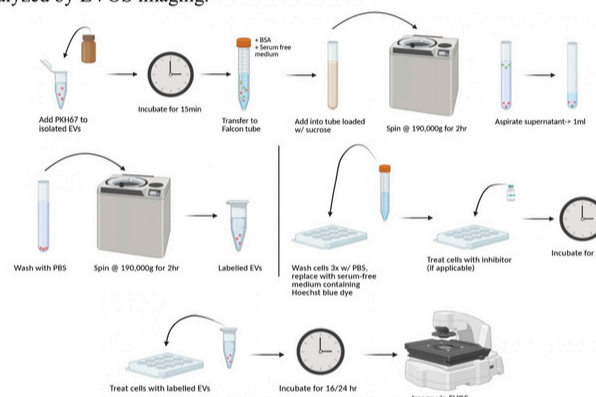
- **Extracellular vesicles (EVs)** are bi-layered particles released by cells through various pathways, playing roles in **cell-cell communication**^[1].
- Cellular uptake of EVs may occur through various mechanisms, such as **caveolin-mediated** and **clathrin-mediated endocytosis**^[2]. This can be **inhibited** by various means, such as **low temperature (4°C)**, **heparin** and **chlorpromazine (CPZ)**^[2].
- The **small intestine** plays a major role in energy homeostasis and systemic health^[3].
- We recently described EV secretion from the intestine^[4]. **The functional roles of gut-derived EVs are not known.**
- EVs may contribute to endothelial dysfunction via their uptake into endothelial cells^[5].
- **Whether gut-derived EVs enter vascular endothelial cells and regulate their functions is unknown.**

OBJECTIVES

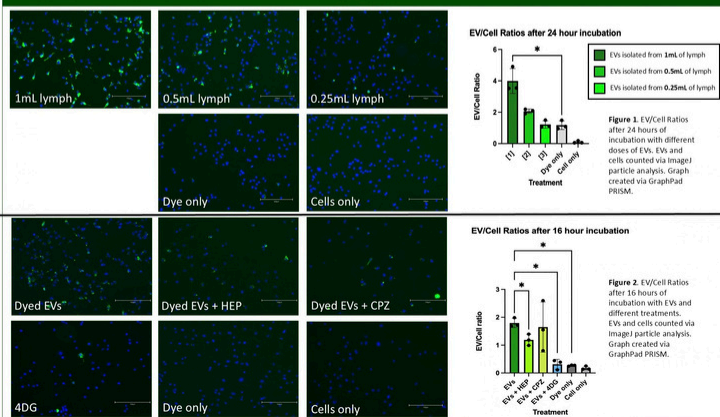
- To examine the **uptake of EVs** isolated from gut lymph by an endothelial cell model, rat aortic endothelial cells (RAOEC).

MATERIALS and METHODS

- EVs were isolated from **rat mesenteric lymph** through ultracentrifugation.
- Isolated EVs were fluorescently labelled with **PKH67 Green dye**.
- The nuclei of **RAOEC** were labelled with **Hoechst Stain**.
- EV uptake was shown by alteration of fluorescence intensity after co-incubating RAOEC with labelled EVs, in the presence and absence of various endocytosis inhibitors (e.g. **cold temperature**, **heparin**, **CPZ**). Fluorescence intensity was analyzed by EVOS imaging.



RESULTS



CONCLUSIONS

- EVs can be **labelled** with PKH67 green dye.
- EVs are taken up by RAOEC in a **dose-dependent** manner.
- Uptake of EVs into RAOEC is **reduced** by low temperature and heparin.

FUTURE DIRECTIONS

- Quantify EV uptake into RAOEC via **flowcytometry**.
- Examine the effects of EV on endothelial functions and health.
- Assess the uptake and functional role of EVs from disease animal models.

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ACKNOWLEDGEMENTS

I extend my gratitude to my fellow lab member, our postdoctoral fellow **Dr. Tianyu Hang**, and my supervisor **Dr. Changting Xiao** for their continued support throughout this project.

This research project was funded by the **Biomedical Summer Research Scholarship** and the **Heart and Stroke Foundation of Canada**.



Hana Shaarawy (Dr. Asmahan AbuArish)

Investigating the Contribution of Ribosomal Dynamics to Integrated Stress Response Defects in Cystic Fibrosis

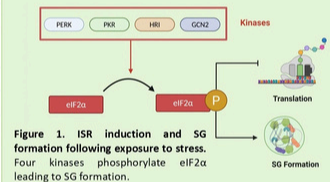
Abstract: Cystic fibrosis (CF) is a respiratory disease caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, most commonly the $\Delta F508$ mutation, resulting in protein dysfunction and chronic proteostatic stress. CF airways exhibit elevated oxidative stress, which may alter epithelial adaptive responses to environmental challenges. Recent work from Dr. AbuArish's laboratory demonstrated that acute cigarette smoke exposure induces robust stress granule (SG) formation in bronchial epithelial cells through activation of the protective integrated stress response (ISR). They also showed that this response is blunted in CF cells, which form fewer and larger SGs. We hypothesized that this defect is caused by reduced ribosome disassembly in CF cells. To test this hypothesis, quantitative immunofluorescence imaging together with pharmacological modulation of ribosome assembly were used. Our findings showed that puromycin-induced ribosome disassembly did not restore the SG formation defect in CF cells, suggesting that ribosome dynamics are not a determining factor. Cycloheximide, which stalls ribosomes, caused rapid SG disassembly in both CF and non-CF cells, highlighting the highly dynamic nature of SGs and their non-pathogenic nature. Collectively, these findings do not support our hypothesis and indicate that impaired SG formation in CF cells is not driven by altered ribosome dynamics.

Investigating the Contribution of Ribosomal Dynamics to Integrated Stress Response Defects in Cystic Fibrosis

Hana Shaarawy & Dr. Asmahan AbuArish

BACKGROUND

- Cystic fibrosis (CF) is a hyperinflammatory respiratory disease with 70% of cases caused by biallelic deletion of phenylalanine 508 in the CFTR gene, also known as $\Delta F508$ mutation¹.
- This mutation causes CFTR misfolding and retention in the ER resulting in chronic proteostatic stress.
- Environmental stressors can exacerbate airway inflammation in CF. Whether this vulnerability reflects defects in adaptive mechanisms that protect the airway epithelium against acute insults remains unknown.
- Recent work from AbuArish's group showed that human bronchial epithelial cells expressing wild type (WT)-CFTR respond to acute exposure to cigarette smoke by activating the integrated stress response (ISR) pathway and forming membraneless organelles called stress granules (SGs)². Cells expressing $\Delta F508$ -CFTR formed fewer and larger SGs, indicating a defect in the ISR pathway.



- SG formation requires ribosome-free mRNAs³. Whether chronically stressed CF cells form fewer and larger SGs due to ribosome stalling on mRNAs⁴ is not known.
- To test if inducing ribosome disassembly restores SG formation in CF cells, puromycin was used.
- Importantly, pathological SGs are static and increase in size⁵ while non-pathological SGs are dynamic and in equilibrium with polysomes.
- Cycloheximide is used to stall ribosomes on mRNAs which induces disassembly of non-pathological SGs.

HYPOTHESIS & OBJECTIVES

Hypothesis : The disparity in SG formation between CF ($\Delta F508$) and non-CF cells in response to cigarette smoke exposure is due to differential ribosome dynamics on mRNAs.

Objectives :

1. Induce ribosome disassembly in both cell types using puromycin and characterize SG formation.
2. Enhance ribosome stalling in both cell types using cycloheximide and characterize SG formation.

MATERIALS AND METHODS

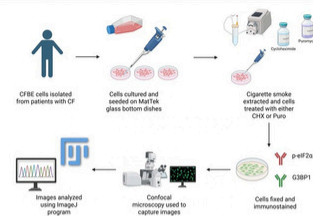
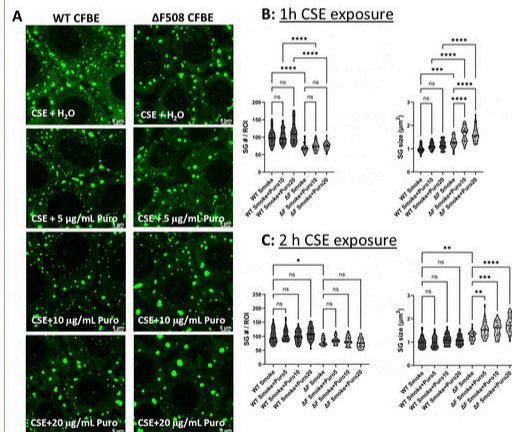


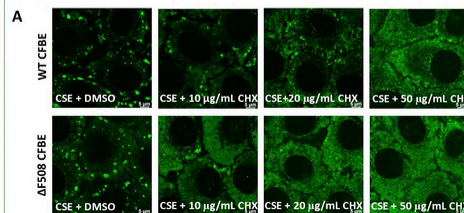
Figure 2: Immunofluorescence, fluorescence confocal imaging and quantitative cluster analysis are the experimental methods used to observe and quantify the effects of modulating ribosome dynamics using Puromycin (Puro) and Cycloheximide (CHX) on SG formation in CFBE cells expressing WT- (non-CF) or $\Delta F508$ -CFTR (CF). Acute stress was induced by exposing cells to cigarette smoke extract for either 1 or 2 hours. Puromycin (Puro) was added in conjunction with CSE for the full exposure time. Cycloheximide (CHX) was added in the last 30 minutes of CSE treatment. Water (H₂O) and DMSO were used as controls for Puro and CHX treatments, respectively.

RESULTS

Inducing ribosome disassembly does not restore SG formation in CF cells



Inducing ribosome stalling similarly disassembles SGs in both CF and non-CF cells



RESULTS

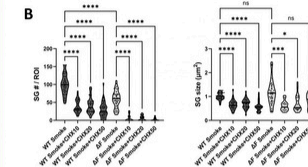


Figure 4B: Effect of ribosome stalling on SG number and size. Quantitative cluster analysis shows that CHX treatment effectively disassembles SGs in cells expressing WT- and $\Delta F508$ -CFTR in a dose dependent manner with highest disassembly rate in response to 50 $\mu g/mL$ CHX. Cells expressing $\Delta F508$ -CFTR show exaggerated response to CHX, with several images having no SGs.

CONCLUSIONS

1. Impaired ribosome disassembly did not account for the defective SG response observed in CF cells as demonstrated by inducing ribosome disassembly using puromycin and measuring SG characteristics in both cell types. Puromycin treatment did not restore SG numbers in CF cells, indicating that mRNA availability is not a limiting factor in SG nucleation.
2. Stalling ribosomes on mRNAs with CHX led to similar SG disassembly in both cell types suggesting SGs are dynamic. This indicates that both cell types form non-pathogenic SGs, hence this aspect can be eliminated as a reason for defective ISR signaling in CF cells.

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ACKNOWLEDGMENTS

I would like to thank Dr. AbuArish and lab members Bisrat Bekele, Mousumi Bhowmik and Evan Chayer for their support. In addition, I would like to thank the funding bodies which allowed me to pursue this project, namely the NSERC USRA and the Biomedical Summer Research Project awards.



Shelton Reece Ziola (Dr. Michael Levin)

Investigating the Effects of Dysfunctional Heterogenous Nuclear Ribonucleoprotein A1 on Mitochondrial Protein Abundance in Multiple Sclerosis

RNA binding protein dysfunction, hallmarked by nucleocytoplasmic mislocalization in neurons, contributes to neurodegeneration in multiple sclerosis (MS). Notably, dysfunctional RNA binding proteins have been implicated in mitochondrial dysfunction in other neurodegenerative diseases and is a key driver of neurodegeneration in MS. To model RNA binding protein induced neurodegeneration, we transduced primary mouse embryonic neurons with dysfunctional MS-patient derived heterogenous nuclear ribonucleoprotein A1 (A1) mutations (N265D, P275S, and K277N) to test the hypothesis that neuronal A1 dysfunction alters mitochondrial electron transport chain (ETC) complex subunits and mitochondrial fission protein abundance. Using Western blotting, we found that expression of ETC complex subunits were not significantly altered by dysfunctional A1 mutations. However, we observed a significant increase in the mitochondrial fission protein dynamin-related protein 1 (DRP1) in neurons expressing K277N. We also observed a significant increase in phospho-DRP1 (S616), a marker of stimulated mitochondrial fission, in neurons expressing P275S and K277N. These findings suggest that A1 dysfunction may be promoting excessive mitochondrial fission, potentially impairing mitochondrial function and contributing to altered energy production. Given the high energy demand of neurons, altered energy production may impair neuronal function and promote cell death, thereby supporting a potential mechanism by which A1 dysfunction contributes to neurodegeneration.

Investigating the Effects of Dysfunctional Heterogenous Nuclear Ribonucleoprotein A1 on Mitochondrial Protein Abundance in Multiple Sclerosis

Shelton R. Ziola^{1,3,4}, Connor E. Johnson MSc^{1,3,4}, Patricia A. Thibault PhD^{1,3,4}, Michael C. Levin MD¹⁻⁴

¹Department of Anatomy, Physiology and Pharmacology, ²Department of Neurology, ³Cameco Multiple Sclerosis Neuroscience Research Center, ⁴Office of the SK MS Clinical Research Chair
University of Saskatchewan, Saskatoon, SK, Canada



Background

- Multiple Sclerosis (MS) patients exhibit significantly higher nucleocytoplasmic mislocalization of the RNA binding protein heterogeneous nuclear ribonucleoprotein A1 (A1) in neurons compared to healthy controls^{1,2}
- Dysfunctional A1, characterized by mislocalization, contributes to neurodegeneration in MS^{1,2}
- Mitochondrial dysfunction is a driver of neurodegeneration in MS³

Objective & Hypothesis

Objective: Determine whether A1 dysfunction impacts mitochondrial protein targets using primary embryonic neurons

Hypothesis: Dysfunctional A1 will alter the abundance of electron transport chain (ETC) and mitochondrial fission proteins in primary embryonic neurons

Materials & Methods

- Primary embryonic neurons were isolated from wild-type embryos
- Primary neurons were transduced with adeno-associated viral vectors expressing A1 (WT) or A1 (Mut) on DIV 9
- Protein lysates were collected on DIV 14
- Protein targets were examined by Western blotting
- Analysis was performed using ImageLab software by normalizing to average total protein. The results for A1 (WT) are compared to A1 (WT)

Results: Effects of Overexpression of A1 Mutations on Electron Transport Chain Complex Protein Abundance in Primary Embryonic Mouse Neurons

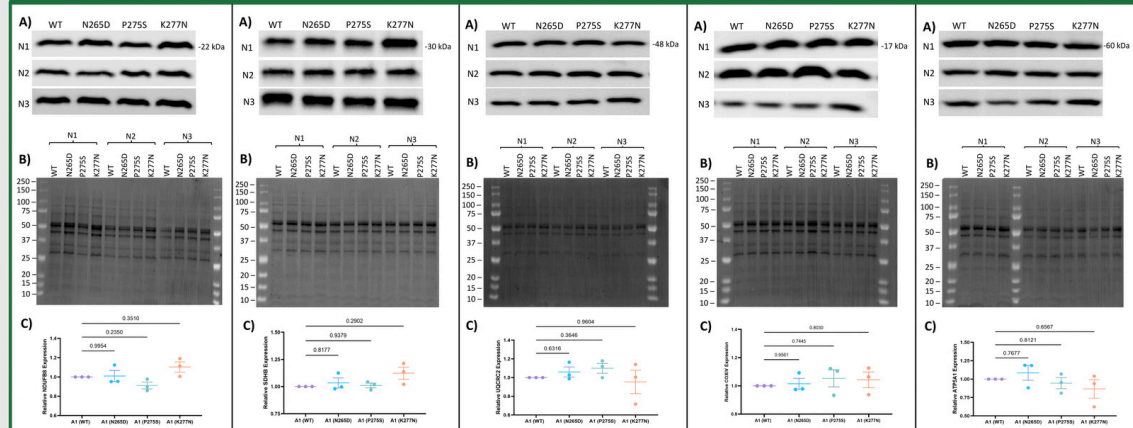


Figure 3. Overexpression of A1 mutations show no change in NADH ubiquinone oxidoreductase subunit B (NDUFB8) (CII) expression. A) Western blot of NDUFB8 expressing A1 (WT) and A1 (Mut). B) Corresponding stain-free total protein blot used for normalization. C) NDUFB8 protein was normalized to A1 (WT) and expressed as mean $\pm$ SEM (n=3) (One-way ANOVA with Dunnett's post-hoc test).

Figure 4. Overexpression of A1 mutations show no change in succinate dehydrogenase subunit B (SDHB) (CII) expression. A) Western blot of SDHB expressing A1 (WT) and A1 (Mut). B) Corresponding stain-free total protein blot used for normalization. C) SDHB protein was normalized to A1 (WT) and expressed as mean $\pm$ SEM (n=3) (One-way ANOVA with Dunnett's post-hoc test).

Figure 5. Overexpression of A1 mutations show no change in ubiquinol-cytochrome c reductase core protein 2 (UQCRC2) (CIII) expression. A) Western blot of UQCRC2 expressing A1 (WT) and A1 (Mut). B) Corresponding stain-free total protein blot used for normalization. C) UQCRC2 protein was normalized to A1 (WT) and expressed as mean $\pm$ SEM (n=3) (One-way ANOVA with Dunnett's post-hoc test).

Figure 6. Overexpression of A1 mutations show no change in cytochrome c oxidase subunit 4 (COXIV) (CV) expression. A) Western blot of COXIV expressing A1 (WT) and A1 (Mut). B) Corresponding stain-free total protein blot used for normalization. C) COXIV protein was normalized to A1 (WT) and expressed as mean $\pm$ SEM (n=3) (One-way ANOVA with Dunnett's post-hoc test).

Figure 7. Overexpression of A1 mutations show no change in ATP Synthase F1 subunit alpha (ATP5A1) (CV) expression. A) Western blot of ATP5A1 expressing A1 (WT) and A1 (Mut). B) Corresponding stain-free total protein blot used for normalization. C) ATP5A1 protein was normalized to A1 (WT) and expressed as mean $\pm$ SEM (n=3) (One-way ANOVA with Dunnett's post-hoc test).

Results: Overexpression of Mislocalizing A1 Mutations in Primary Embryonic Mouse Neurons Increases the Expression of the Mitochondrial Fission Protein DRP1

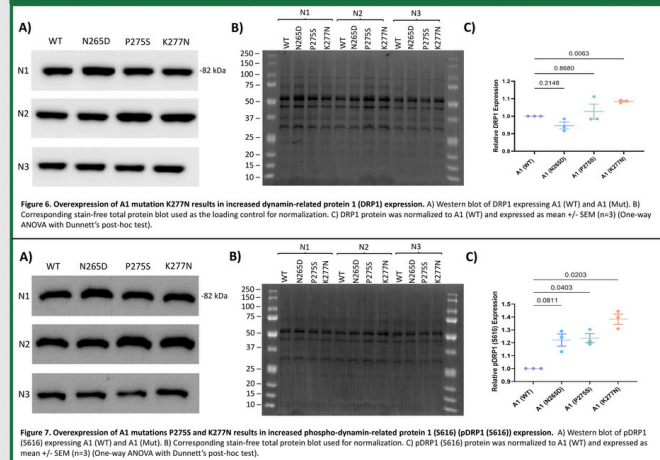


Figure 6. Overexpression of A1 mutation K277N results in increased dynamin-related protein 1 (DRP1) expression. A) Western blot of DRP1 expressing A1 (WT) and A1 (Mut). B) Corresponding stain-free total protein blot used as the loading control for normalization. C) DRP1 protein was normalized to A1 (WT) and expressed as mean $\pm$ SEM (n=3) (One-way ANOVA with Dunnett's post-hoc test).

Figure 7. Overexpression of A1 mutations P275S and K277N results in increased phospho-dynamin-related protein 1 (pDRP1) (S616) expression. A) Western blot of pDRP1 (S616) expressing A1 (WT) and A1 (Mut). B) Corresponding stain-free total protein blot used for normalization. C) pDRP1 (S616) protein was normalized to A1 (WT) and expressed as mean $\pm$ SEM (n=3) (One-way ANOVA with Dunnett's post-hoc test).

Conclusion

- Overexpression of A1 mutations does not significantly affect overall protein abundance in targeted subunits of mitochondrial ETC complexes I-V
- Overexpression of mutant A1 (K277N) significantly increases the expression of DRP1, a mitochondrial fission protein
- Overexpression of mutants A1 (P275S) and A1 (K277N) significantly increase the expression of pDRP1 (S616), a marker of activated mitochondrial fission
- Increased expression of the mitochondrial fission protein DRP1 suggests enhanced mitochondrial fragmentation, which may contribute to impaired mitochondrial function, energy failure, and neuronal cell death
- This data therefore suggests that A1 dysfunction, through mislocalization, may contribute to neurodegeneration by promoting excessive mitochondrial fission

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Biochemistry, Microbiology & Immunology





Adina Antu (Dr. Oleg Dmitriev)

Nanobody-assisted Structural Analysis of Copper Transporter ATP7B

ATP7B is a membrane copper transporter that plays an important role in maintaining cellular copper homeostasis. Mutations in the gene encoding ATP7B results in abnormal copper accumulation in cells, leading to Wilson disease. ATP7B contains six metal-binding domains (MBDs) involved in its regulation; however, this mechanism is poorly understood, partly because its complete structure has yet to be solved. Existing cryo-electron microscopy structures lack the first four MBDs due to their highly mobile and flexible nature. We hypothesize that nanobody binding may stabilize the MBDs in a physiologically relevant conformation and facilitate cryo-electron microscopy imaging of these domains. Nanobodies are genetically engineered single-domain antibodies that are highly versatile tools in protein biochemistry due to their small size and stability. This project aimed to study the binding of two nanobodies, 5A51 and 2R21 which target MBD4 and the linker loop between MBD3 and MBD4, respectively. Western blot analysis was used to confirm binding, following which the detection limits of both nanobodies were compared. Our results demonstrated successful binding and similar detection limits for both nanobodies. Additionally, nanobody-mediated pull down experiments were performed to isolate the MBD1-4 fusion protein, with both nanobodies successfully pulling down the target protein.



Halle Beblow (Dr. Kerry Lavender)

Comparative analysis of interferon-alpha subtype potency against Epstein-Barr virus

Mammals produce interferon-alpha (IFN- α) subtypes, proteins that play a pivotal role in the innate immune response to viral infections. Although these subtypes were once considered functionally redundant, evidence suggests that the 12 human IFN- α subtypes differ in their antiviral activity against specific viruses. This study evaluated the effects of individual IFN- α subtypes on Epstein-Barr virus (EBV) challenge.

Peripheral blood mononuclear cells (PBMCs) cells were plated at 500,000 cells per well. After 24 hours, cells were treated with 100 U/ml of individual IFN- α subtypes. 24 hours later, cells were administered EBV at a multiplicity of infection (MOI) of 0.1 and were incubated for an additional 72 hours. Following infection, PBMCs were counted, collected, and EBV viral load was quantified using droplet digital PCR (ddPCR).

Treatment with IFN- α subtypes resulted in an overall trend toward reduced EBV copy number compared to untreated cells. These findings support the growing evidence that IFN- α subtypes exhibit differential antiviral activity and provide a foundation for future studies investigating subtype-specific mechanisms of EBV inhibition.

Comparative analysis of interferon-alpha subtype potency against Epstein-Barr virus

Halle Beblow, Hajar Miranzadeh and Kerry J. Lavender

Department of Biochemistry, Microbiology and Immunology, College of Medicine, University of Saskatchewan

Introduction

Type I interferon alpha (IFN α) subtypes

- IFN α plays a role in direct antiviral immunity.¹
- Each subtype has distinct antiviral activities due to different expression of interferon-stimulated genes (ISGs).¹
- We were interested in the 12 human IFN α subtypes (1, 2, 4, 5, 6, 7, 8, 10, 14, 16, 17, 21).

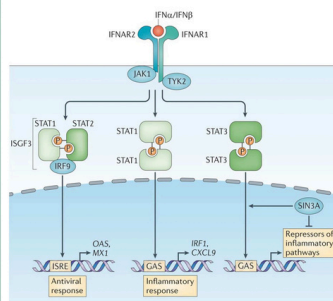


Figure 1: JAK-STAT signaling cascade for IFN α subtypes. Ivashkiv & Donlin. (2014). Immunology.

Epstein-Barr virus (EBV)

- EBV is a gamma herpesvirus that is present in more than 90% of humans.²
- EBV targets both epithelial and B cells, then establishes latency within the host through B cell infection.²

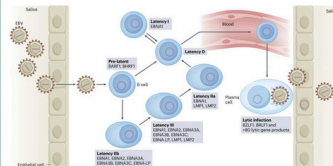


Figure 2: EBV infection pathway of humans. Munz, C. (2025). Nature Reviews Microbiology.

Objective and Hypothesis

- **Objective:** Evaluate the effect of the IFN α subtypes on EBV challenge.
- **Hypothesis:** Initial EBV infection will be most potentially controlled by specific IFN α subtypes.

Methods

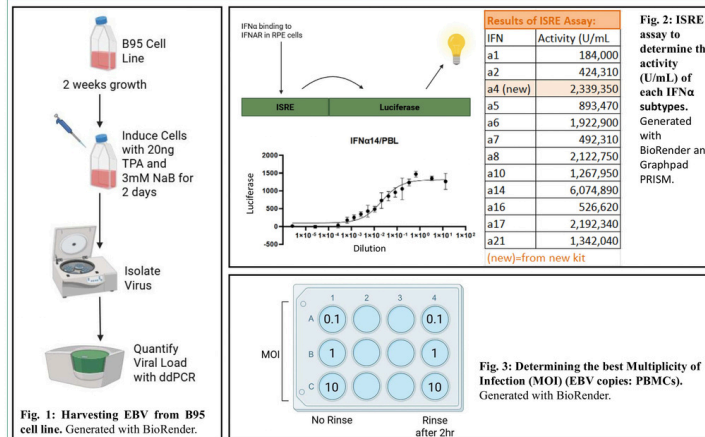


Fig. 1: Harvesting EBV from B95 cell line. Generated with BioRender.

Fig. 3: Determining the best Multiplicity of Infection (MOI) (EBV copies: PBMCs). Generated with BioRender.

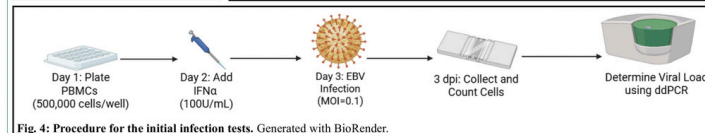


Fig. 4: Procedure for the initial infection tests. Generated with BioRender.

Results

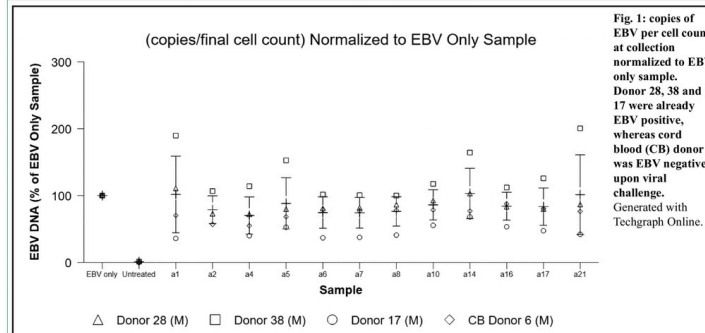


Fig. 1: copies of EBV per cell count at collection normalized to EBV only sample. Donor 28, 38 and 17 were already EBV positive, whereas cord blood (CB) donor 6 was EBV negative upon viral challenge. Generated with Techgraph Online.

Conclusion: Donor 28, 17 and CB 6 exhibited an overall trend toward reduced EBV copy number following IFN treatment, while Donor 38 showed a distinct response profile.

Future Directions/Improvements

- Test more donors for the initial infection suppressive effects of IFN α subtypes on EBV infection, including more EBV negative donors.
- Test the effects of IFN α subtypes on latent reactivation and cell immortalization to see how they impact other parts of the EBV lifecycle.
- Use *GAPDH* to allow more accurately determine the amount of EBV DNA per cell.

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Acknowledgements

Lavender Lab Members

- Dr. Kerry Lavender
- Dr. Hajar Miranzadeh
- Vianne Chang
- Satyajit (Shatu) Biswas

Funding

- Natural Sciences and Engineering Research Council of Canada (NSERC)
- University of Saskatchewan College of Medicine





Josh Cameron (Dr. Aaron White)

Exploring the Interactions between E. coli Curli and Human Amyloid Beta Peptides

Neurodegenerative diseases of humans involve the accumulation of proteins called amyloids in the central nervous system. Escherichia coli, which is present in roughly 90% of the population's microbiome, produce an amyloid protein called curli. Curli has a similar 3D structure to amyloid beta ($A\beta$), the amyloid involved in Alzheimer's disease. The goal of my project is to determine if E. coli curli can influence the accumulation of $A\beta$. I am working to generate a recombinant E. coli strain that we can purify curli from, which will allow me to test the interactions between E. coli curli and $A\beta$. During the summer, I introduced two mutations into the promoter for CsgD, the major activator of curli production. When attempting to introduce these mutations into our E. coli strain, the recombinant plasmid, carrying the mutated csgD promoter, integrated into the lac operon, which was the wrong spot. In my future work, I will knock out the lac operon and retry introducing the csgD promoter mutations. Purification of E. coli curli and testing the interactions with $A\beta$ aggregation would be the next steps in my project.

INTRODUCTION

Amyloids and Neurodegenerative Diseases

- Amyloid fibrils are large, stable aggregates of proteins with a cross- β structure [1] (Fig. 1)

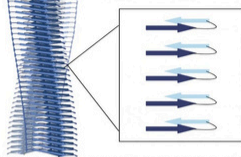


Figure 1: The Cross- β Structure of Amyloids. Created in BioRender

- Neurodegenerative diseases (NDs) involve the loss of mental and physical function that progressively worsens. Amyloids are involved in many NDs [1,2] (Table 1).

Table 1. List of major human neurodegenerative diseases and associated amyloid proteins.

Disease	Amyloid Protein
Alzheimer's Disease	Amyloid beta peptides
Parkinson's Disease	Alpha-synuclein
Creutzfeldt-Jakob Disease	Prion protein
Amotrophic Lateral Sclerosis	Superoxide dismutase

Curli made by *E. coli* and *Salmonella*

- Some bacteria produce functional amyloids [2]. One example is curli, an amyloid fimbriae produced by *Escherichia coli* and *Salmonella* that is used by the bacteria to form biofilms [3].
- Salmonella* has been shown to produce curli within its host [4].

Is There a Microbial Link to Neurodegenerative Disease?

- Cross-seeding is a process in which an amyloid can act as a seed to start or speed up the aggregation process of a different amyloid protein [1].
- Curli shares a similar structure to the Alzheimer's Disease amyloid, amyloid beta (A β) [5].
- We hypothesize that *E. coli* curli and human A β can cross-seed, leading to increased A β fibrilization.

Building an Optimal Strain to Study Curli

- This work is in a Saskatchewan *E. coli* strain, E4BF2, that has a cellulose knockout for cleaner curli purification [6].
- One objective is to introduce a mutation in the *csgD* promoter known to boost curli production [7] (Fig. 2)

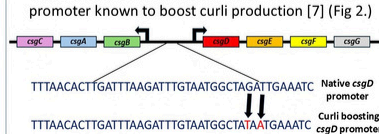


Figure 2: *csgBAC* and *csgDEFG* Operons and *csgB-D* Intergenic Region. When the *csgD* promoter's -10 region is mutated from TAGATT to TATAAT, there is a significant boost in curli expression.

MATERIALS and METHODS

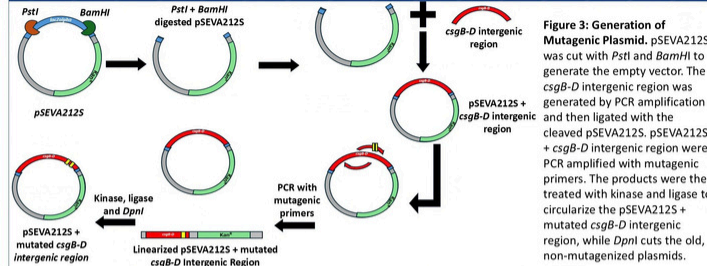


Figure 3: Generation of Mutagenic Plasmid. pSEVA2125 was cut with *Pst*I and *Bam*HI to generate the empty vector. The *csgB-D* intergenic region was generated by PCR amplification and then ligated with the cleaved pSEVA2125. pSEVA2125 + *csgB-D* intergenic region were PCR amplified with mutagenic primers. The products were then treated with kinase and ligase to circularize the pSEVA2125 + mutated *csgB-D* intergenic region, while *Dpn*I cuts the old, non-mutagenized plasmids.

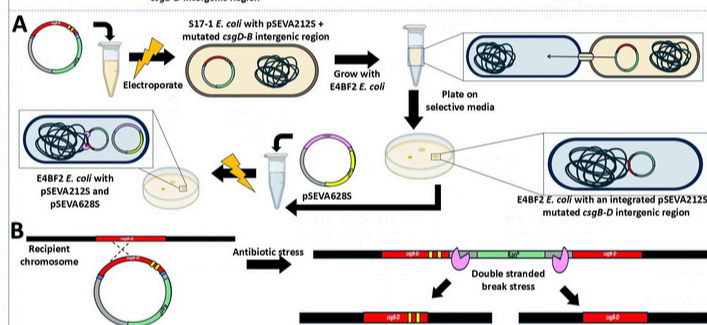


Figure 4: Introducing the *csgD* Promoter Mutation to E4BF2 *E. coli*. (A) pSEVA2125 was electroporated into an auxotrophic donor, which conjugated pSEVA2125 to E4BF2. The mix was plated onto minimal media supplemented with kanamycin to select conjugants. Conjugants were transformed with pSEVA628S, encoding gentamicin resistance and *I-SceI* (Pink partial circles). (B) Antibiotic stress leads to integration of pSEVA2125, forming the merodiploid. pSEVA628S encoded *I-SceI* enzymes create double stranded breaks, resolving the merodiploid to either wild-type or mutant. In part made with BioRender.

RESULTS

- Following the methods in Fig. 3, E4BF2 *E. coli*'s *csgB-D* intergenic region was cloned into pSEVA2125 (Fig. 6 A), and the TAGATT to TATAAT mutation was successful (Fig. 6 B).
- Unfortunately, introducing the mutation into E4BF2 *E. coli*'s genome did not work as planned. pSEVA2125 integrated into the *lac* operon (Fig. 7) as opposed to the *csgB-D* intergenic region.



Figure 6: Representation of where pSEVA212 Inserted into E4BF2. Upon sequencing the merodiploids, it was found that pSEVA2125 was recombining into the *lac* operon. Sequencing data not shown.

FUTURE WORK

- To ensure correct integration of pSEVA2125, E4BF2 *E. coli*'s *lac* operon will be knocked out.
- This will be done using the Lambda Red system (Fig. 7).

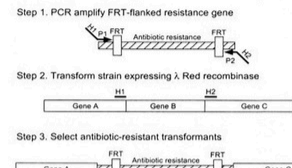


Figure 7: Lambda Red System for Recombination. Adapted from Datsenko KA, and Warner BL (2000).

- After removal of the *lac* operon, the *csgD* promoter mutation is expected to insert into the chromosome.
- Once the mutation is introduced, *E. coli* curli can be purified, and its interactions with A β tested (Fig. 8).

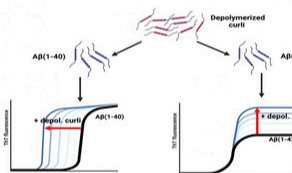


Figure 8: Summary of Interaction between *Salmonella* Curli and Amyloid Beta. Adapted from Flores PA (2023).

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ACKNOWLEDGEMENTS

The authors would like to thank the members of the White Lab; Dr. Shaun Wachter, Megan Tomlin, Ryan Bahrey, Rosemary Nnajide, Matt Scrivens, and Laurel Tarr.





Isfar Chowdhury (Dr. Ahmed Mostafa)

Lipidomics and HLA Molecular Mismatch in Alloimmune Kidney Transplant Rejection

Human leukocyte antigen (HLA) molecular mismatch, structural incompatibility between donor and recipient HLA molecules, predicts alloimmune kidney rejection and is quantified using the Epitope Registry (Epitope-based), PIRCHE-T2 (T-cell epitopes), and PIRCHE-B (B-cell epitopes). Lipidomics, global plasma lipid profiling, may offer a non-invasive complement to biopsy for detecting rejection-associated metabolic change. We hypothesized that molecular mismatch burden correlates with circulating lipid signatures, and that this relationship differs by rejection type. In 121 kidney transplant recipients (Saskatchewan cohort) with paired baseline and 90-day lipidomic and mismatch data, patients were stratified by outcome: antibody-mediated rejection (AMR), cell-mediated rejection (CMR), or no rejection. Spearman correlations (Benjamini-Hochberg corrected) were computed between nine mismatch scores and 66 lipid species. In the AMR group specifically, Eregistry DQB1 showed a triglyceride-dominant correlation pattern, led by diacylglycerol 32:2 ($\rho=0.67$, $q=0.047$), concentrated in glycerolipid metabolism (10/18 pathway lipids, $p<0.0001$). Univariate Cox regression identified PIRCHE-T2 DR+DQ as the strongest predictor of AMR-free survival (hazard ratio [HR] 1.49, 95% confidence interval [CI] 1.02-2.20, $p=0.042$). These findings support a locus- and rejection-type-specific link between mismatch and lipid metabolism, warranting external validation and multimodal integration with donor-specific antibody and donor-derived cell-free DNA testing.



Andrew Delainey (Dr. Jenny Wachter)

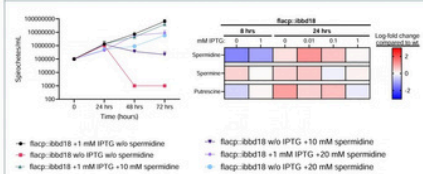
Spermidine Acts as a Co-Regulator of RpoS Dependent Gene Expression and Bacteriophage Induction in Borrelia burgdorferi

Borrelia burgdorferi, the causative agent of Lyme disease, undergoes an enzootic cycle between Ixodes ticks and vertebrate hosts and must tightly regulate gene expression during transmission. The sigma factor RpoS controls numerous genes associated with vertebrate infection and is repressed during in vitro growth by the protein BBD18. Previous work demonstrated that loss of BBD18 results in RpoS overexpression, spirochete lysis, and prophage induction, while supplementation with the polyamine spermidine can prevent these effects. This study investigated the role of spermidine in BBD18-dependent gene expression and Φ BB-1 bacteriophage induction. BBD18 interaction with the 5' untranslated region of *potA* was supported by RNA co-immunoprecipitation and electrophoretic mobility shift assays, while RT-qPCR demonstrated that BBD18 represses *potA* expression and that spermidine further reduces *potA* expression. RT-qPCR analysis also showed that spermidine supplementation decreases *rpoS* and downstream *ospC* expression. Additionally, spermidine generally reduced Φ BB-1 bacteriophage copy numbers in the culture supernatant. Together, these findings support a role for spermidine as a co-regulator of RpoS-dependent gene expression and prophage induction. The results further suggest that elevated spermidine concentrations in vertebrate blood may contribute to BBD18-independent regulation and proliferation during vertebrate infection.

INTRODUCTION

Borrelia burgdorferi, the causative agent of Lyme Disease, exists in a biphasic zoonotic cycle between an *Ixodes* tick vector and vertebrate hosts [1]. Numerous genes required for adaptation to the vertebrate host are under the control of the sigma factor RpoS which is repressed in culture and in the tick vector by the protein BBD18 [1]. During *in vitro* culture, *Borrelia burgdorferi* requires BBD18 expression to prevent overexpression of RpoS and associated lysis [2]. However, BBD18 expression is not essential during the natural infectious cycle for unknown reasons [2].

Our previous work has demonstrated that *Borrelia burgdorferi* overexpressing RpoS can be rescued from lysis by supplementation of the growth medium with 10 mM of the polyamine spermidine (Figure 1). Metabolic analysis of flacp::bbd18 (IPTG-inducible bbd18) cultures showed a significant increase in spermidine levels 24 hours following inhibition of bbd18 expression and loss of BBD18 protein (Figure 2). Also, *Borrelia burgdorferi* imports spermidine using the PotABCD ATP-binding cassette (ABC) transporter which is suspected to also be regulated by BBD18 [3].



BBD18 acts as a transcriptional repressor of *rpoS* [2]. When *Borrelia burgdorferi* is cultured *in vitro*, BBD18 is expressed and *rpoS* is repressed [2]. However, when bbd18 expression is controlled through an IPTG-inducible promoter, inhibition of bbd18 expression leads to *rpoS*/RpoS overexpression and:

1. Spirochete lysis.
2. Induction of lytic ΦBB-1 prophages.
3. Increased (over)expression of vertebrate-specific genes such as *OspC* [2].

These effects are not observed when the media is supplemented with spermidine, and interestingly, vertebrate blood is enriched with spermidine. This suggests a potential role for spermidine in the regulation of the BBD18-RpoS system and *Borrelia*'s vertebrate infectivity. This project seeks to evaluate the role of spermidine on *Borrelia burgdorferi*'s gene expression and its importance during the pathogen's enzootic cycle.

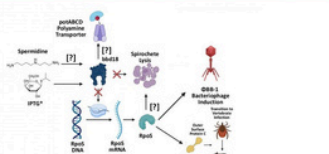


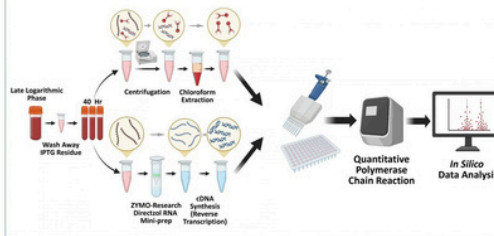
Figure 3: mechanistic diagram of BBD18-RpoS genetic regulatory system in *B. burgdorferi*. Spermidine's role in this system is unestablished. Additionally, the potABCD polyamine transporter is suspected to be regulated by BBD18.

METHODS

Figure 4: Four growth conditions were cultured in BSK II media for 40 hours at 34°C and 2.5% CO₂ from a starting density of 1.00 × 10⁶ cells/mL:

1. [IPTG] = 1 mM, [SP] = 10 mM
2. [IPTG] = 1 mM, [SP] = 0 mM
3. [IPTG] = 0 mM, [SP] = 10 mM
4. [IPTG] = 0 mM, [SP] = 0 mM

RNA was extracted and cDNA was synthesized for use in RT-qPCR (and RNA-seq). Additionally, supernatant was extracted and phage DNA was separated from non-phage DNA for use in qPCR.



RESULTS

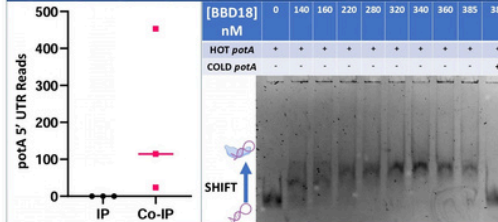


Figure 5: (Left): graphed potA 5' UTR (untranslated region) reads from RNA-seq (immunoprecipitation of crosslinked and un-crosslinked BBD18). Figure 5: (Right): Electrophoretic mobility shift assay using recombinant BBD18 protein and FAM labeled, potA run on a 6% TBE acrylamide gel at 100 volts for 60 minutes. Image exposed under fluorescence made for 250 seconds. "Cold" run with a large excess of unlabeled potA-RNA.

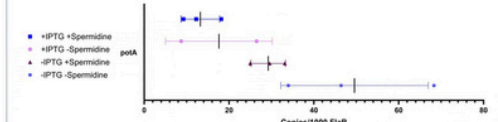


Figure 6: RT-qPCR analysis using *potA*, *potB*, and *potC* primers. All conditions were run in biological triplicates, and qPCR was done in technical triplicates. Flab was used as an internal standard to calculate relative expression using a ΔΔCt method.

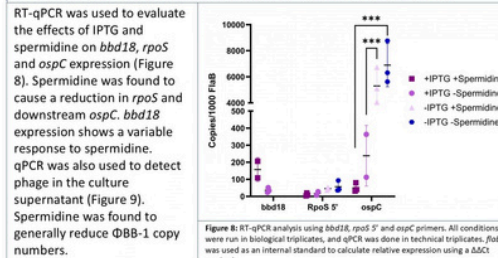


Figure 7: RT-qPCR analysis using *bbd18*, *rpoS* 5', and *ospC* primers. All conditions were run in biological triplicates, and qPCR was done in technical triplicates. Flab was used as an internal standard to calculate relative expression using a ΔΔCt method.

Since previous work indicated an increase in spermidine in the absence of BBD18, we used two methods to evaluate binding of BBD18 to the *potA* mRNA. RNA-BBD18 Co-IP experiments (Supriya Ramesh, Figure 5) have shown an enrichment with the 5' UTR of the *potA* mRNA indicating *in vivo* interaction. Additionally, EMSA using the 5' UTR of *potA* mRNA and BBD18 shows a mobility shift (Figure 6); this indicates *in vitro* binding of BBD18 to the *potA* mRNA. The combination of *in vitro* and *in vivo* evidence for BBD18 interaction with *potA* prompted us to complete RT-qPCR evaluating the dependence of *potA* expression on BBD18 and spermidine (Figure 7). BBD18 was found to act as a transcriptional repressor of *potA*. Spermidine was also found to repress *potA* expression.

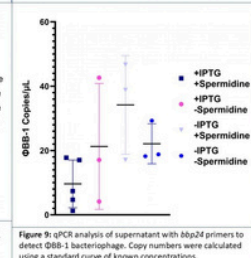


Figure 8: qPCR analysis of supernatant with *bbb24* primers to detect ΦBB-1 bacteriophage. Copy numbers were calculated using a standard curve of known concentrations.

CONCLUSIONS

Our current hypothesis is that BBD18 is dispensable during vertebrate infection because spermidine levels are high enough in the vertebrate blood to prevent *rpoS*/RpoS overexpression and associated lysis. This hypothesis is supported by the findings of this experiment that spermidine supplementation of the growth medium leads to decreased expression of *rpoS* and associated downstream genes such as *ospC*. RT-qPCR and EMSA data in conjunction with previous RNA Co-Immunoprecipitation experiments strongly suggest that BBD18 acts as a transcriptional repressor of the *potABCD* operon. This aligns with its role in relation to *rpoS* where it is also a transcriptional repressor. I hypothesize that BBD18 functions broadly as a general repressor of many genes in *Borrelia burgdorferi* which depend on the stage of the zoonotic cycle. This project has also demonstrated that induction of ΦBB-1 prophages is negatively regulated by spermidine. This aligns with previous observations that *Borrelia burgdorferi* spirochetes could be saved from lysis (despite lacking BBD18) by supplementation of the medium with 10 mM of spermidine.

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ACKNOWLEDGEMENTS

This research was made possible by the generous funding provided by the National Research Council of Canada (NSERC) and the University of Saskatchewan College of Medicine. Additionally, I would like to thank the entire Wachter laboratory and VIDO team for their collaboration and assistance with this work. In particular, I would like to thank senior VIDO laboratory technician Satyender Hansra for her exceptional mentorship over the previous two summers. All figures were created using: BioRender, Graphpad Prism and Adobe Macromedia Fireworks. EMSA and RNA Co-IP experiments were completed completely or in collaboration with Lucie-Anne Corvellec-Mocnik and Supriya Ramesh respectively.



Presly Goodwin (Dr. Jenny-Lee Thomassin)

Microbiota-Derived Metabolites Activate the Type II Secretion System of Citrobacter rodentium

Citrobacter rodentium is a natural murine pathogen used as a surrogate animal model for enteropathogenic and enterohemorrhagic *Escherichia coli* (EPEC and EHEC) due to shared core virulence factors. One such virulence factor is the type II secretion system (T2SS), which bacteria use to secrete proteins, including toxins, that contribute to infection. *C. rodentium* also possesses two-component systems (TCS) that sense the host environment and metabolites to regulate gene expression, with several shown to influence virulence.

This project builds on previous studies that defined the activation conditions of four T2SS components: *gspA*, *gspC*, *gspD*, and *gspG*. This study demonstrates that various host-derived metabolites influence T2SS activation, with galactose having the most notable effect. In addition, this research investigates the influence of various TCS on *gspC* and *gspG* activation using transcriptional fusions of T2SS components with TCS deletion mutants. Results revealed differences in activation among the clones used, suggesting that poly(A) slippage may influence activation. Further work will investigate the poly(A) status of existing clones to determine whether the transcriptional fusions are locking the genes into an “on” or “off” state.



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Microbiota-Derived Metabolites Activate the Type II Secretion System of *Citrobacter rodentium*

Presly Goodwin¹, Nabeela Kanwal¹, Hannah Braun¹, and Jenny-Lee Thomassin¹

¹Department of Biochemistry, Microbiology, and Immunology, University of Saskatchewan

Introduction

Type II secretion system

- T2SS
- Encoded on two operons
- Nanomachine transports folded proteins
- Essential for infection

Two-component system

- TCS
- Senses host signals/metabolites
- Signal transferred through cell
- Response regulator turns genes on/off

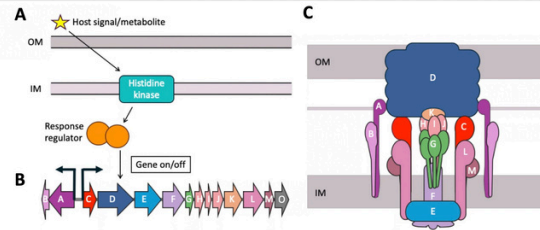


Figure 1: Schematic of how two-component systems influence T2SS activity. Two-component systems sense host signals (A), such as metabolites, to turn genes on and off in the T2SS operon (B) to impact activation of the T2SS (C).

Hypothesis: *C. rodentium* T2SS expression is controlled by specific bacterial signal transduction systems in response to nutrients present during host colonization.

Methods

- Transcriptional fusions of T2SS components with *lacZ*
- *gspA*, *gspC*, *gspD*, and *gspG*
- Beta-galactosidase assay to quantify transcript levels

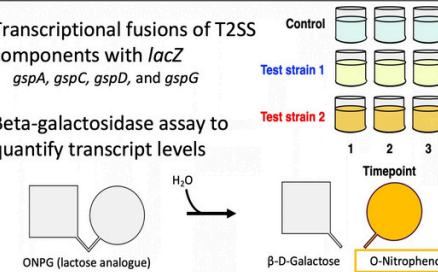


Figure 2: Graphic schematic of beta-galactosidase assay methodology. ONPG is a lactose analogue cleaved by LacZ, producing β -D-Galactose and O-Nitrophenol. O-Nitrophenol produces a yellow colour that is used to measure transcript activity.

Results

Different host-derived products activate the T2SS

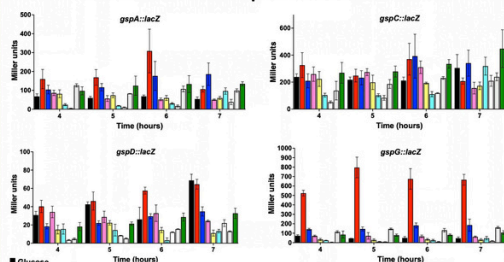


Figure 3: Activation of T2SS components is altered by host metabolites. LacZ activity (Miller units), indicative of fusion protein production was determined over time in the indicated media or in minimal medium supplemented with metabolites found in host. Shown are means $\pm$ standard deviation from three independent experiments.

Galactose concentration impacts *gspG* activation

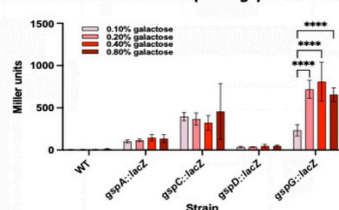


Figure 4: Activation of T2SS components in different galactose concentrations. LacZ activity (Miller units) determined after 5 hours in minimal media supplemented with different galactose concentrations.

TCS have varying effects on T2SS activation

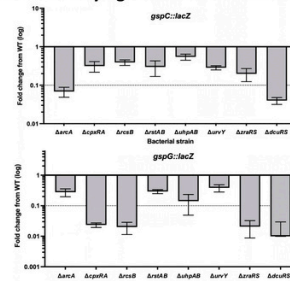


Figure 5: TCS deletions alter activation of *gspC* and *gspG* in the T2SS. Transcriptional fusions of TCS deletions and T2SS components were made. Activation of *gspC* and *gspG* in the presence of TCS deletions were determined by beta-galactosidase assay after growth in M9+0.4% galactose after 5 hours.

Poly(A) slippage may cause phase variation

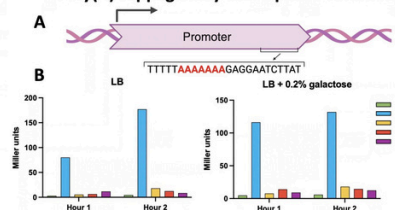


Figure 6: Poly(A) slippage in the T2SS promoter may alter activation. The T2SS promoter contains a Poly(A) sequence (A), which may contribute to the differences in activation between *gspC::lacZ* clones in LB and LB supplemented with galactose (B).

Significance

- T2SS is responsive to a microbiota-produced metabolite
- Evidence for phase variation
- Feature of microbiota-responsive secretion systems

Future Directions

- Correlation between high T2SS activation and secretion
- Impact of signal transduction systems on secretion
- Investigate Poly(A) region in the promoter
- Does phase variation contribute to T2SS regulation?

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Acknowledgements

University of Saskatchewan

Thomassin laboratory: Dr. Jenny-Lee Thomassin, Hannah Braun, and Eric Toombs

Funding sources: College of Medicine- Office of the Vice Dean of Research; NSERC (CGS-D)





Anna Gosselin (Dr. Oleg Dmitriev)

Differential Effects of Copper Binding to the Cell Motility Regulator MEMO1

MEMO1 facilitates human cell motility by promoting lamellipodia formation; however, the molecular mechanism underlying this activity remains poorly understood and may involve copper binding. In this study, we investigated the copper-binding properties of MEMO1 and demonstrated that wild-type MEMO1 directly binds Cu(I). Microscale thermophoresis was used to characterize Cu(I) binding and determine its affinity for MEMO1. Because Cu(I) is readily oxidized, samples were prepared and experiments were conducted under anaerobic conditions. Wild-type MEMO1 bound Cu(I) with a dissociation constant (K_d) in the micromolar range. The C244S mutant retained some Cu(I)-binding activity, whereas binding was abolished in the H49A mutant, suggesting an important role for His49 in Cu(I) coordination. Characterizing the metal-binding properties of MEMO1 provides insight into its biochemical function and may help clarify how copper binding contributes to MEMO1-mediated cell motility.

Copper-binding Properties of the Cancer Metastasis Modulator MEMO1

Anna Gosselin, Paria Nouri, Oleg Dmitriev

Department of Biochemistry, Microbiology and Immunology

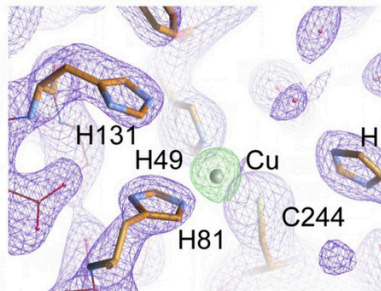
Introduction

Copper is an essential trace element required for many biological processes. However, copper levels are often elevated in tumors and in the blood of cancer patients, where increased copper availability may enhance the activity of copper-binding proteins involved in cancer progression.

One potential copper-binding protein is Mediator of Cell Motility 1 (MEMO1), a highly conserved 33-kDa protein involved in cell migration and metastasis. MEMO1 promotes cytoskeletal remodeling and lamellipodia formation and has been implicated in the progression of cancers such as triple-negative breast cancer. Despite these established roles, its primary molecular function remains poorly understood.

MEMO1 is structurally similar to metal-dependent proteins, suggesting that metal binding may contribute to its function. Investigating whether MEMO1 directly binds copper may therefore provide insight into the molecular mechanisms underlying its role in cell motility and cancer progression.

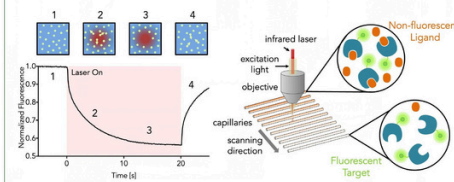
MEMO1 metal binding site



We hypothesize that MEMO1 binds Cu(I), which may contribute to its role in cancer cell migration and progression.

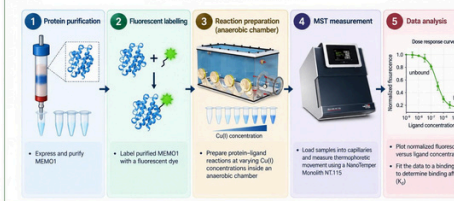
Methods

Microscale thermophoresis (MST) is a biochemical technique used to quantify biomolecular interactions by measuring the movement of molecules within a microscopic temperature gradient. Molecular properties such as size, charge, and hydration shell influence thermophoretic movement and can change upon ligand binding. In MST, fluorescently labelled molecules are loaded into capillaries and exposed to a localized temperature gradient generated by an infrared laser. Changes in fluorescence distribution are monitored across a range of ligand concentrations, allowing binding interactions to be detected and binding affinity (K_d) to be determined.



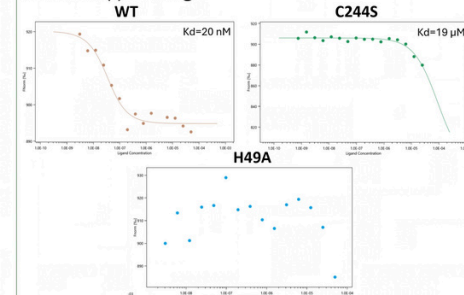
Purified MEMO1 was fluorescently labelled and incubated with increasing concentrations of Cu(I) under anaerobic conditions. Samples were analyzed using microscale thermophoresis (MST), and changes in thermophoretic behaviour were used to evaluate Cu(I) binding and determine binding affinity.

MST workflow



Results

MST analysis demonstrated saturable Cu(I) binding by WT MEMO1, with binding occurring in the nanomolar range ($K_d = 20$ nM). The C244S mutant retained a saturable binding response but exhibited substantially weaker affinity ($K_d = 19$ μ M). In contrast, H49A showed no saturable Cu(I)-binding response, suggesting that His49 plays an important role in Cu(I) binding.



All conditions: n = 3 independent replicates

Conclusion

MEMO1 binds Cu(I), supporting a potential role for copper in MEMO1 function. Mutation of Cys244 reduced Cu(I) binding affinity, while mutation of His49 abolished the saturable binding response, suggesting these residues contribute differently to Cu(I) binding. Further investigation is needed to determine how copper binding influences MEMO1-mediated cell motility and its role in cancer progression.

Acknowledgements

This research was supported by the University of Saskatchewan College of Medicine Biomedical Summer Research Projects program



Atharv Govardhan (Dr. George Katselis)

Blood Proteomics to Evaluate the Impact of Whole-Body Vibration on Cognitive Impairment Using a Rat Model

Whole-body vibration (WBV) is a common occupational exposure, and growing evidence suggests it may affect cognitive function and brain health [1]. Studies examining WBV have reported changes in learning, memory, and other aspects of cognitive performance, although the underlying mechanisms are not fully understood [2]. Processes such as inflammation, oxidative stress, and altered neuronal signalling have been proposed as possible contributors to the neurological effects of WBV [3]. This study investigated whether WBV exposure is associated with changes in blood proteins related to cognitive impairment using a rat model. Adult rats were exposed to different WBV frequencies, namely 4 Hz and 30 Hz, while a control group (0 Hz) did not receive any vibration exposure. Blood samples (pre- and post-) were then collected and analyzed using mass spectrometry-based proteomics to identify differences in protein expression between the groups. Proteins showing significant changes were then further examined using bioinformatics and pathway analyses to identify biological processes that they may be involved in. The blood proteomics data we found helped us better understand the relationship between WBV exposure and cognitive impairment. Identification of these potential blood-based biomarkers associated with these effects can be used in the future to predict neurodegenerative diseases.

Blood Proteomics to Evaluate the Impact of Whole-Body Vibration on Cognitive Impairment Using a Rat Model

Atharv Govardhan¹, Daniel Chao², Stephan Milosavljevic³, George S. Katselis^{2,4}

¹Biochemistry, Microbiology and Immunology; ²CCRAH; ³School of Rehabilitation Science; ⁴Department of Medicine; College of Medicine, Univ. of Saskatchewan

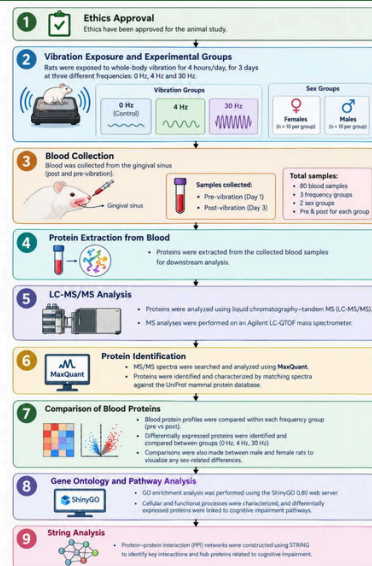
Introduction

- Whole-body vibration (WBV) is a common occupational exposure, particularly among agricultural and machinery workers, and can exceed recommended safety levels¹.
- Prolonged WBV exposure may negatively affect cognitive function and overall neurological health.
- Research has reported changes in learning, memory, and cognitive performance following WBV exposure².
- Low-frequency vibrations (~4–6 Hz) may be transmitted through the body toward the head, potentially affecting brain function.
- The molecular mechanisms underlying WBV-related cognitive changes remain unclear, highlighting the need for further investigation.
- Blood proteomics** can help identify circulating protein changes and potential biomarkers associated with WBV-related cognitive impairment³.

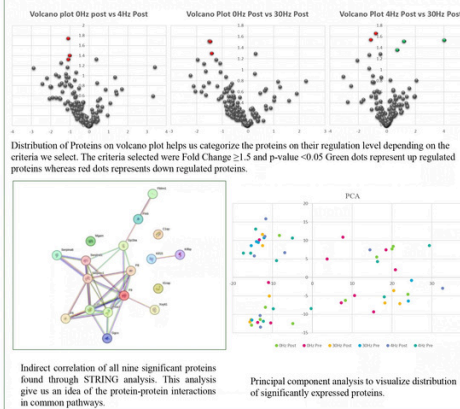
Objectives

- Characterize the molecular impact of WBV** by identifying blood protein changes following exposure to **0 Hz, 4 Hz and 30 Hz WBV** using mass spectrometry-based proteomics.
- Define the proteomics signature of WBV exposure** by comparing **pre- and post-exposure blood profiles** to identify differentially expressed protein biomarkers.
- Determine the cognitive consequences of WBV** by assessing changes in learning, memory, and cognitive performance across exposure groups.
- Link molecular and behavioural outcomes** by examining whether WBV-induced changes in blood proteins correspond with the severity of cognitive impairment.
- Determine potential blood-based biomarkers** that may reveal the underlying biological response to WBV and provide insight into mechanisms contributing to **WBV-associated cognitive dysfunction**.

Materials and Methods



Results



Conclusions

- | Protein Accession # | Protein Names | Regulation |
|---------------------|--|-------------------|
| P16296 | Coagulation factor IX | Down (0 vs 4 Hz) |
| P31722 | Complement C1q subcomponent subunit C | Down (0 vs 4 Hz) |
| Q63621 | Interleukin-1 receptor accessory protein | Down (0 vs 4 Hz) |
| A0ACMRQ61 | Apolipoprotein N | Down (0 vs 30 Hz) |
| P16296 | Coagulation factor IX | Down (0 vs 30 Hz) |
| P53813 | Vitamin K-dependent protein S | Down (0 vs 30 Hz) |
| D5ZTX4 | Glucan 1,4-alpha-glucosidase | Down (4 vs 30 Hz) |
| P31211 | Corticosteroid-binding globulin | Down (4 vs 30 Hz) |
| A0A8SZV49 | Filamin A | Up (4 vs 30 Hz) |
| A0A0G2JXT8 | Filamin B | Up (4 vs 30 Hz) |
| P31722 | Complement C1q subcomponent subunit C | Up (4 vs 30 Hz) |
| Q7TSP2 | Kinesin-like protein KIF15 | Up (4 vs 30 Hz) |
- The table depicts all the significant proteins we identified when comparing blood proteomics between rats vibrated on different frequencies.
 - C1q protein can bind to synaptic structures associated with amyloid pathology and facilitate their removal by microglia. This becomes particularly relevant to neurodegeneration because excessive complement-mediated synaptic pruning has been implicated in **Alzheimer's disease and other neurodegenerative conditions**.
 - If WBV causes Blood-Brain barrier dysfunction, systemic inflammation could potentially interact with CNS complement pathways.
 - IL-1 receptor accessory protein (IL1RAP) is a required co-receptor for IL-1 receptor signaling. The IL-1 pathway is strongly associated with **neuroinflammation**.
 - Recent work has further shown that IL1RAP is expressed in **CNS astrocytes, microglia, and neurons**, with a neuron-specific isoform involved in CNS signaling⁴.
 - Protein S (PROS1) is a ligand for the **TAM receptor family**, including MERTK, and is involved in phagocytosis and immune regulation. Recent literature describes PROS1 functions in the CNS. Even more compellingly, a study of Alzheimer's disease mice found **PROS1 in the hippocampus**, including inside microglia and extracellularly. PROS1 increased in the hippocampus of 5XFAD Alzheimer's mice and was associated with microglial activation and phagocytosis⁵.

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Acknowledgements

- The authors wish to thank Brooke Thompson, Zarlish Mubashar, and Rachel Guerra.
- Funding was provided by a Biomedical Summer Research Project scholarship, College of Medicine, University of Saskatchewan.



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Colby Maduck (Dr. Jenny-Lee Thomassin)

Generation of OmpT Variants for Functional Analysis

OmpT proteases are a unique family of proteases in Gram-negative bacteria that preferentially cleave extracellular substrates between two basic amino acids. OmpT, an ompT protease from *Escherichia coli*, preferentially cleaves peptides and contributes to virulence by inactivating the human antimicrobial peptide LL-37. As a result, the presence of the ompT gene is used as a diagnostic marker to identify pathogenic *E. coli*. Relatively little work has been performed to explore the dynamic range of OmpT activity that can be measured from intact bacterial cells in complex fluids. Therefore, the objective of this project was to generate OmpT variants that are predicted to have 10 to 10,000-fold reductions in protease activity and assess their production in *E. coli*. Point mutations were introduced into EHEC ompT on the pEHompT plasmid using overlap and inverse PCR methods for site-directed mutagenesis. Plasmids with sequence-confirmed mutations were transformed into *E. coli* BL21 for protein production. Production of OmpT variants was assessed by Western blotting using a polyclonal OmpT antibody. OmpT protein levels were similar for all OmpT variants. These variants will be used in downstream experiments to determine the linear range of OmpT activity that can be measured in complex fluids.

Generation of OmpT Variants for Functional Analysis



Colby Maduck and Jenny-Lee Thomassin

Department of Biochemistry, Microbiology and Immunology, University of Saskatchewan

Introduction

OmpT Proteases

- Unique protease family
- Features of serine and aspartate proteases

OmpT

- Pathogenic *Escherichia coli*
- Cleaves antimicrobial peptides
- High activity associated with more severe infections

Can OmpT activity be used to create a diagnostic tool?

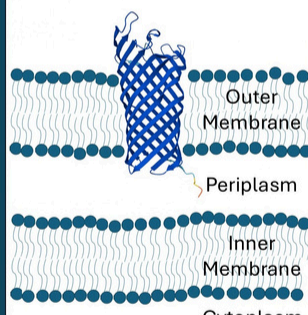


Figure 1. OmpT in the bacterial cell. Schematic showing OmpT in the outer membrane. The five extracellular loops facing the environment govern substrate specificity by limiting access to the enzyme's active site in the barrel.

Methods and Results

(a) Site-directed mutagenesis of *ompT*

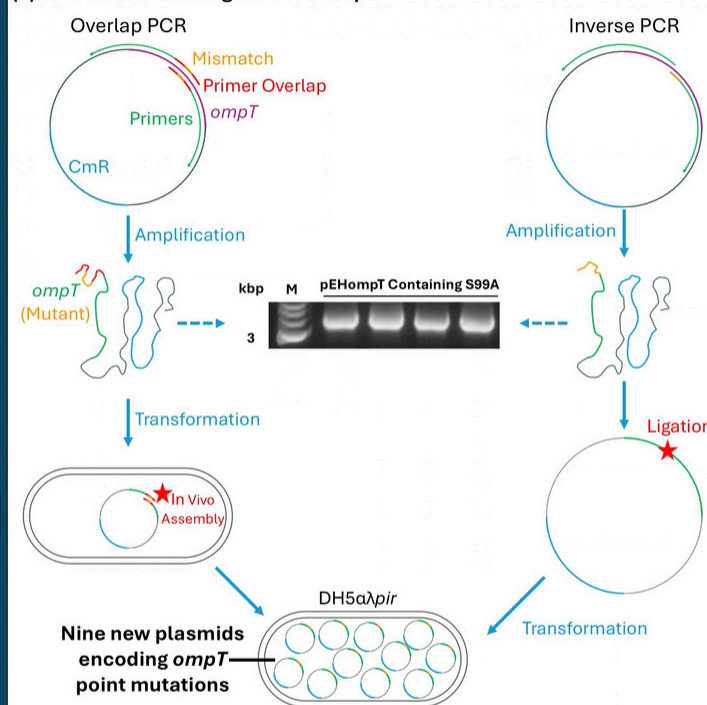
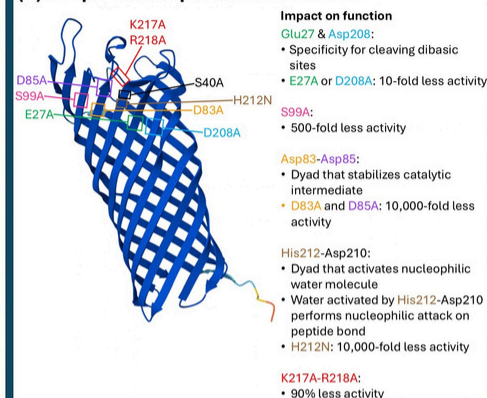


Figure 2. Generation of point mutations in EHEC *ompT*. Point mutations were generated using either overlap or inverse PCR. For overlap PCR, specific mismatches were integrated into the middle of the primer sequence (orange), whereas for inverse PCR, specific mismatches were integrated at the 5' end of one primer (yellow). Following amplification of pEHompT (*ompT*(S99A) shown), template DNA was restricted with DpnI, ligated (inverse PCR), then transformed into DH5αpir. Mutagenesis was verified by nanopore sequencing.

(b) OmpT variant production in cells



(c) OmpT variants are produced at similar levels

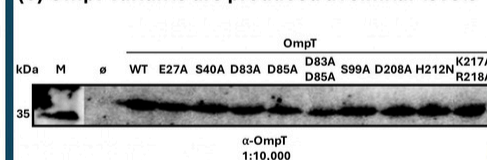


Figure 3. OmpT variant production in *E. coli* BL21. OmpT was detected by Western blot. Bacteria were grown to mid-log phase and normalized by optical density. Cells were resuspended in electrophoresis sample buffer and boiled. Proteins were separated by Tris-Tricine SDS-PAGE, transferred to a PVDF membrane, and probed with polyclonal OmpT antibody. M denotes molecular weight marker, Ø denotes an empty vector *ompT* null control, and WT denotes EHEC OmpT.

Objectives

1. Generate OmpT variants
2. Assess OmpT variant production

Future Directions

- OmpT variants will be used to study unique catalytic activity of OmpT
- OmpT variants will be used to test point-of care detection tests of pathogenic *E. coli*

Conclusions

- Successfully generated *ompT* point mutants
- OmpT variants produced and detected in *E. coli*

Acknowledgements

- **University of Saskatchewan**
- **Supervisor:** Dr. Jenny-Lee Thomassin
- **Thomassin Laboratory Members**
- **Funding:** University of Saskatchewan College of Medicine



Isha Noor (Dr. Ninad Mehta)

*HLA-B *-21 Leader Mismatch and CMV Persistence Following Kidney Transplantation*

Background: HLA-B *-21 dimorphism (methionine [M] vs. threonine [T]) determines whether a cell supplies the peptide stabilizing HLA-E, a ligand for NK-cell receptors. Recipients accustomed to *-21M signaling may lose this support if their donor kidney supplies no *-21M peptide. We hypothesized that loss of donor *-21M supply impairs NK-cell control of viral replication post-transplant.

Methods: We genotyped HLA-B *-21 in 38 donor-recipient pairs and performed PCR for CMV. Pairs where the recipient carried ≥ 1 *-21M allele but the donor carried none were classified "exposed" (n=8); all others "unexposed" (n=30). CMV DNAemia duration, clearance time, and peak viral load were compared using rank-sum testing and regression adjusted for testing frequency.

Results: Exposed pairs showed significantly longer CMV DNAemia (median 380.5 vs. 8.5 days; $p=0.0020$) and slower clearance (median 408.5 vs. 32.5 days; $p=0.016$), while peak viral loads were similar ($p=0.31$). The association persisted after adjustment and correction.

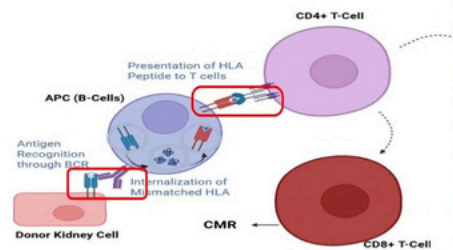
Conclusions: Loss of donor *-21M leader supply was associated with prolonged CMV DNAemia and delayed clearance, without altering peak viral load, suggesting HLA-B *-21 mismatch impairs control of established infection rather than initial containment. These findings support *-21 genotyping as a viral-risk marker.

HLA-B -21 Leader Mismatch and CMV Persistence Following Kidney Transplantation

Isha Noor, Ninad Mehta, Ahmad Mostafa and Cody Lewis

University of Saskatchewan, College of Medicine; Department of Pathology and Laboratory Medicine

INTRODUCTION



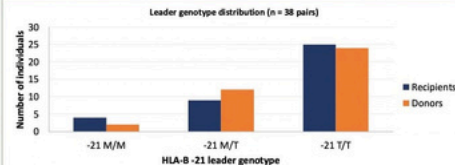
HLA-B -21 variation may influence antiviral immune responses through HLA-E and natural killer (NK) cells. At position -21, HLA-B can contain either methionine (-21M) or threonine (-21T), with -21M providing a peptide that stabilizes HLA-E. Following kidney transplantation, a recipient with ≥ 1 -21M allele may receive a -21T/T donor kidney, resulting in reduced donor HLA-E ligand supply. Because immunosuppression increases susceptibility to viral infections such as CMV, this study investigated whether donor-recipient HLA-B -21 mismatch is associated with prolonged CMV persistence.

OBJECTIVES

To investigate whether donor-recipient differences in the HLA-B -21 leader genotype are associated with CMV replication and persistence following kidney transplantation.

1. Determine whether loss of donor HLA-B -21M leader supply is associated with prolonged CMV DNAemia.
2. Compare CMV DNAemia duration between exposed and non-exposed transplant pairs.
3. Assess whether HLA-B -21 mismatch is associated with peak CMV viral load.
4. Evaluate whether the association remains after accounting for differences in CMV testing intensity.

MATERIALS AND METHODS



The following outcomes were measured

- CMV DNAemia duration
- Persistent DNAemia ≥ 90 days
- Time to CMV clearance
- Number of positive CMV samples
- Fraction of samples positive
- Peak CMV viral load
- Statistical Analysis

The study compared exposed vs. non-exposed groups and used:

- Rank-sum testing
- Kaplan-Meier analysis
- Regression models
- Adjustment for number of CMV assays
- Leave-one-out analysis
- Permutation-based correction for multiple testing

RESULTS

Median CMV DNAemia duration by leader direction

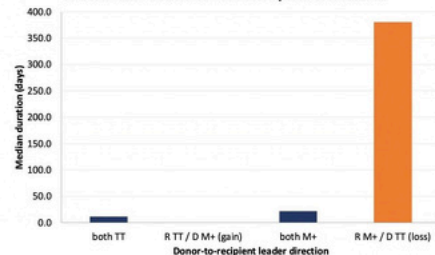


Figure 1. Median days shown for each donor/recipient cell combination. Recipient monocytes persisted longest (375 days) after donor T-cell engraftment, corresponding to delayed CMV clearance in -21M mismatched transplants.

Direction category	Median DNAemia duration (d)	n
both TT	11.5	16
R TT / D M+ (gain)	0.0	9
both M+	22.0	5
R M+ / D TT (loss)	380.5	8
Kruskal-Wallis p (4 group comparison)	0.0176	

Figure 3. Median CMV DNAemia duration across the four donor-recipient leader configurations. The gradient is confined to the loss category. Kruskal-Wallis p = 0.018 for duration; the same test on peak viral load gives p = 0.49.

Model / term	Odds ratio	95% CI lower	95% CI upper	Y position
M1: EXPOSED (unadjusted)	9.857	1.613	60.245	7
M2: EXPOSED (adj. N assays)	9.051	1.120	73.125	6
M2: N CMV assays	1.104	1.030	1.182	5
M3: EXPOSED (adj. assays + B MM)	5.680	0.621	51.912	4
M3: HLA-B allele MM	3.657	0.444	30.138	3
M4: Recipient M-dose	1.585	0.470	5.350	2
M4: Donor M-dose	0.309	0.047	2.033	1

Figure 5. Odds ratios for persistent CMV DNAemia with 95% confidence intervals, log scale, reference line at 1. Confidence intervals are wide throughout, which is the honest picture of an analysis with 8 exposed cases and 13 events.

Peak CMV Viral Load by Exposure Group (p = 0.31)

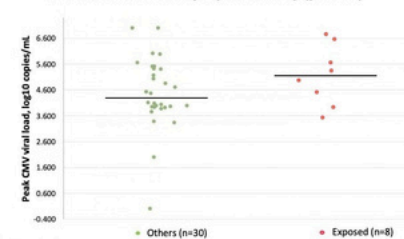


Figure 2. Peak CMV viral load, median value of 4.28 log10 copies/ml (Others) versus median value of 5.16 log10 copies/ml (Exposed), no statistically significant difference.

Probability of remaining CMV DNAemia-positive

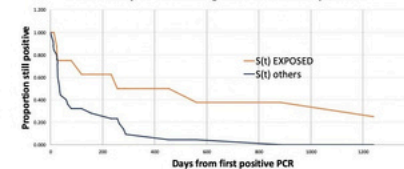


Figure 4. Kaplan-Meier estimate of time to CMV clearance. Median 408.5 days in exposed pairs versus 32.5 days in others; log-rank p = 0.016. Two cases with no post-transplant DNAemia are not at risk of clearance and are excluded (n = 36).

Adjusted Odds Ratios for Persistent CMV DNAemia

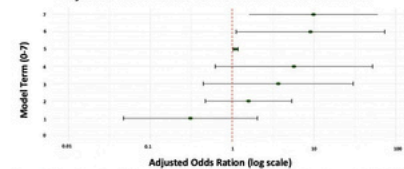


Figure 6. Adjusted odds ratios for prolonged CMV detection. Values >1 indicate increased risk, while values <1 suggest protective effects.

CONCLUSIONS

1. Loss of donor -21M leader supply was associated with substantially prolonged CMV DNAemia.
 2. The HLA-B -21 mismatch was associated with CMV persistence, but not a statistically significant difference in peak viral load.
 3. The association appeared to depend on the donor-recipient direction of the HLA-B -21 mismatch rather than either genotype alone.
 4. Recipients exposed to loss of donor -21M leader supply had substantially delayed CMV clearance.
 5. The association persisted after accounting for CMV testing intensity.
- In this cohort of kidney transplant donor-recipient pairs, loss of donor HLA-B -21M leader supply was associated with substantially prolonged CMV DNAemia and delayed viral clearance.

ACKNOWLEDGEMENTS

This project was supported by the Office of the Vice-Dean Research (OVDR) through the Dean's Summer Research Project program. I sincerely thank my mentors for their invaluable guidance and the members of the Histocompatibility and Immunogenetics Laboratory (HIL) for their mentorship and ongoing support as well as the Microbiology Lab located at Royal University Hospital.



Matt Scrivens (Dr. Aaron White)

Generating Single Gene Knockouts in Salmonella enterica Serovar Typhimurium and Testing their Survival in Water

Salmonella enterica serovar Typhimurium is a Gram-negative bacteria known to cause gastrointestinal disease in humans. Though Salmonella infection is typically associated with consumption of raw poultry, other food products can become contaminated as well. One method of contamination is when fecal runoff enters a water source used for irrigation. This water is then used to irrigate crops, which then in turn become contaminated. Previous research has shown that Salmonella is very good at surviving in water. Therefore, our lab is interested in determining which genes are essential for Salmonella water survival. Seven genes were selected as possible water survival genes based on their function in Legionella. Lambda red recombination was used to generate seven mutant strains of salmonella, each with a suspected water survival gene knocked out. These mutants were then tested in water trials. Once a week, total colony forming units were enumerated for each mutant and graphed in excel. Although data collection is ongoing, two knockouts ($\Delta yciC$ and $\Delta rpoZ$) are showing promising decline compared to wildtype Salmonella.

Matthew Scrivens^{1,2}, Rylan D. Bahrey^{1,2}, Megan Tomilin^{1,2}, and Aaron P. White^{1,2}

1. Vaccine and Infectious Disease Organization, University of Saskatchewan
2. Department of Biochemistry, Microbiology, and Immunology, University of Saskatchewan

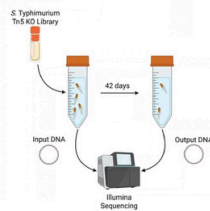
INTRODUCTION

- Salmonella enterica* is a species of Gram-negative bacteria known to cause disease in humans [1].
- The World Health Organization estimates that 180 million people are infected with *Salmonella* worldwide each year, with 298,000 infections resulting in death [1].
- Although poultry is the main reservoir for *Salmonella*, water sources can become contaminated from fecal runoff [1,2].
- Produce irrigated with contaminated water can in turn become contaminated [1].
- Our lab is interested in which genes enable *Salmonella enterica* serovar Typhimurium to survive in water.

Gene name	Role from UniProt
gltD	Part of a transport system that regulates nitrogen metabolism
gltH	Electron transport system for the ribonucleotide reductase system hrdH
gltK	Provides RNA polymerase assembly
yjcC	Multi-pass membrane protein
yjcK	Protein-disulfide isomerase activity / stress response activity
yjcL	Notes in metal ion binding and DNA binding
STM14_1856	Recycles H ₂ to yield ATP and protect oligonucleotides against O ₂ damage under carbon limited conditions
narW	Chaperone activity and roles in nitrogen metabolism
yrfA	Inner membrane protein
LBB	Cobalamin converter. Roles in membrane transport

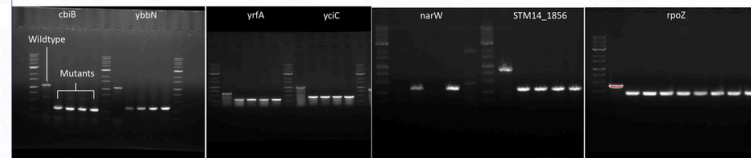
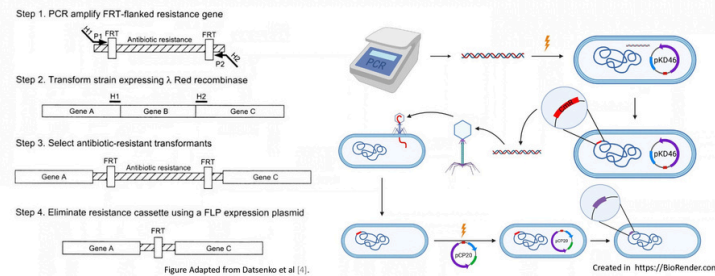
- Previously, our lab created a library of mutants using transposon 5 techniques.
- I used Lambda Red Recombination to knockout genes we suspect to be involved in water survival [3,4].

BACKGROUND

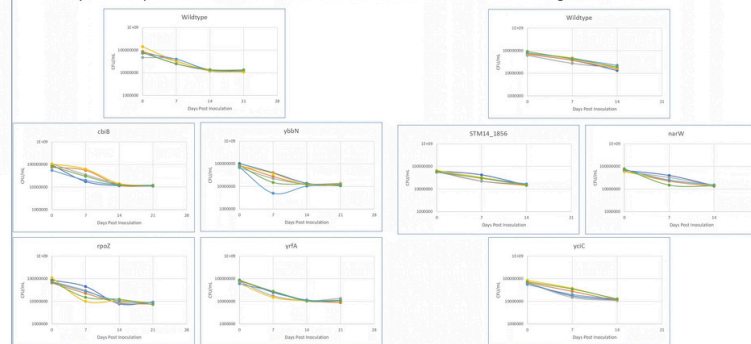


- Previously, Transposon 5 techniques were used to determine which genes may be essential to *Salmonella* Typhimurium water survival.
- Seven *Salmonella* Typhimurium genes were selected: narW, STM14_1856, rpoZ, cbiB, ybbN, yrfA, and yjcC.
- Gene knockout was verified via colony PCR.
- Each mutant was subjected to water trials and drop dilutions were performed once weekly.

RESULTS



- Lambda Red Recombination was used to knock out seven genes in *Salmonella* Typhimurium.
- Colony PCR was performed once the final mutant was created to confirm successful gene knock out.



- Each mutant was grown to a concentration of 8×10^8 cells/mL and added to 39 mL of water.
- Once a week, I performed drop dilutions of each water trial to monitor the survival rates of the mutants.
- Values were plotted in excel.

CONCLUSIONS

- I successfully knocked out seven genes in *Salmonella* Typhimurium using Lambda Red Recombination, verified by colony PCR.
- Each mutant was inoculated in water and compared to wildtype *Salmonella*.
- Salmonella* with either rpoZ or yjcC knocked out are declining more than wildtype *Salmonella*.
- We've identified two genes that are potentially needed for water survival, though it is still too early to tell.
- This data can tell us about metabolic pathways in *Salmonella* which may have been overlooked.
- Furthermore, this research may be used to develop water treatment methods that target *Salmonella* specifically.

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ACKNOWLEDGEMENTS

We would like to thank the following: Josh Cameron, Laurel Tarr, Griffin Lehnert, Shaun Wachter, Chinenye Nnajiye, and Adam Webster.

VIDO receives operational funding from the Government of Saskatchewan through Innovation Saskatchewan and the Ministry of Agriculture and from the Canada Foundation for Innovation through the major Science Initiatives Fund.



Gabriel Swetlikoff (Dr. Michael Wozny)

Development of a Gene Knock-in Protocol Using Cas12a RNPs for Fluorescent Labelling of Mitochondrial Antiviral Signaling Protein

Mitochondrial antiviral signaling protein (MAVS) is found on the surface of mitochondria, and is involved in signaling RNA virus infection. MAVS spatial arrangement is altered by viral infection, but the mechanism remains unclear. Fluorescent tagging can help answer this question by providing an effective method to track proteins in-vivo, allowing us to monitor their spatial response to RNA viruses in the cell. Stable knock-in of fluorescent tag sequences into protein-coding genomic DNA is possible through homologous repair by using CRISPR/Cas systems combined with a DNA template. Previous research using Cas12a RNPs for knock-ins are limited, creating the need for protocol development. Thus the objective of this study was to develop a protocol using Cas12a Ribonucleic proteins (RNPs) and a linear DNA template to engineer HEK293-T and SH-SY5Y cell lines which express MAVS with an N-terminal mScarlet fluorescent tag. PAM sequences were identified from genomic DNA and used to design the guide RNA and template DNA. The cells were electroporated with varying combinations of cell, RNP, and template DNA concentrations. While the desired cell lines were not produced, the study provided preliminary investigation that will be used to improve knock-ins for future studies involving Cas12a RNPs.

Development of a Gene Knock-in Protocol Using Cas12a RNPs for Fluorescent Tagging of Mitochondrial Antiviral Signaling Protein

Gabriel Swetlikoff¹, Dr. Michael Wozny¹

¹University of Saskatchewan Department of Biochemistry, Microbiology and Immunology



Abstract

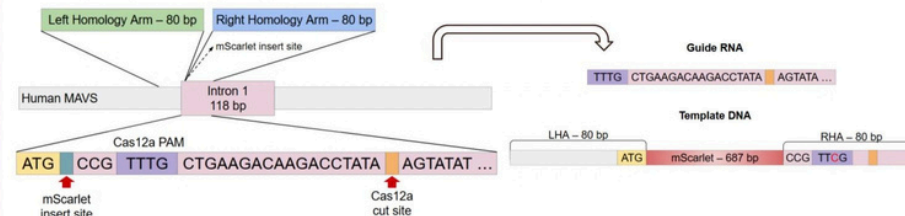
Mitochondrial antiviral signaling protein (MAVS) is found on the surface of mitochondria, and is involved in signaling RNA virus infection. MAVS spatial arrangement is altered by viral infection, but the mechanism remains unclear. Fluorescent tagging can help answer this question by providing an effective method to track proteins in-vivo, allowing us to monitor their spatial response to RNA viruses in the cell. Stable knock-in of fluorescent tag sequences into protein-coding genomic DNA is possible through homologous repair by using CRISPR/Cas systems combined with a DNA template. Previous research using Cas12a RNPs for knock-ins are limited, creating the need for protocol development. Thus the objective of this study was to develop a protocol using Cas12a Ribonucleic proteins (RNPs) and a linear DNA template to engineer HEK293-T and SH-SY5Y cell lines which express MAVS with an N-terminal mScarlet fluorescent tag. PAM sequences were identified from genomic DNA and used to design the guide RNA and template DNA. The cells were electroporated with varying combinations of cell, RNP, and template DNA concentrations. While the desired cell lines were not produced, the study provided preliminary investigation that will be used to improve knock-ins for future studies involving Cas12a RNPs.

Introduction

- Cas12a and RNPs decrease off-target effects in complex cells with infrequent homologous repair
- Successful knock-ins using Cas12a RNPs in human cells has not previously been published
- Electroporation to deliver RNPs and template DNA into cells; tested prior with GFP plasmid
- Tested cell concentrations, guide RNA : Cas12a, and template DNA concentrations

Methods and Results

1. Design of gRNA targeting MAVS N-terminus and template DNA

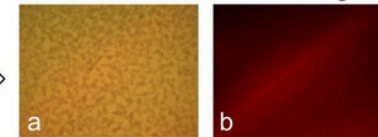


2. Electroporation of HEK293-T and SH-SY5Y cells

Cells per 10 μ L	Cas12a RNPs	Template DNA
500 000	50 pmol	150 pmol
	100 pmol	100 pmol
		200 pmol
		300 pmol
250 000	100 pmol	100 pmol
		200 pmol
		300 pmol

Electroporation
1100 mV, 20 ms,
2 pulses

No detectable fluorescent signal



Electroporated HEK293 cells
(a) transilluminated and Cy5 channels overlaid
(b) Cy5 channel fluorescence only

Conclusions and future directions

- We were not able to develop an N-terminus mScarlet knock-in protocol for MAVS in either the HEK293-T or SH-SY5Y cell lines
- These are only preliminary investigations into fluorescent tag knock-in using Cas12a RNPs
 - Future investigations will include RNP assembly efficiency and activity assays, reagent and buffer optimization, and electroporation optimization
- If this method of tagging is successful, it will be used to tag other proteins with a variety of fluorescent markers and provide baseline research into using Cas12a RNPs in human cells



Stuti Thakkar (Dr. Jess Sheldon)

*Investigating iron piracy in the opportunistic, emerging, multidrug-resistant pathogen
Morganella morganii.*

Morganella morganii is an emerging, multidrug-resistant Gram-negative bacterium that resides harmlessly in the gut and mucosal surfaces of humans and animals. However, as an opportunistic pathogen, *M. morganii* can cause hospital-acquired urinary tract, wound, and bloodstream infections amongst others. Iron acquisition is essential for bacterial survival and virulence, and hosts restrict iron and other metals through nutritional immunity during infection. In response, many Gram-negative bacteria rely on the biosynthesis of small iron-binding molecules known as siderophores and the uptake of xenosiderophores produced by neighboring microbes. To determine whether *M. morganii* produces its own siderophores and/or can utilize those generated by other bacteria and fungi, siderophore production was assessed using Chrome Azurol S (CAS) assays in iron-limited medium, and xenosiderophore uptake was evaluated by supplementing this restricted media with ferrichrysin, ferricrocin, coprogen, or rhizoferrin as an iron source. All *M. morganii* strains showed significantly lower CAS activity than the *Pseudomonas aeruginosa* positive control, indicating no detectable siderophore production under the tested conditions, and growth rescue assays demonstrated dose-dependent increases in growth when supplemented with xenosiderophores. Conclusively, *M. morganii* exhibits broad iron-acquisition strategies shaped by its diverse host and environmental niches, pointing to a potential reservoir.

Investigating iron piracy in the opportunistic, emerging, multidrug-resistant pathogen *Morganella morganii*

Stuti Thakkar,¹ Christine Joyce Francisco,^{1,2} Camille Hamula,³ Ninad Mehta,³ and Jessica R. Sheldon¹

1. Department of Biochemistry, Microbiology and Immunology, College of Medicine, University of Saskatchewan, Canada

2. Department of Forest & Conservation Sciences, Faculty of Forestry, University of British Columbia, Canada

3. Department of Laboratory Medicine, Royal University Hospital, Saskatoon, Saskatchewan, Canada; Department of Pathology and Laboratory Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

Introduction

- Gram-negative
- Commensal & opportunistic
- Nosocomial infections
- Emerging multidrug resistance
- One Health pathogen
- Iron dependent growth

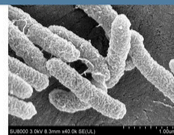


Figure 1. SEM image of *M. morganii*

Clinical Relevance

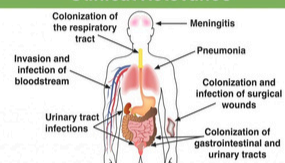


Figure 2. *M. morganii* causes a wide range of infections

Iron Acquisition & Siderophore Biology

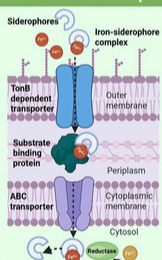


Figure 3. TonB-dependent siderophore uptake

- Hosts tightly bind iron, so bacteria must rely on specialized iron-acquisition mechanisms to overcome limitation.
- Bacteria adapt by producing and/or stealing siderophores from neighboring microbes to scavenge Fe^{3+} .
- Trojan-horse antibiotics can use this pathway, enabling antimicrobial compounds to enter.

Hypotheses

M. morganii produces endogenous siderophores and relies on siderophores from other microbes to acquire iron under iron-limited conditions.

Objectives

- Determine whether *M. morganii* produces endogenous siderophores
- Assess whether *M. morganii* can use xenosiderophores as an iron source

Methods and Results

1. Siderophore Activity Measurement – Chrome Azurol S Assay

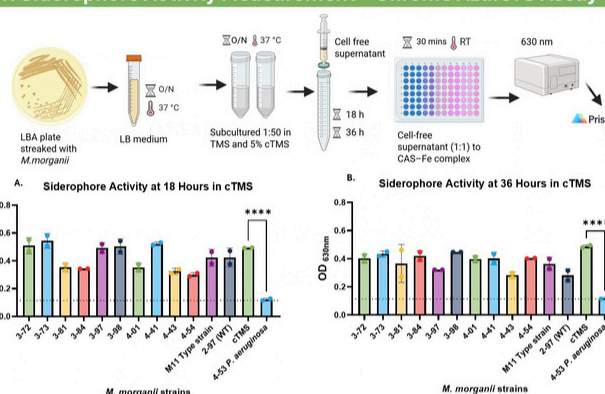


Figure 4. Siderophore activity of *M. morganii* in chelexed Tris Minimal Succinate (cTMS) measured by CAS assay. Cell-free supernatants were mixed 1:1 with CAS reagent, and absorbance at 630 nm (OD_{630nm}) was measured after 30 min of incubation in the dark. Lower absorbance shows higher iron-chelating activity. (A) 18 h and (B) 36 h graphs show that *M. morganii* exhibits minimal CAS reactivity compared with the positive control. Data represent mean $\pm$ SD from biological duplicates, and significance was determined by one-way ANOVA (**** $p < 0.0001$), where all other strains are significantly different compared to the positive control, *Pseudomonas aeruginosa*.

2. Xenosiderophore Supported Growth Under Iron Limitation

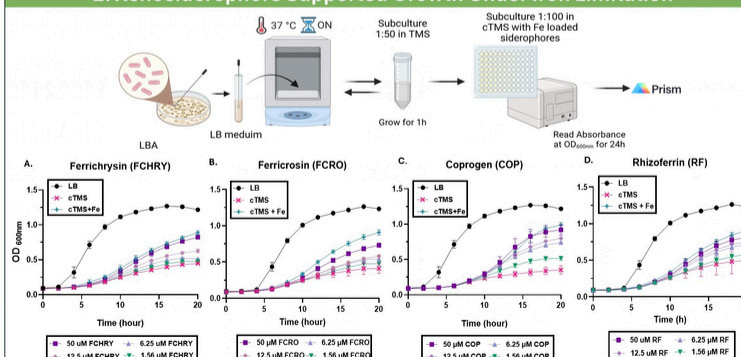


Figure 5. *M. morganii* utilizes fungal xenosiderophores as iron sources under iron-restricted conditions. Overnight LB cultures were transitioned through TMS into cTMS containing individual fungal xenosiderophores. Growth curves show *M. morganii* responses to increasing concentrations of (A) Ferrichrysin, (B) Ferricrocin, (C) Coprogen, and (D) Rhizoferrin. Iron-replete controls (+Fe) contained 30 μ M $FeCl_3$; LB served as a rich-media positive control and unsupplemented cTMS as the iron-restricted negative control. Optical density (OD) at 600 nm was recorded every 30 min for 20 h, and all conditions were performed in biological quadruplets. Data represent mean $\pm$ SD.

Conclusions

- Low CAS activity across *M. morganii* isolates at both 18 h and 36 h indicates minimal to no endogenous siderophore production.
- M. morganii* can utilize fungal xenosiderophores, including the hydroxamates ferrichrysin, ferricrocin, and coprogen, as well as the polycarboxylate siderophore rhizoferrin.
- M. morganii* displays dose-dependent iron uptake when provided with fungal siderophores.

Future Directions

- Test siderophore piracy from other bacteria to evaluate whether *M. morganii* can use xenosiderophores during co-infection.
- Perform RNA-seq under iron-deplete conditions to assess transcriptional responses under iron limitation.
- Generate targeted mutants in key candidate genes to define their functional roles.
- Assess iron-dependent growth of each mutant to determine individual contributions.

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Acknowledgements

I would like to thank Christine Joyce Francisco for her early foundational contributions. I am deeply grateful to Dr. Jess Sheldon, my principal investigator, for her guidance, mentorship, and support throughout this study. I also thank all members of the Sheldon Lab for their assistance, feedback, and encouragement.

Community & Indigenous Health





Gurraj Hothi (Dr. Segun Oyedokun)

Evaluating an Enhanced Supervision Model in a Canadian Practice-Ready Assessment Program: A Multi-Method Program Evaluation

Introduction: Rural and remote regions in Canada continue to face significant shortages of family physicians. The Saskatchewan International Physician Practice Assessment (SIPPA) evaluates readiness of internationally trained physicians to practice in Saskatchewan and, in 2023, implemented a redesigned supervision model. This evaluation examined how the enhanced framework supports physician readiness, quality of care, workload, wellness, and rural retention.

Methods: A multi-method program evaluation combined descriptive analysis of administrative supervision data with qualitative interviews conducted between June and August 2026. Administrative data characterized supervision activities, progression, and workload experiences. Interview data were analyzed using Braun and Clarke's reflexive thematic analysis.

Results: Among physicians with workload data, 69.4% reported sustainable or somewhat sustainable workloads, while 22.2% indicated workload frequently affected wellness. Qualitative findings identified three domains: Educational and Professional Development, Well-Being and Relational Experience, and System and Structural Contexts. Graduates valued high-quality feedback, documentation skill development, mentorship, and accessible support. Challenges included workload overwhelm, isolation, and administrative burdens. Physician leaders emphasized rural emergency department demands and the need for clearer communication between SIPPA supervisors and clinic leadership.

Conclusion: The enhanced SIPPA supervision model strengthens clinical competence, confidence, documentation skills, and readiness for independent practice. However, broader workplace and system factors continue to shape physician wellness, workload, and retention. Future refinements should prioritize clearer expectations, improved onboarding, practical transition-to-practice supports, stronger communication with physician leaders, and targeted skill-based workshops.

Evaluating an Enhanced Supervision Model in a Canadian Practice-Ready Assessment Program

Raj Hothi, Udoka Okpalauwaekwe, Obianuju Asiedu, Taofiq Olusegun Oyedokun

In-Progress Poster as data analysis is ongoing

INTRODUCTION

- Canada's primary healthcare system continue to face significant challenges related to a persistent **shortage of family physicians**.¹
- Access disparities are especially pronounced in rural and remote communities, where physicians tend to be unevenly distributed and where healthcare infrastructure is under considerable strain.²
- Practice-Ready Assessments (PRAs) like the *Saskatchewan International Physician Practice Assessment (SIPPA)* have emerged as a strategy to facilitate international medical graduates (IMGs) to practice family medicine in Canada.²
- Physicians within SIPPA first undergo a 12-week clinical field assessment, followed by a two-year period of supervised practice in a rural community. Key elements of supervision include: clinical chart reviews, an emergency department chart review, a periodic review and weekly rounds.
- Research increasingly suggests that structured supervision and mentorship are critical to successful transition into independent practice.³
- In 2023, SIPPA revamped their supervision model. Grounded in Kern and Thomas' 6-step Model and experiential learning theory, the supervision program is designed to **foster reflective practice, professional identity formation, and competence through guided participation and feedback**.
- This project evaluated how well the **redesigned supervision framework supports physician readiness, quality of care, and long-term retention in rural Saskatchewan**.

OBJECTIVES

This project had 3 main objectives:

- Describe engagement with the enhanced supervision model using routinely collected administrative program data.
- Explore the experiences and perceptions of SIPPA physician candidates and program leaders regarding the enhanced supervision model, including:
 - SIPPA's influence on physician readiness for independent practice
 - Quality of care
 - Workload and wellness, and
 - Transition into Canadian family medicine.
- Identify perceived strengths, challenges, and opportunities to inform ongoing refinement of the SIPPA enhanced supervision model and guide future practice-ready assessment programs.

METHODS

This was a multi-method program evaluation combining:

- Quantitative:** a descriptive analysis of routinely collected administrative supervision data, analyzed using IBM SPSS Statistics.
- Qualitative:** interviews with SIPPA physician candidates, graduates and program leaders, analyzed using Braun and Clarke's reflexive thematic analysis.

Administrative data were used to describe the supervision model, its practice context, and documented program activities. The qualitative inquiry formed the principal component of the evaluation and was used to understand how enhanced supervision was experienced, perceived, and translated into practice. We reported the study in accordance with the Standards for Reporting Qualitative Research (SRQR)

Ethical approval was obtained from the University of Saskatchewan Behavioural Research Ethics Board (Beh-REB #6321).

RESULTS - QUANTITATIVE

Characteristics of Enhanced Supervision:

Chart 1: At the 1-Year checkpoint, most physicians were practicing in multiple settings (these categories are not mutually exclusive):

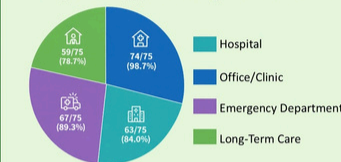


Chart 2: Documented supervision elements

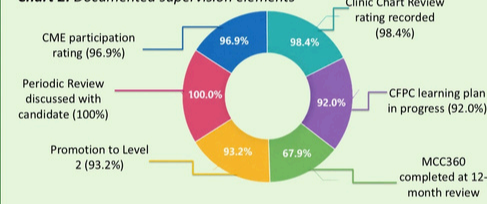
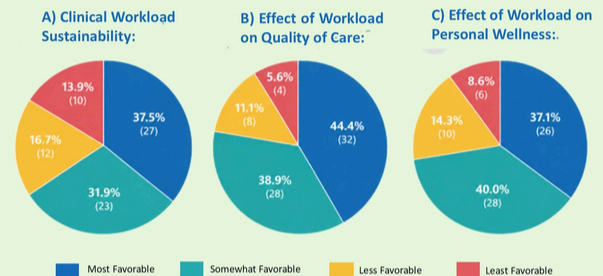


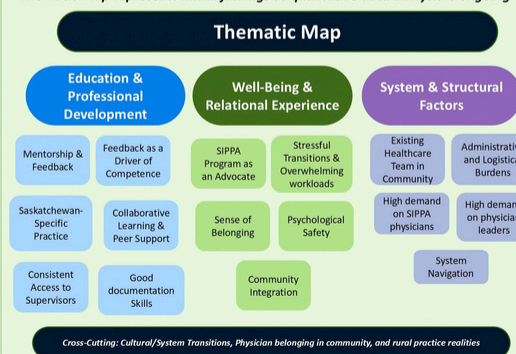
Chart 3: Physician-Reported workload sustainability and perceived effects on care and wellness:



Workload-monitoring data were summarized using each physician's most recent complete assessment. Assessments were available only for 72 physicians for clinical workload sustainability and the perceived effect of workload on quality of care

RESULTS - QUALITATIVE

Thematic Map represents initial findings as qualitative data analysis is ongoing



- Common themes that emerged from interviews with SIPPA graduates included strong support in educational and professional development, the SIPPA program caring about their wellbeing and systemic concerns stemming from staffing shortages, difficulties in working in rural regions with minimal supports and harsh transitions into independent practice
- Common themes among physician leaders: communication concerns and barriers, high demand on leaders to both manage and teach, and there being a process gap, not an educational one.

CONCLUSIONS

Conclusions are preliminary as data analysis is ongoing

- Integrated supervision enhances competence but not retention.** SIPPA's structured mentorship and feedback model effectively builds clinical confidence, documentation skills, and readiness for independent practice, however, physician retention remains primarily influenced by community structure, team supports, and systemic factors beyond supervision.
- Systemic alignment, integrating recommendations from alumni, and wellness supports are essential.** To sustain physician well-being and rural workforce stability, future program development should bridge gaps between the SHA, SIPPA, and physician leaders on the ground, reduce administrative burdens on SIPPA physicians, and continue encouraging psychological safety.

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ACKNOWLEDGEMENTS

Thank you to Drs. Segun Oyedokun and Udoka Okpalauwaekwe for their support, encouragement and expertise on this project, as well as Obianuju Asiedu, Dr. Jon Witt, Carla Fehr, and the rest of the SIPPA team. Our deepest gratitude to our research participants as well as the SIPPA physicians, graduates and physician leaders who gave this project meaning and purpose. Finally, this project was made possible by a Deans Summer Project Award from the University of Saskatchewan College of Medicine.



Sukhman Kaur (Dr. Michelle Collins)

Prevalence of Genetic Variants in Patients with Cardiomyopathies: A Saskatchewan Cohort Review in Comparison to International Data

Introduction: Cardiac diseases have a significant genetic etiology, yet population-specific data on variant prevalence among Saskatchewan patients remains limited.

Objective: To characterize the distribution of genetic variants associated with cardiomyopathies in SK and compare with international trends.

Methods: Medical genetics findings were reviewed for patients with cardiac conditions referred for genetic testing. This analysis focused on HCM, DCM, ARVC/ARVD, LQTS to determine prevalence of pathogenic/likely pathogenic variants for each. International data on two major cardiomyopathies (HCM and DCM) were obtained from the Atlas of Cardiac Genetic Variation, ClinVar, and relevant peer-reviewed literature, and compared to provincial findings.

Results: HCM cohort - SK showed a smaller distribution of MYH7 and TNNT2 compared to international data, while MYBPC3 remained the most prevalent gene, consistent with global trends. Variants reported in Dutch, Hungarian, diverse Caucasian cohorts and Hutterite populations globally were observed locally. DCM cohort – SK has a higher distribution of LMNA and BAG3, while TTN followed a similar trend compared to international data.

Conclusion: Our findings provide valuable information on cardiomyopathy associated genetic variants in Saskatchewan population, demonstrating trends suggestive of shared ancestral background amongst affected individuals and offering clinicians locally relevant data to inform screening and patient care.

Prevalence of Genetic Variants in Patients with Cardiomyopathies: A Saskatchewan Cohort Review in Comparison to International Data

Sukhman Kaur¹, Ibrahim Al-Moualad Al-Azem¹, Emma Eger², Bitu Hashemi³, Brandon Chalazan³, Michelle M. Collins²

¹ College of Medicine, University of Saskatchewan, ²Department of Anatomy, Physiology and Pharmacology, University of Saskatchewan, ³Division of Medical Genetics, Department of Pediatrics, Saskatchewan Health Authority

INTRODUCTION

- Limited information available for prevalence of genetic variants of cardiac conditions, especially cardiomyopathies, in Saskatchewan population.
- Identifying genetic contribution can be essential in identifying trends of certain variants seen in common cardiac conditions in the province.
- International comparisons can provide additional context for understanding the prevalence and population characteristics of this province.

OBJECTIVE

- Characterize the distribution and classification of genetic variants associated with cardiac conditions in Saskatchewan
- Compare pathogenic and likely pathogenic (P/LP) variant patterns for two major cardiomyopathies (hypertrophic cardiomyopathy and dilated cardiomyopathy) with reported international populations.

METHODS

- Charts obtained from the provincial database for patients referred for genetic testing by SK cardiology departments from 2014–2024

- 890 referred
- 331 pediatric patients (66 declined testing)
- 559 adult patients (34 declined testing)

- 790 included in analysis
- 265 pediatric patients
- 525 adult patients

- Referrals spanned 15 cardiac conditions in pediatric cohort and 14 in adult cohort.

- 4 conditions selected for focus: cardiomyopathies (HCM, DCM, ARVC/ARVD) and channelopathy (Long QT syndrome).

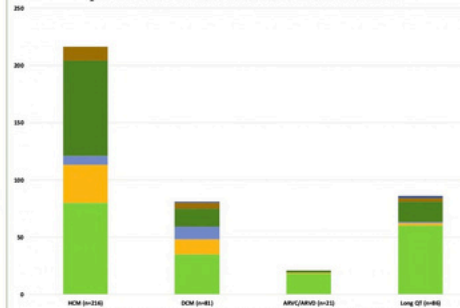
- Hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/ARVD, Long QT syndrome (LQTS).

- P/LP variant rates determined for each

- HCM and DCM P/LP variant provincial prevalence compared with international data

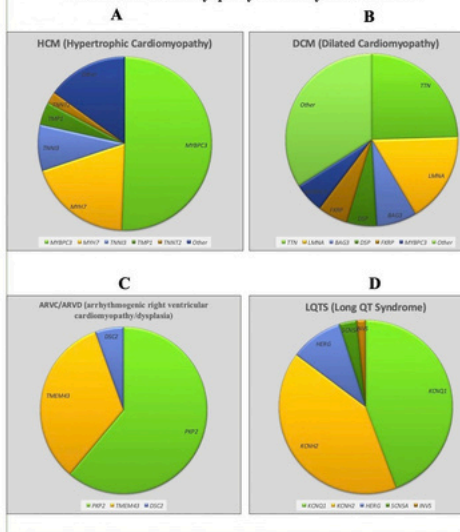
RESULTS

Figure 1: Summary of genetic yield: variants identified in patients with cardiac conditions in Saskatchewan



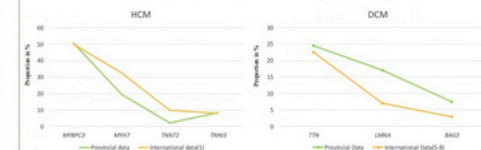
We observed the highest yield of pathogenic and likely pathogenic variants in HCM, with a total of 93 variants identified, followed by 61 in Long QT syndrome, 53 in DCM, and 18 in ARVC/ARVD.

Figure 2: Pathogenic and Likely Pathogenic (P/LP) genetic variants identified in cardiomyopathy and arrhythmic disorder



RESULTS CONT'D

Figure 3: Distribution of genetic variants in HCM and DCM patients: Provincial vs. International comparison (1, 5-8)



P/LP Variant	International data	Saskatchewan data (n=216, 93 P/LP variants)
p.Trp792Val ⁴¹ (MYBPC3)	25% of cases of HCM in the Netherlands (Dutch founder variant) ¹⁵	19.35% (18/93)
P.P958R ⁹⁵ (MYBPC3)	7.78% (7/90), from n=242 Hungarian population ¹⁶	5.38% (5/93)
Arg92Trp (MYBPC3)	2.4% (3/124) from a diverse Caucasian HCM cohort ¹⁶	5.38% (5/93)
TRAPPC1 (c.1287-5G>A), CFTR (c.3882T>A), THOC6 (c.136 G>A)	genetic variants considered pathogenic for other medical conditions found in Hutterite population ¹⁷⁻¹⁹	1.08% (1/93) for each variant listed

CONCLUSION

- HCM: similarities to published data- MYBPC3 is most prevalent; differences – SK has smaller distribution of MYH7 and TNNI2. Variants reported in Dutch, Hungarian, diverse Caucasian cohorts and Hutterite populations globally were also observed in SK.
- DCM: similar trend for TTN; differences – SK has higher prevalence of LMNA (16.98%, 9/53), and BAG3 (7.55%, 4/53).
- Our findings provide valuable information on cardiomyopathy associated genetic variants in Saskatchewan population and demonstrate a trend that indicates shared ancestral background amongst affected individuals, offering clinicians locally relevant data to inform screening and patient care.

International data was obtained from the Atlas of Cardiac Genetic Variation, ClinVar, and supplemented by relevant peer-reviewed literature.

Limitations & Future Directions: Limited access to some international databases and country-specific data may affect comparability; broader searches across additional and less-accessible sources are needed to strengthen the accuracy and comprehensiveness of international findings.

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ACKNOWLEDGEMENTS

I would like to thank the USask College of Medicine Dean's Office and MacGill-Groves Foundation for funding this summer project, Dr. Michelle Collins for her continued guidance throughout this project and Danielle Wong at the Saskatchewan Health Authority Clinical Library for her support in searching pre-existing data on SK population.



Jakob Philipchuk (Dr. Mina Niazi)

Illness Perception and Mediterranean Diet Adherence Among Adults with Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common liver disease in Canada. A Mediterranean-style diet is an effective approach to its management, yet real-world adherence is low among non-Mediterranean populations. This study evaluates baseline diet adherence and its relationship with disease severity and separately characterizes illness perception among Canadian adults with MASLD.

Objective: To characterize baseline Mediterranean-style diet adherence (MEDAS) and its relationship with hepatic steatosis (CAP) and fibrosis (kPa); to describe post-consultation illness perception (BIPQ) and its association with disease severity; and to evaluate whether prior dietary counselling is associated with better adherence and disease understanding.

Methods: 45 adults with MASLD completed the MEDAS and BIPQ at their initial hepatology consultation. FibroScan quantified steatosis and liver stiffness. Correlations and group comparisons were performed, with partial correlation adjusting for food insecurity and GLP-1 agonist use.

Results: Greater adherence was correlated with lower CAP ($r=-0.364$, $p=0.016$). Prior counselling was associated with greater disease understanding (median coherence 8.0 vs 6.0, $p=0.048$) but not greater adherence to Mediterranean diet. Despite strong belief in diet as a treatment, adherence remained low (median MEDAS 5.0/14).

Conclusions: Structured, behaviourally focused interventions may be required to enhance adherence to evidence-based dietary recommendations in MASLD.

Illness Perception and Mediterranean Diet Adherence Among Adults with Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)



Jakob Philipchuk¹ & Mina Niazi^{1,2}

¹University of Saskatchewan, College of Medicine; ²Saskatchewan Health Authority

INTRODUCTION

- Metabolic dysfunction-associated steatotic liver disease (MASLD) is a chronic liver disease defined by hepatic steatosis in the presence of ≥ 1 cardiometabolic risk factor.
- MASLD is the most common liver disease in Canada, with an estimated prevalence of up to 35% among adults [1].
- Weight loss is central to management. Modest reductions in body weight improve hepatic steatosis, while more substantial weight loss of $\geq 10\%$ is associated with improvement or reversal of liver fibrosis [2].
- A Mediterranean-style diet is the most consistently recommended and best-studied dietary pattern for MASLD, reducing hepatic steatosis even in the absence of weight loss [3, 4].

OBJECTIVES

- To characterize baseline Mediterranean-style diet adherence (MEDAS) in a Canadian cohort of adults with MASLD and examine its relationship with hepatic steatosis (CAP) and fibrosis (kPa)
- To describe illness perception (BIPQ) in this population and examine its association with disease severity (e.g., fibrosis and illness threat)
- To evaluate whether prior dietary counselling is associated with greater diet adherence and greater illness coherence (disease understanding)

MATERIALS & METHODS

Cross-sectional observational study of adults (≥ 18 years) with MASLD/MASH recruited at their initial hepatology consultation in Saskatchewan, Canada; questionnaires completed post-appointment.

Measures: MEDAS (habitual Mediterranean diet adherence); BIPQ (illness perception, 8 domains); FibroScan (CAP, dB/m; liver stiffness, kPa); cardiometabolic risk factors (CMRFs), prior dietary counselling, food insecurity, and GLP-1 agonist use recorded.

Analysis (SPSS): Descriptives as mean $\pm$ SD or median (IQR); Pearson/Spearman correlations; t-test/Mann-Whitney U for group comparisons; partial correlation adjusting for food insecurity and GLP-1 agonist use. Two-sided $p < 0.05$

RESULTS

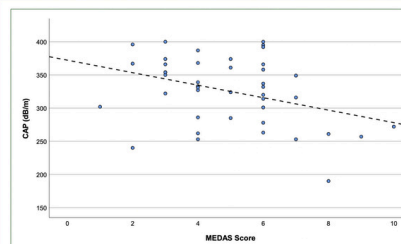


Figure 1. Mediterranean diet adherence (MEDAS score) versus hepatic steatosis (CAP, dB/m). Higher adherence was associated with lower steatosis ($r = -0.364$, $p = 0.016$). Dashed line represents the linear fit. Each point is one participant.

Results were unchanged by food insecurity ($n=3$) or GLP-1 agonist use ($n=5$) (all $p > 0.7$)

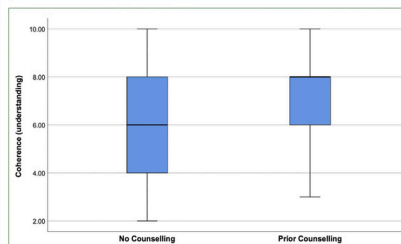


Figure 2. Illness Coherence (BIPQ understanding) by prior counselling. Participants who had received prior dietary counselling reported significantly greater understanding of their liver disease than those who had not (median 8.0 [6.0-8.0] vs. 6.0 [3.8-8.0]; $U = 133.5$, $p = 0.048$). Boxes show median and IQR; whiskers show range.

Cardiometabolic burden

CMRF count was not associated with steatosis ($r_s = 0.163$, $p = 0.297$) or fibrosis ($r_s = 0.037$, $p = 0.812$) in this cohort.

Advice specifics

Neither Mediterranean-specific dietary advice ($p = 0.715$) nor perceived clarity of advice ($r_s = 0.206$, $p = 0.276$) was associated with greater adherence.

Illness threat

More severe liver fibrosis was correlated with greater illness threat perception ($r_s = 0.366$, $p = 0.017$); steatosis severity was not associated with patient concern ($r_s = 0.071$, $p = 0.649$).

Belief-behaviour gap

Patients strongly believe that a Mediterranean-style diet is beneficial (treatment-control median 9.0/10), yet actual adherence was low (MEDAS 5.0/14).

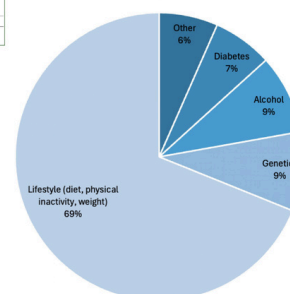


Figure 3. Patient-perceived primary cause of liver disease ($n=45$). Participants ranked up to three contributing factors; only the first-listed cause is shown, grouped by a single reviewer. Most patients attributed their disease to modifiable factors amenable to intervention.

Characteristic	Value
Age, years	57.2 $\pm$ 12.4
Female sex	26 (57.8%)
BMI, kg/m ²	35.1 $\pm$ 7.2
CAP, dB/m	332 (285-366)
Steatosis S3	33 (73.3%)
Liver stiffness, kPa	7.1 (5.1-10.9)
Advanced fibrosis (F3-F4)	14 (31.1%)
Total CMRFs	2.0 (2.0-3.0)
Prior dietary counselling	30 (66.7%)
Mediterranean diet advised	12 (26.7%)
MEDAS score	5.0 $\pm$ 2.0
BIPQ total	29.5 (22.3-37.8)

Table 1. Participant demographics and clinical characteristics ($n=45$).

CONCLUSION

Higher Mediterranean diet adherence was associated with lower hepatic steatosis (CAP), even in a non-Mediterranean cohort with generally low adherence.

Prior dietary counselling was associated with greater disease understanding, but not with greater dietary adherence.

Patients recognized diet as an important aspect of disease management (median treatment-control 9.0/10), yet actual adherence remained low. This suggests structured interventions may be needed.

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ACKNOWLEDGMENTS





Erika Whyte (Dr. Angelica Lang)

How do shoulder kinematics change in a progressive overhead lifting task?

Background: Overhead lifting is associated with upper-limb injury risk, and shoulder kinematics may be influenced by increasing load and sex. This study investigated shoulder kinematics during a progressive overhead lift and identified potential differences between sexes.

Methods: Thirty healthy adults (15 women, 15 men; mean age of 44.5 ± 14.3) completed four sets of five overhead lifts with progressively increasing load and effort. Shoulder, trunk, and arm motion were captured using a Vicon optical motion capture system. Humeral and scapular kinematics were assessed across lifting sets and between sexes using statistical parametric mapping (SPM) and two-way mixed ANOVAs.

Results: Increasing load altered shoulder kinematics in both sexes. Humeral elevation and external rotation decreased as load increased. Scapular upward rotation increased with load in both sexes, with set $\times$ sex interactions ($p = .002$) at some levels of humeral elevation. Males demonstrated greater increases in upward rotation across progressive sets than females.

Conclusion: Shoulder kinematics change with progressive overhead loading, with males and females demonstrating different scapular adaptations. These findings suggest that sex should be considered when evaluating shoulder mechanics and developing strategies for workplace injury prevention.

How do shoulder kinematics change in a progressive overhead lifting task?

¹Erika R. Whyte, ¹Kenzie B. Friesen, & ¹Angelica E. Lang

¹Canadian Centre for Rural and Agricultural Health, College of Medicine, University of Saskatchewan,



Introduction

- Overhead lifting is associated with increased upper-limb injury risk [1]
- Injury risk is often evaluated using humeral elevation. However, humeral rotation and scapular movement are also important components of shoulder mechanics [2], [3]
- Shoulder kinematics may vary with sex [4], while increasing load may alter movement strategies [5], both of which are important considerations for injury prevention

Purpose: To investigate shoulder kinematics during a progressive overhead lift and identify potential differences between sexes

Methods

- Thirty healthy adults were recruited: 15 women and 15 men (mean age: 44.5 ± 14.3 years).
- Participants completed four sets of five overhead lifts with progressively increasing load and effort.
- Shoulder, trunk, and arm motion was tracked using a Vicon optical motion capture system



Figure 1: Motion capture marker and EMG sensor placement (left) and overhead lifting task (middle, right).

- Humeral and scapular angles were calculated for each lift.
- Scapular orientations were extracted at 15° increments of humeral elevation for each task.
- Humeral angles were compared across the full lift cycle with statistical parametric mapping (SPM).
- Two-way mixed ANOVA was used to compare scapular and humeral kinematics across sets and between sexes, and to assess sex $\times$ set interactions.

Results

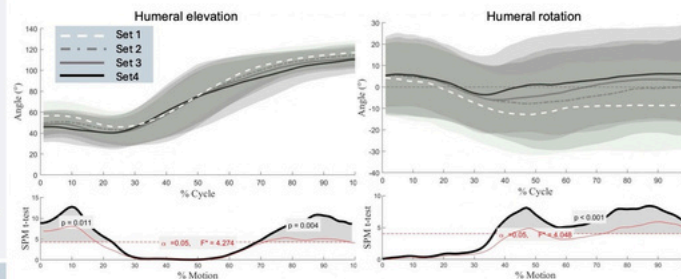


Figure 1: Humeral elevation and rotation across four progressive lifting sets, with SPM identifying regions of significant differences throughout the lifting cycle.

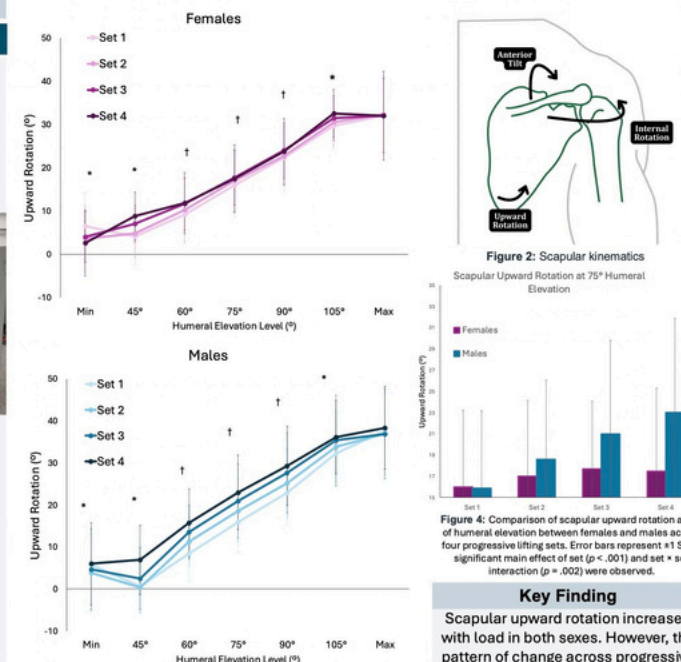


Figure 3: Scapular upward rotation ($\pm 95\%$ CI) of dominant arm at different levels of humeral elevation. * denotes significant main effect of set ($p < 0.05$), † denotes significant set $\times$ sex interaction ($p < 0.05$).

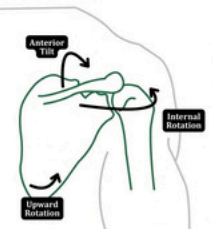
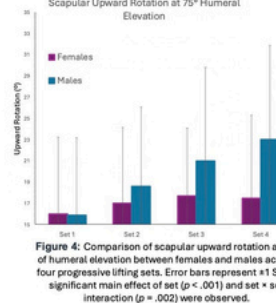


Figure 2: Scapular kinematics
Scapular Upward Rotation at 75° Humeral Elevation



Key Finding
Scapular upward rotation increased with load in both sexes. However, the pattern of change across progressive lifting sets differed between females and males, consistent with a significant set $\times$ sex interaction.

Results

- Increasing load altered shoulder kinematics in an overhead lift task in both sexes.
- Both humeral elevation and external rotation decreased as the load increased over the sets.
- These compensations have been reported in previous research [5] and likely reflect strategies to rely on the bigger shoulder muscles and trunk movement.
- There were notable sex and set interactions for scapular upward rotation.
- Males increasing the upward rotation more in the middle humeral elevation, possibly to compensate for lower joint flexibility.
- Increased upward rotation can be a positive adaptation to avoid damage to the rotator cuff.

Conclusions

- Shoulder kinematics change for both sexes during a progressive overhead lift.
- Males adjust their scapular kinematics differently than females, even though the load was normalized to individual effort, which may be related to lower overall work-place injury in males
- Sex should be considered in workplace injury prevention and treatment

Acknowledgements

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Maheen Zafar (Dr. Jacob Alhassan)

The sense of belonging and its health impacts: A review of Canadian evidence

Belonging refers to the feeling of being included, accepted or connected to a group or a community. Previous research shows that belonging influences mental and physical health through different health outcomes although no current synthesis exists on patterns of belonging and health impacts in Canada. This scoping review identified the existing evidence on health and equity dimensions of the impacts of the sense of belonging in Canada.

The scoping review was conducted by searching 6 health science databases through searches on three core concepts: belonging, health and Canada. Peer-reviewed English-language studies published between 2000-2026 on the health impacts of belonging in Canada were included. Grey literature, other review types and studies not directly reporting health impacts were excluded. Identified studies were synthesized thematically to identify patterns of health impacts.

Higher sense of belonging was better for health due to improved mental health (self-rated mental health, lower suicidal ideation, depression and anxiety) and better physical health (self-rated general health, health utility, lower risk of incidence of diabetes, diabetes-related hospitalization, and chronic conditions, particularly arthritis).

Positive impacts were however context-dependent, varying across demographic groups. A sense of belonging improved health especially for women, older adults, and some population groups.

The sense of belonging and its health impacts: A review of Canadian evidence

Maheen Zafar, Dr. Jacob Alhassan



INTRODUCTION

Sense of belonging refers to the feeling of being included, accepted or connected to a group or a community. A sense of belonging is an important social determinant of health, that is associated with physical and mental health outcomes.¹ Previous research has shown that a stronger sense of belonging has been associated with various positive physical and mental health outcomes.¹ There is no current synthesis of Canadian literature on the health impacts of belonging.

PURPOSE

The aim of the scoping review is to map and synthesize the existing evidence on the association between a sense of belonging and health in Canada, with an emphasis on physical and mental health.

RESEARCH QUESTION

What are the health impacts of belonging in Canada?

METHODS

The search strategy focused on three core concepts—belonging, health, and Canada—and incorporated relevant synonyms and related terms for each concept.

Six databases were searched: MEDLINE Ovid, PsycINFO, Embase, Public Health, CINAHL, and Web of Science.

Included: Peer reviewed English language studies published between 2000-2026 that examined the health outcomes of belonging in Canada were included.

Excluded: Grey literature, other review types, and studies not directly reporting health impacts.

Data was extracted from studies and synthesized thematically to identify patterns in health impacts.

METHODS

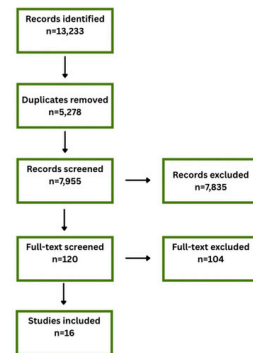


Figure 1. Study Selection Process

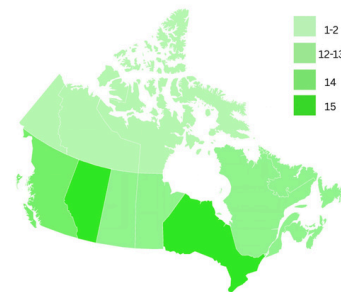
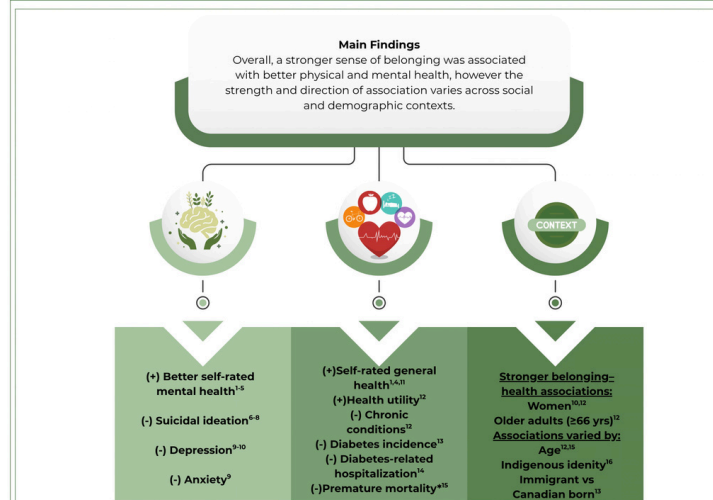


Figure 2. Geographic Coverage of Included Studies

RESULTS



*Premature mortality findings varied by age group

CONCLUSION

Overall, a stronger sense of belonging was associated with better mental and physical health outcomes. Although these associations differed depending on the health outcome and population group being examined.

These findings highlight how social and cultural contexts shape experiences of belonging and influence health outcomes.

RESEARCH GAPS

Most studies had a cross-sectional design, limiting conclusions about temporality and causality.

Indigenous people living on reserves and in other Indigenous communities were underrepresented in the literature, with limited research examining the health impacts of belonging across First Nations, Métis, and Inuit populations.

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ACKNOWLEDGEMENTS

Thank you to Dr. Alhassan and Anu Yadav for their support. Thank you to the University of Saskatchewan College of Medicine for the funding to complete this Dean's summer research project. Map created using IMEJIS.IO; flowcharts designed using Canva.

Medical Education





Daymond Bernath (Dr. Susan Petryk)

Disability Disclosure, Accommodation, and Ableism in Medical Education: A Mixed-Methods Study

Project Title: Disability Disclosure, Accommodation, and Ableism in Medical Education: A Mixed-Methods Study

Background: Learners with disabilities remain underrepresented in medical education and may encounter barriers impacting their learning experience. National data suggests many learners choose not to disclose their disability to their medical program. Existing literature has primarily examined the prevalence of disabilities and the types of accommodation provided, with limited exploration of institutional culture and the attitudes of peers and faculty that may influence disclosure and inclusion.

Methods: This study utilized a mixed-methods model consisting of an anonymous online survey for quantitative data followed by optional semi-structured interviews for qualitative data collection. Quantitative and qualitative data was then analysed using descriptive statistics and Braun and Clarke's reflexive thematic analysis respectively

Results: Preliminary results are showing that 28% of students identifying with a disability still have not requested accommodations. Our study population describes the institutional culture as encouraging and supportive, however, concerns surround impact on residency and how disclosure may negatively impact an individual's experience.

Conclusion: Disability in the medical education has a positive foundation to stand on with work still needed in areas such as stigma, ableism, and psychological safety. Medical learners would appreciate more awareness and openness in discussions surrounding disability and accessibility and clarification on the real-world impact on residency applications and matching.

Disability Disclosure, Accommodation, and Ableism in Medical Education: A Mixed-Methods Study

Daymond Bernath¹, Dr. Susan Petryk^{1,3}, Sanjida Newaz², Shirmin Kader², Kirat Shukla², Hamza Moustapha¹
College of Medicine, University of Saskatchewan¹, Research Department, Saskatchewan Health Authority², Saskatchewan Health Authority³

Introduction

Motivation:

- Learners with disabilities are underrepresented within the medical education
- Many learners with disabilities choose not to disclose to their program

Gap:

- Majority looks at how to treat patients with disabilities
- Commentary and Reflections
- Focus on individual disabilities rather than disability as a whole
- Few studies look at direct perspectives of medical learners

Purpose:

- Examine patterns of disability disclosure, perceptions of stigma, and awareness of disability-related support within a medical education context
- explore both the experiences of medical learners to better understand interpersonal and institutional factors that may shape disclosure decisions and inclusion

Objectives

- Better understand the disability experience within the medical education and appreciate existing strengths and gaps
- Development of recommendations to inform faculty development initiatives, learner orientation activities, and institutional policies related to accessibility
- Utilization of findings to support ongoing institutional efforts in promoting accessibility and equity

Acknowledgements

This project was made possible through the support of the University of Saskatchewan, College of Medicine, Dean's Project Funding

Contact

Daymond Bernath
University of Saskatchewan, College of Medicine
E-mail: daymond.bernath@usask.ca

Materials and Methods

Mixed-methods design involving an anonymous online survey followed by qualitative interviews

Quantitative Analysis



Qualitative Analysis



Qualitative and quantitative findings were integrated during the interpretation phase to provide a comprehensive understanding of disability disclosure and inclusion within medical education

Preliminary Results

Figure 1 – Accommodations Received Breakdown INSTITUTIONAL ACCOMMODATIONS BREAKDOWN

■ Accommodations Provided ■ Did Not Request
■ Requested But Not Yet Received ■ Accommodations Not Provided

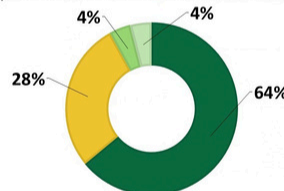


Figure 2 – Distribution of Qualitative Results

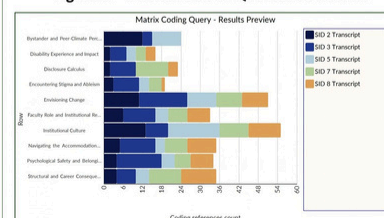


Table 1 - Statistical Comparison of Attitudes and Beliefs (Welch's t-tests)

Attitude/Belief Statement	Group	N	Mean	SD	t	df	p
The medical profession benefits from including physicians with disabilities	Yes	23	5.61	0.583	-2.896	54.98	0.005
Physicians with disabilities may have greater empathy for patients	Yes	23	5.30	0.765	-2.202	51.19	0.032
Students needing extra time on exams can be just as capable	Yes	23	5.61	1.158	3.198	47.16	0.002
Accommodations give students with disabilities an unfair advantage	Yes	25	1.40	0.500	3.231	56.42	0.002
Mental health condition poses a risk to patient safety	Yes	25	1.76	0.723	0.738	51.71	0.464
Disclosing a disability during residency	No	34	4.32	1.249	4.08	1.256	
applications would hurt chances	Yes	25	4.08	1.256			

Figure 3 – Institutional Culture Word Cloud



Figure 4- Psychological Safety & Belonging



Discussion

- Inclusion and accessibility surrounding disability in medical education is ongoing, however, future progress must involve increased conversation and openness about disability
- Medical learners emphasize the impact of staff information delivery has on perception of acceptance and inclusion
- Medical learners with disabilities would like more clarity surrounding true impact of disclosure on residency applications and career outlook
- Effectiveness/variety of accommodations may need be reconsidered as only 64% of participants who had accommodations found them to be either very effective (20%) or somewhat effective (44%)

Figure 5 – Envisioning Change Word Cloud



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Emmanuel Fabella (Dr. Eric Sy)

Patient Oriented Discharge Summaries in the ICU: A Scoping Review

Introduction: Intensive care unit (ICU) discharge is an at-risk transition marked by communication gaps, adverse events, and fragmented care. Patient-oriented discharge tools may help, but ICU use is poorly described.

Methods: Database search was done on MEDLINE, Embase, CINAHL, and Google Scholar (inception to May 2026) for patient- or family-oriented ICU discharge tools. Two reviewers independently screened and extracted data, resolving conflicts by consensus. Data were analyzed thematically.

Results: Of 4,892 records, 30 studies were included (18 adult; 12 pediatric/neonatal). Four themes were identified. First, design was largely agreed on: standardized, tailorable templates (26/30) and plain language (22/30), though reading level was assessed in 6/30. Second, adult and pediatric tools addressed different problems, recounting an ICU stay patients could not recall (10/18 vs 2/12) versus teaching caregiving skills (8/12 vs 0/18). Third, implementation limited use: nurses delivered most tools (14/30), timing varied by setting, clinician time the main barrier (10/30), patient-partner collaboration the main facilitator (15/30). Fourth, tools were well received (satisfaction 17/30; improved understanding 13/30), with unintended distress in 8/30, and adverse events measured in one study (no difference).

Conclusions: Patient-oriented ICU discharge tools may improve communication of patient-related information. Further research should define core contents, increase implementation, and measure effectiveness outcomes.

Patient-Oriented Discharge Summaries in the ICU: A Scoping Review

Emmanuel Fabella¹, Lexington Kinnear¹, Emma Kowal, Basit Gilani, Jonathan Mailman^{2,3}, Eric Sy^{1,4}

¹ College of Medicine, University of Saskatchewan, Regina, SK · ² Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC

³ Pharmacy Services, Royal Jubilee Hospital, Victoria, BC · ⁴ Department of Critical Care, Saskatchewan Health Authority, Regina, SK

BACKGROUND & OBJECTIVE

- Transitions out of the intensive care unit (ICU) are high-risk periods during which important information is lost, contributing to adverse events and discontinuity of care.
- Patient-oriented discharge summaries (PODS)** give patients and families clear written information on their stay, care needs, and follow-up plan.
- PODS are established in general hospital settings, but the literature on their use in critical care has never been synthesized.

Objective. Map the literature on ICU-specific PODS and similar patient- and family-oriented tools and to inform a PODS for our setting.

METHODS

- Design.** Scoping review (JBI), reported per PRISMA-ScR protocol registered a priori on OSF.
- Sources.** MEDLINE, Embase, CINAHL Plus with Full Text, Google Scholar to 26 May 2026, plus backward citation searching. Strategy developed with a health sciences librarian and peer-reviewed by a second.
- Eligibility.** Any patient- or family-directed discharge communication tool in neonatal, pediatric, or adult ICU; PODS, transfer letters, booklets, checklists, diaries, care pathways. Clinician-directed documentation excluded; English only.
- Analysis.** Duplicate screening and charting in Covidence, third reviewer resolving disagreements. No critical appraisal. Open-coded into 97 codes across four domains.

STUDY SELECTION

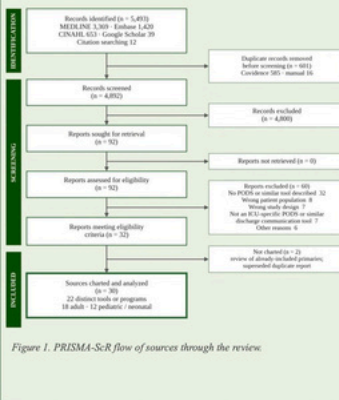


Figure 1. PRISMA-ScR flow of sources through the review.

RESULTS

4,892
records screened

30
sources included

22
tools or programs

18 / 12
adult / pediatric

4
randomized trials

- 4,892 records screened, 30 studies were included (18/30, 60% adult; 12/30, 40% pediatric or neonatal). **Four themes were identified.**

1. Design characteristics were largely agreed on

- Standardized template allowing tailoring: 26/30 (87%).
- Plain language: 22/30 (73%); reading level measured in 6/30 (20%).
- Written material with verbal delivery: 18/30 (60%). No study supported written material alone.

2. Adult and pediatric tools addressed different problems

- Adult tools recounted an ICU stay patients could not recall: 10/18 (56%) vs 2/12 (17%).
- Pediatric tools taught caregiving skills: 8/12 (67%) vs 0/18 (0%).

3. Implementation limited use

- Nurses delivered most tools: 14/30 (47%).
- Delivery timing varied by setting: across the admission in 8/12 (67%) pediatric vs 4/18 (22%) adult.
- Main barrier: clinician time and workload, 10/30 (33%). Completion time was quantified in 2 studies, using different measures.
- Main facilitator: patient-partner collaboration, 15/30 (50%).
- Availability did not equal use: a tool available since 2013 was recalled by 2 of 7 nurses (DesMadryl 2021).

4. Tools were well received; effectiveness was rarely measured

- Satisfaction: 17/30 (57%). Improved understanding: 13/30 (43%).
- No or limited measured effect: 13/30 (43%).
- Unintended patient/family distress: 8/30 (27%); 42% of diary and 20% of summary recipients in Castillo 2020.
- Readmissions and associated adverse events measured in 1 study, with no reported differences (Moyer 2014).
- Continuity of care named as the rationale in 8/30 (27%) and measured in none.

Content diverges sharply by setting

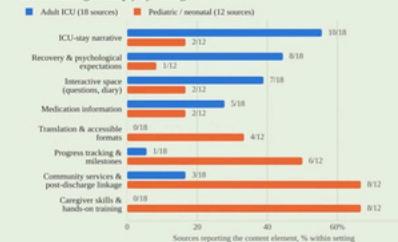


Figure 2. Content elements by ICU setting. Bars show the percentage of sources within each setting; counts are the raw numerator and denominator.

Design is agreed on — and rarely verified

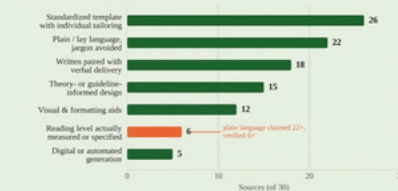


Figure 3. Most frequently applied design codes across all 30 sources.

Most-reported barriers



Most-reported facilitators



Figure 4. Most frequently reported barriers and facilitators across all 30 sources.

CONCLUSIONS

- Patient-oriented discharge tools in the ICU may improve communication of patient-related information.
- Design characteristics were largely agreed on, but adult and pediatric tools addressed different problems and no core content set has been defined.
- Satisfaction and improved understanding were commonly reported; clinical and health-service outcomes were largely unmeasured.

IMPLICATIONS

For practice

- No study supported written material alone; 18/30 (60%) paired it with verbal delivery.
- Availability did not equal implementation: plan for the mandate, the training, and the workflow slot.
- Some recipients found the information distressing; offering choice over whether and when to receive it was the only tested response.

For future research

- Define the core contents, separately for adult and for pediatric/neonatal ICU.
- Increase implementation: quantify completion time and cost, and test what sustains use.
- Measure outcomes related to effectiveness: clinical, health-service and process outcomes alongside satisfaction, and compare delivery timing directly within a setting.

LIMITATIONS

- English-language studies only, potentially reproducing the language gap the review identifies.
- No critical appraisal, so how often a finding is reported is not a measure of the strength of the evidence behind it.
- Frequencies count studies, not independent investigations.

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ACKNOWLEDGEMENTS

Supported by a Dean's Summer Project Award (2026), College of Medicine, University of Saskatchewan. We thank the U of S health sciences librarians who developed and peer-reviewed the search strategy.



Daly Haas (Dr. Marla Davidson)

Evaluating the Impact of Wellness Initiatives on Resident Wellbeing and Learning Environment Perceptions

Introduction: Medical residents face complex workplace demands that can negatively impact their wellbeing and engagement in training. This mixed methods study evaluated resident use of resources from the USask Postgraduate Medical Education Resident Resource Office (RRO) and its association with resident wellbeing and learning environment perceptions.

Methods: Three years of retrospective learning environment evaluations and RRO utilization records were analyzed. A cross-sectional survey measuring awareness and use of RRO resources, fatigue, burnout, grit, resiliency, and overall wellbeing was sent to all USask residents (N=525), with 36 respondents.

Results: RRO use continued to increase each year, and residents were satisfied and comfortable with their experiences. While overall RRO utilization was not associated with general wellbeing, burnout, resilience or grit, residents who accessed three or more RRO resources reported significantly higher fatigue scores. Residents reporting poor or fair health rated the learning environment less favourably. Improved awareness of available RRO resources was identified as a priority for increasing resource use.

Discussion: Further research is needed to better understand the relationship between resident wellbeing and wellness resource utilization and to identify strategies that promote awareness and engagement with available supports. Larger sample sizes are needed to clarify these relationships.

Evaluating the Impact of Wellness Initiatives on Resident Wellbeing and Learning Environment Perceptions

Daly Haas, Marla Davidson, Michelle Koehn, Tanya-Robertson-Frey, Loni Desanghere

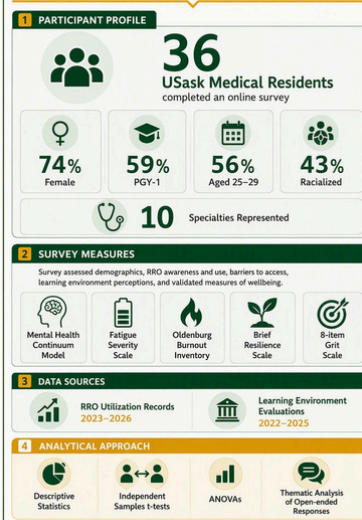
BACKGROUND

- ❖ Medical residents face substantial demands that can negatively impact resident wellbeing and engagement.¹⁻⁵
- ❖ Wellness initiatives have become an important strategy to support resident wellbeing.^{6,7}
- ❖ The USask PGME Resident Resource Office (RRO) offers residents individualized support and proactive wellness initiatives.
- ❖ Resident engagement with wellness resources, barriers to access, and the impact of wellness programming on resident wellbeing and learning environment perceptions remain underexplored.

OBJECTIVES

- ❖ Assess the relationship between RRO utilization and learning environment perceptions.
- ❖ Compare wellbeing outcomes among residents with different levels of RRO engagement.
- ❖ Identify barriers to accessing RRO resources.

METHODS



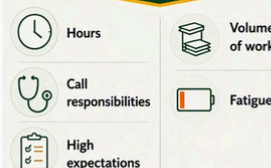
RESULTS

Resident Wellbeing



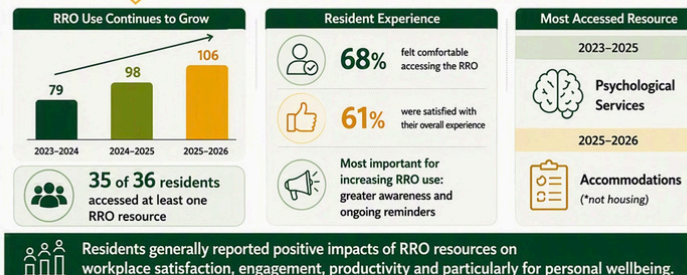
Despite fairly positive self-reported wellbeing, many residents reported indicators of psychological strain.

Greatest Threat to Resident Wellbeing: WORKLOAD



"[I am] feeling overwhelmed, emotionally and physically drained from the amount of workload."

RRO Use and Perceptions



Association Between RRO Use and Resident Outcomes

Retrospective learning environment evaluation (2022-2025):

Residents reporting poor/fair health or experiencing/witnessing incivility and harassment reported significantly lower learning environment ratings across all domains.

Current resident survey:

No significant differences in learning environment perceptions were observed between residents with lower (<3 resources) and higher (≥3 resources) levels of RRO engagement (all $p > 0.05$).

Residents who accessed three or more RRO resources showed significantly greater fatigue ($p < .05$).

No significant differences between groups on overall wellbeing, burnout, resilience or on the mental health continuum.

CONCLUSIONS

- ❖ Residents reporting higher fatigue were more likely to engage with RRO supports.
- ❖ Workload, along with awareness, accessibility, and time constraints, were important barriers to resource use.
- ❖ Poorer wellbeing was associated with more negative learning environment perceptions.
- ❖ Greater use of RRO resources was not linked to improved wellbeing or learning environment outcomes.
- ❖ Wellness resources may be most effective when combined with broader organizational and structural wellness initiatives.
- ❖ Larger, longitudinal studies are needed to better understand how different wellness resources influence resident wellbeing and learning environment experiences.

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ACKNOWLEDGEMENTS

Thank you to all participants for taking the time to complete the survey.

Thank you to PGME for assisting in the development and editing of this project.



Xavier LaBelle (Dr. Segun Oyedokun)

Needs Assessment for Emergency Medicine Program Development in South Sudan

INTRODUCTION: South Sudan faces significant emergency care challenges, including limited trained personnel, infrastructure, and resources, with no structured emergency medicine (EM) residency program. This study aimed to identify needs and priorities for sustainable EM training development.

METHODS: A mixed-methods needs assessment purposively sampled hospital and emergency department leaders, emergency practitioners, and university and Ministry of Health leadership. Three REDCap surveys assessed workforce and system capacity, clinical competencies and training needs, and institutional readiness. Semi-structured stakeholder interviews explored needs, barriers, resources, and sustainability. Surveys were analyzed descriptively. Thematic analysis and mixed-methods triangulation are ongoing.

RESULTS: Preliminary findings demonstrated strong demand for EM development. Among practitioners ($n = 151$), 86.1% were interested or very interested in formal EM training, while 100% of institutional respondents ($n = 26$) considered academic EM important or very important. Only 40.7% reported having physicians with formal EM training. Key competency gaps included psychiatric emergencies, point-of-care ultrasound, electrocardiogram interpretation, and intubation. Funding, infrastructure, ambulance/referral systems, and human resources emerged as key barriers. Stakeholders emphasized local ownership and capacity building.

CONCLUSIONS: Findings support locally led EM residency development in South Sudan alongside investment in workforce, infrastructure, sustainable financing, and local capacity building.

INTRODUCTION

- South Sudan faces significant healthcare challenges which are reinforced by the ongoing conflict and economic instability including limited human resources, inadequate infrastructure, and high levels of trauma.^{1,2}
- South Sudan only has a small number of trained emergency medicine (EM) specialists, and currently there is no structured EM residency or training program that exists.
- The use of a needs assessments is an effective first step in building and developing an EM residency program by identifying gaps and priorities to guide program development.³
- Conducting a needs assessment is a key step in the World Health Organization (WHO) Twinning Partnerships for Improvement (TPI) framework for program implementation and sustainable capacity building.⁴

STUDY OBJECTIVE

To perform a comprehensive needs assessment of emergency medicine education, infrastructure, human resources, and system organization at the University of Juba and affiliated healthcare facilities.

METHODS

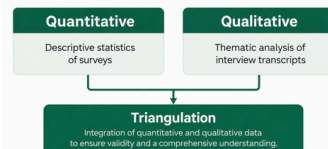
Study Design

- A mixed-methods needs assessment combining quantitative data analysis and qualitative stakeholder input.

Data Sources

- Purposive sampling of key stakeholders
- Quantitative: REDCap Surveys
- Qualitative: Semi-Structured Interviews with key stakeholders on USask supported Zoom

Data Analysis



RESULTS

Participants/Data Sources

Survey A – Hospital/ED Leadership (n=55): Staffing, infrastructure, resources & system capacity
Survey B – Emergency Care Practitioners (n=151): Competencies, training needs & barriers
Survey C – University/MoH Leadership (n=26): Institutional priorities, readiness & sustainability
Interviews – Key Stakeholders (n=16): Perceived needs & priorities, barriers, resources, and sustainability

Emerging Findings	Quantitative Support	Qualitative Support
HUMAN RESOURCES: Limited Trained EM Workforce	40.7% reported having physicians with formal EM training (Survey A) - Median emergency care experience: 2 years (Survey B) 86.1% interested or very interested in formal EM training (Survey B) 100% considered academic EM important or very important (Survey C)	- Shortage of trained personnel, specialists, and knowledgeable staff were repeatedly identified. "a proper emergency care human resource cannot exist without... academic trainings." - Stakeholders advocated for locally available postgraduate EM training as a strategy to address workforce shortages. "[An EM] residency program is one of the most important things we are advocating for"
EDUCATION: Strong Support for Formal EM Training	Preferred training: Bedside 70.2% and Classroom 46.4% rather than virtual	- Stakeholders emphasized practical, comprehensive emergency training to prepare clinicians for time-sensitive emergencies. "Emergency cannot wait... you need ready-trained staff being there, to tackle the emergency."
EDUCATION: Competency & Curriculum Needs		- Infrastructure, equipment, medications, and critical-care resources were repeatedly identified as limitations. "The major challenge is the limited resources [and] the working environment..."
INFRASTRUCTURE: Limited Clinical & Training Resources		
SYSTEM ORGANIZATION: Ambulance & Referral Barriers	- Ambulance Reliability (Survey A) 38.5% reported ambulance services as sometimes or never available	- Ambulance availability, transportation, communication, and security concerns emerged as referral barriers. "Ambulances are for the living... But in South Sudan, ambulances are for the dead."
IMPLEMENTATION: Funding is a Major Barrier	88.1% identified funding as a training barrier (Survey B) 7.7% potential Year-1 stipend support (Survey C)	- Financial constraints were repeatedly described as key barriers to program establishment and sustainability. "Funding is of course, the key thing."
SUSTAINABILITY: Local Ownership & Capacity Building		- Local ownership and development of South Sudanese faculty were emphasized as essential for sustainability. "We must own it and see it as our own... to serve the interests of our people."

TABLE 1 – Mixed-Methods Triangulation of Emerging Findings

DISCUSSION

- Limited formal EM training highlights a clear need for EM residency training and strong stakeholder support suggests readiness for its development and implementation.
- Identified competency gaps and preferences for bedside/classroom learning can guide the development of contextually relevant, competency-based curriculum.
- Human resources, infrastructure, equipment, and financial constraints limit emergency care delivery and residency implementation.
- Existing institutional resources provide a foundation for program development. Having sustainable financing, local faculty development, capacity building, and South Sudanese ownership will be critical.



CONCLUSIONS

- There is strong stakeholder support and a need for formal EM training in South Sudan. A sustainable EM residency will require local ownership, capacity building, adequate resources, and sustainable financing.

These findings can inform development of a locally led, contextually appropriate EM residency program in South Sudan.

ACKNOWLEDGMENTS

We thank the University of Juba, Ministry of Health, participating institutions and all survey and interview participants. Ethics approval: University of Saskatchewan Behavioural REB and South Sudan MoH-RERB.

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Vaidehee Lanke (Dr. Scott Adams)

Evaluating artificial intelligence models for gastrointestinal polyp detection

Early and accurate detection and characterization of gastrointestinal (GI) polyps is essential for clinical management and prevention of GI malignancies and conditions. Artificial intelligence tools have the potential to assist clinical in accurately and efficiency detecting and characterizing polyps. However, AI models vary significantly in their architecture, training and validation datasets and availability, raising questions about model generalizability and real-world applicability. The objective of this project was to systematically evaluate and compare the performance of AI models for polyp detection and characterization across multiple datasets and evaluation metrics, including polyp detection, segmentation and classification and model generalizability.

Evaluating artificial intelligence models for gastrointestinal polyp detection

Vaidehee Lanke, Scott Adams

Introduction

- Gastrointestinal (GI) polyps are lesions detected during endoscopes and may represent precursors to malignancies¹.
- Early and accurate detection and characterization of polyps is important¹.
- Artificial intelligence (AI) tools have the potential to assist clinicians in accurately and efficiently detecting and characterizing polyps^{2,3}.
- AI models vary significantly in their architecture, training and validation data and availability, ranging from open source to commercially developed models, raising questions about model generalizability and real-world applicability^{4,5}.

Objectives

Systematically evaluate and compare the performance of AI models for polyp detection and characterization across multiple datasets and evaluation metrics.

Primary objectives:

- Evaluate AI model performance in polyp detection, segmentation and lesion classification

Secondary objectives:

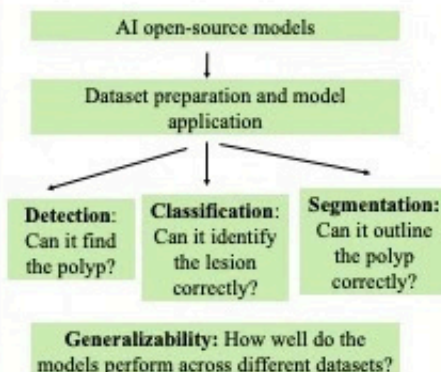
- Assess the generalizability of AI models across multiple different datasets
- Compare the performance of open-source vs commercial AI models

Materials and Methods

Open-source models Commercial models

- ColonFormer
- PraNet
- HarDNet-MSEG
- ColonSegNet
- Polyp-PVT
- Baseline AI models
- EndoBRAIN
- Endo-AID
- GI Genius
- SKOUT

Dataset	Description
HyperKvasir	10,662 labelled GI endoscopy images
Kvasir-SEG	1000 polyp images with corresponding segmentation masks
CVC-ClinicDB	612 annotated polyp images and corresponding segmentation masks
SUN Dataset	49,136 samples of 100 different polyp types, including shape and size
PolypDB	3934 still polyp images
ETIS-LaribPolypDB	196 polyps images, 29 colonoscopy sequences



Results and Impact

Results: Our anticipated results will provide a standardized comparison of AI models for GI polyp detection and characterization, including performance across multiple evaluation metrics, strengths and limitations in detection, segmentation and lesion classification and extent of generalizability across different datasets.

Impact: This project hopes to contribute an evidence-based framework for understanding the value and role of AI tools in GI medicine and identify areas for future model development, validation and clinical application.

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Acknowledgements

Thank you to the College of Medicine for the Dean's Summer Research Project funding.



Elise Morphy (Drs. Kirsten Smith & Alicia Thatcher

Thriving as Co-Educators: A Scoping Review of People with Intellectual and Developmental Disabilities in Health Professional Curriculum

Background: People with intellectual and developmental disabilities (PWIDD) have been historically undervalued as knowledge producers in health professions education (HPE). Co-education initiatives with PWIDD can improve student learning outcomes, which may contribute to narrowing health inequities faced by PWIDD.

Objective: To map and synthesize the literature on the experiences of PWIDD as co-educators in health professions education.

Methods: Guided by the PRISMA-ScR framework, a scoping review was conducted through systematic searches of four databases: MEDLINE, EMBASE, CINAHL, and ERIC. One reviewer screened titles, abstracts, and full-text articles against predefined inclusion criteria. Data were extracted and synthesized using descriptive and thematic analysis.

Results: The database search identified 1,182 unique records, of which eight met inclusion criteria. Eight additional articles were identified through backward reference searching, resulting in 16 included studies. Key facilitators of co-educator involvement included Reasonable Adjustments, Safe and Supportive Learning Environments, and Optimizing Agency. Benefits included Psychological Wellbeing, Meaningful Employment and Role Participation, and Learning and Skill Development.

Conclusions: Findings highlight factors that support meaningful involvement of PWIDD as co-educators in HPE and may guide institutions seeking to implement co-education initiatives. Future research should prioritize the perspectives of co-educators with IDD and examine institutional facilitators and barriers to implementation.

Thriving as Co-Educators: A Scoping Review of People with Intellectual and Developmental Disabilities in Health Professional Curriculum

Morphy, E., Robinson, M., Guliak, D., Thatcher, A., Smith, K.

INTRODUCTION & BACKGROUND

People with intellectual and developmental disabilities (PWIDD) are experts in their experiences, yet have been historically undervalued as knowledge producers in health professions education (HPE)¹. Evidence suggests that co-education initiatives with PWIDD can improve student learning outcomes² which may contribute to narrowing health inequities faced by PWIDD³ that are due to limited knowledge and stigmatizing attitudes on the part of healthcare workers in caring for this population⁴.

Despite the value of co-education initiatives in partnership with PWIDD, little is known about the impact of participation on the co-educators themselves or the facilitators that enable their involvement.

OBJECTIVES

To map and synthesize the literature on the experiences of PWIDD as co-educators in health professions education.

METHODS

A scoping review guided by the PRISMA extension for scoping reviews⁵ was undertaken to answer the research question. The search strategy was first developed in MEDLINE based on the PCC framework:

Population: PWIDD involved in co-education

Context: HPE classrooms

Concept: Support needs, facilitators, benefits

The search strategy was translated into a total of four databases—MEDLINE, EMBASE, CINAHL, and ERIC—and executed on June 17th, 2026. Backward reference searching supplemented the database search.

One reviewer screened titles, abstracts, and full-text articles against predefined inclusion criteria.

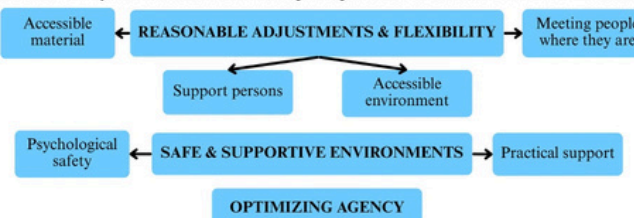
Eligibility Criteria:

- Satisfies PCC framework criteria
- Minimum one facilitator or benefit described
- Conference abstracts, opinion pieces, commentaries excluded

Data were extracted and synthesized using descriptive and thematic analysis.

RESULTS

The database search identified 1182 unique records, of which eight met inclusion criteria. An additional eight articles were identified through backward reference searching, resulting in sixteen included studies. Key facilitators and benefits of participation for co-educators with IDD included:



"Participants referred to the University as a 'safe place' where reasonable adjustments were made by the researchers to create an environment where they felt welcome and valued. Most felt sufficient reasonable adjustments were made to allow them to be independent, whilst researchers were positive and calm which made the experience fun"⁶

Figure 1. Support Needs & Facilitators



"When I was speaking, I felt like I was in control, that I had all this powers again"⁶

"I like making sure that the right people are passing their exam"⁷

"[B]eing employed provides opportunities to occupy valued social roles"⁸

Figure 2. Benefits

SEARCH STRATEGY

	Search concepts	Search terms used in database
POPULATION	1 Health professions education	exp Education, Professional/ or exp Schools, Health Occupations/ or exp Students, Health Occupations/ or exp Health Personnel/ed or exp Health Occupations/ed (nurs* or dent* or medic* or pharmacist* or occupational therap* or physician assistant* or physical therap* or physiotherap* or speech language patholog* or nutrition* or dietitian* or health profession* or optomet* or allied health* or interprofessional* or healthcare or multidisciplinary or transdisciplinary or psych* or health occupation* or doctor or clinical) adj3 (education or school* or student* or classroom* or learn* or train* or curricular* or clerkship or instruct*)//i,ab,kf.
CONCEPT	2 PWIDD involved in co-education	
CONTEXT	3 People with IDD	persons with disabilities/ or persons with intellectual disabilities/ or exp developmental disabilities/ or exp intellectual disability/ or exp learning disabilities/ (mental* or intellectual* or development* or learn*) adj3 (disab* or handicap* or impair* or challenge* or delay* or disorder*)//i,ab,kf.
	4 Co-educators with lived experience	(co-educat* or coeducat* or co-product* or coproduc* or lived experience or patient experience or personal experience or standard/ed patient* or co-design* or codesign* or patient collabor* or patient educator* or patient-as-educator* or patient narrative* or patient partner* or patient-as-partner*)//i,ab,kf.
	5	
	6	
	7	
	8	

Figure 3. Search Strategy

DISCUSSION & CONCLUSIONS

Co-education is important, but should not come at the expense of overburdening the co-educators involved⁸. The support needs and facilitators described may guide educational institutions seeking to implement co-education initiatives for health professions students on caring for PWIDD. When executed properly, they help ensure a positive and meaningful experience for all parties involved, including the co-educators with IDD who stand to gain the benefits described in this review.

This review reveals a gap in literature which captures the direct lived experiences of co-educators with IDD in HPE settings. Future research in this field should aim to prioritize and highlight the voices of PWIDD who are co-educators in health professions classrooms. Additionally, it would be valuable to understand the facilitators and barriers to implementation of these co-education initiatives for educational institutions themselves as they play an essential role in ensuring these experiences are appropriately designed and funded.

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ACKNOWLEDGEMENTS

This project was funded through the University of Saskatchewan College of Medicine's Dean's Project Program. We gratefully acknowledge health sciences librarian Erin Watson for her assistance in developing our search strategy.



Hamza Moustapha (Dr. Ibraheem Othman)

Artificial Intelligence in Pre-Clerkship Medical Education: A Review and Synthesis of the Literature

Artificial intelligence (AI) is becoming increasingly present in medical education and clinical practice. Generative AI tools are already being used by medical students for learning. The purpose of this focused narrative review was to examine the current literature on the use of AI in medical education, with particular attention to pre-clerkship students and Canadian studies. This review utilized PubMed to identify English-language, peer-reviewed articles from 2021 onwards, exploring the ways in which students were using AI, how prepared students felt in using AI, students' AI-related concerns, how students assessed the reliability of information generated by AI, and what they would like to learn through formal teaching. A recurrent expectation expressed by students surveyed across the reviewed studies was that AI would feature in their future careers, and many indicated an interest in getting more formal education about it. Furthermore, participants reported a range of uses for AI. While many students reported receiving limited structured teaching about AI and its risks, they also reported many concerns. Some of these included the potential for inaccurate information, bias, issues with privacy, academic integrity, and appropriate use. Additionally, studies reviewed here highlight the importance of educating students to critically appraise and verify information generated by AI. However, the reviewed studies have a number of limitations which must be noted when applying the findings of the existing evidence to specific settings, including low response rates, self-reported data, and differences in how studies defined AI and measured students' experiences with it. More local data is needed about how pre-clerkship medical students at the University of Saskatchewan are currently using AI and what they think schools should be teaching in terms of future AI education.

Artificial Intelligence in Medical Education: Canadian Evidence, Key Themes, and Future Research Directions

Hamza Moustapha¹, Dr. Ibraheem Othman²
University of Saskatchewan College of Medicine

Introduction

As AI becomes more common in medical education, questions about how students engage with it, its reliability, and responsible use are especially relevant during pre-clerkship, where students are building foundational knowledge and forming study habits. [3,7] Students anticipate using AI in their careers and are open to formal teaching, but many already use it without any formal instruction. [1,3,4] Much of the Canadian evidence comes from voluntary, self-reported surveys with limited response rates, so it may not reflect students' experiences here at the University of Saskatchewan. [1,3,4] This literature review provides a foundation for a planned survey of pre-clerkship students at the University of Saskatchewan.

Objectives

1. Describe how students report using AI, how they view its role in medicine, and how prepared they feel using it.
2. Identify the benefits and concerns med students report, considering the limited evidence on how they check AI-generated information.
3. Summarize the published AI curriculum content and evaluated educational outcomes.
4. Identify gaps in evidence to guide future research with pre-clerkship students, including our proposed USask survey.

Search Methods

- **Design:** Focused narrative review; PubMed searched on 20 September 2026.
- **Screening:** English-language publications from 2021 onward were screened by title and abstract.
- **Selection:** Canadian and pre-clerkship evidence was prioritized. Relevant broader health-professions and AI education studies were also considered.
- **Synthesis:** Papers on clinical AI without an educational focus and protocols were excluded; 11 publications were synthesized by theme.

PubMed Search:

("artificial intelligence"[Title] OR [AI[Title] AND (adoption[Title] OR curriculum*[Title])] AND (student*[Title] OR "medical education"[Title] OR "health professions education"[Title] OR curriculum*[Title]) AND (Canada*[Title/Abstract] OR survey*[Title] OR review*[Title] OR readiness[Title] OR experience*[Title])

Findings from Canadian Learner Studies

FUTURE RELEVANCE AND CURRENT USE



FORMAL TEACHING AND DEMAND



CONCERNS AND CHECKING



Additional Canadian Learner findings

Intended Future Use – Ringeval et al. [4]

In a survey of 177 Canadian med students, those with strong intentions to use clinical AI saw it as relevant to their future work and important teach in medical school. The study did not track whether they later used it.

Checking AI answers – Guirguis et al. [5]

In a qualitative study of 51 U of Ottawa health professions who had used AI, 29 respondents described checking its answers against course materials and other trusted sources. Only 8 participants were in Notes

Limitations

Search scope

- Review based on PubMed search, other relevant medical education papers may have been missed
- Priority given to Canadian evidence - focused narrative review rather than exhaustive search
- Review did not formally assess each study's risk of bias

Who was studied?

- Participation was voluntary, potential overrepresentation of students interested in AI
- Some samples included other health professions or students beyond pre-clerkship
- Participation was low: Pucchio's respondents represented 4.5% of Canadian med students, Tran and Ringeval reported 4.3% and 12%, respectively

What students reported

- Students reported using AI in different ways, limited detail about how it is used specifically for school
- Little evidence on how students check info and which sources they trust
- Students interested in AI teaching, but views on acceptable use and specific guidance still needed

Difficulty Comparing

- Differences in AI definitions across studies, from gen AI tools to clinical AI tech
- Differences in outcomes measured: current use, expected future use, interest in formal AI education
- Questions asking about the same concepts worded differently between studies, difficult to compare student preferences

Overall Interpretation: While the literature provides helpful insights toward AI in medical education, it cannot be assumed to reflect the perspectives of Usask pre-clerkship students. Therefore, a local study is needed to examine these questions further.

Directions for USask Survey

The review suggests a pre-clerkship needs assessment built around six domains:

1. **Actual use**
How often they use AI and what they use it for
2. **Perceived preparedness**
Whether they feel able to use AI responsibly and recognize errors
3. **Verification**
Which sources do students consult before trusting an answer
4. **Benefits and concerns**
Where AI creates and/or creates difficulty, including accuracy, bias, privacy, overreliance, academic dishonesty
5. **Acceptability**
Which uses seem appropriate or inappropriate, and how that depends on the task/setting
6. **Educational needs**
What students would like to be taught and which teaching formats they prefer

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Acknowledgements

This work was supported by the University of Saskatchewan College of Medicine Dean's Project funding. I thank Dr. Ibraheem Othman for his supervision and guidance.

Contact:

Hamza Moustapha
University of Saskatchewan
College of Medicine
him138@usask.ca

Medical Imaging



Aniket Bither (Dr. Nzekwu Chukwuemeka)

Quality Improvement in Thyroid Fine Needle Aspiration: A Retrospective Review of Ultrasound, and Surgical Outcomes in Regina, Saskatchewan

Background: Thyroid nodules are common imaging findings, and ACR TI-RADS was developed to standardize ultrasound risk stratification and limit unnecessary biopsy. However, interobserver variability in feature interpretation can inflate scores and drive over-biopsy. Regina faces a growing thyroid biopsy backlog (750+ pending, ~6 new referrals weekly).

Methods: We examined ultrasound-guided thyroid FNAs performed in Regina since 2018, comprising a surgery-selected cohort of 570 patients, 730 nodules, and 858 biopsies. TI-RADS score, Bethesda cytology, and surgical pathology were compared to assess concordance.

Results: Non-diagnostic Bethesda I (7.8%) and indeterminate Bethesda III (19.9%) results accounted for over a quarter of biopsies. Suspicious cytology rose from 5.1% (TR3) to 12.0% (TR4) to 26.9% (TR5), and surgical malignancy rose from 35.3% to 50.8% to 68.8% across the same categories. Non-malignant outcomes remained common among TR4/TR5 surgeries (49.2% and 31.2%), indicating over-classification. Notably, within Bethesda IV cytology, malignancy rose from 35.3% (TR3) to 60.9% (TR5), while Bethesda III malignancy stayed flat (~40–44%) regardless of TI-RADS category.

Conclusion: TI-RADS reliably stratifies malignancy risk overall and adds meaningful discrimination within Bethesda IV cytology specifically, but not within Bethesda III. Indeterminate cytology and TR4 over-classification both contribute to procedural burden.



Introduction

- Thyroid nodules are extremely common on ultrasound (reported prevalence 66% in adults)
- Standard workup: ultrasound-guided fine-needle aspiration (FNA), **cytology reported using the Bethesda System**
- ACR TI-RADS was introduced to standardize ultrasound risk stratification and reduce unnecessary biopsies, **scoring nodules by composition, echogenicity, shape, margins, and echogenic foci**
- TI-RADS relies on subjective feature interpretation prior literature reports only fair-to-moderate interobserver agreement (about 40–60%) for key features (echogenicity, margins, echogenic foci)
- Subjective "up-classification" (example: TR3 to TR4) can drive unnecessary biopsy and surgery without true biologic change
- Local Challenge: Growing biopsy backlog (>750 pending requisitions) driven by potential over-biopsy**

Objectives

- Objective 1:** Quantify diagnostic yield (Bethesda I & III rates).
- Objective 2:** Correlate preoperative TI-RADS scores with final surgical histopathology.
- Objective 3:** Identify histopathologic outcomes among surgically treated TR4/TR5 nodules.
- Objective 4:** Use these findings to inform quality improvement initiatives (structured triage) aimed at reducing the biopsy backlog

Acknowledgments

I would like to thank SHA and Kirat Shukla for their contributions and help related to this project. I would also like to thank Dr. Emeka Nzekwu for his guidance on this project. I would also like to thank Zain Khan and Kunal Amjad for their contributions on this project.

Methods

- 1) Data extracted from REDCap database (Dept. of Radiology, Regina General & Pasqua Hospital); cleaned in R
- 2) Cohort: Surgical subset of thyroid FNA biopsies from Jan 1, 2018 onward; excluding the cancelled procedures and missing-ID cases
- 3) Two linked datasets: biopsy-level (linked to preceding ultrasound/TI-RADS score) and nodule-level (surgical outcome and the final pathology)
- 4) Quality indicators: Bethesda I/III rates; TI-RADS cytology and pathology correlation; non-malignant rate among TR4/TR5 surgical cases

Results

Characteristic	Overall Database	2018+ Analysis Cohort
Patients, n	763	570
Nodules, n	1,013	730
Biopsies, n	1,113	858
Ultrasounds, n	2,758	2,006
Single-nodule patients, n	569	-
Multi-nodule patients, n	193	-

Table 1: Cohort Characteristics

Bethesda Category	n	%
I	69	8.0
II	344	40.2
III	171	19.8
IV	119	13.8
V	86	10.0
VI	89	10.4
Missing	6	0.7
Total	858	100.0

Table 2: Bethesda Cytology Distribution (n=858 (total biopsy))

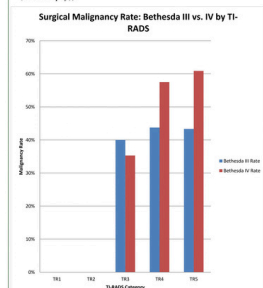


Figure 3: Surgical Malignancy Rate by TI-RADS Category, Stratified by Bethesda III vs. IV

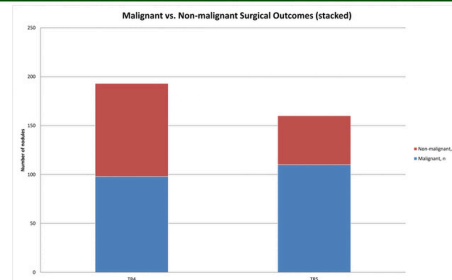


Figure 1: Surgical Outcomes of High-Risk (TR4/TR5) Nodules (n=353 resected / 528 total)

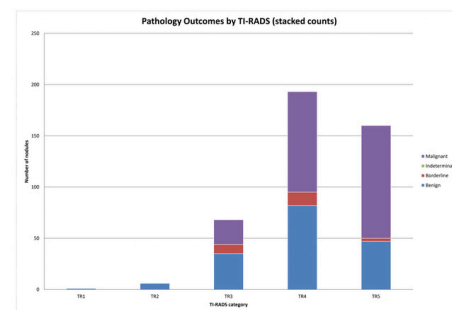


Figure 2: TI-RADS vs. Final Surgical Pathology (n=428 surgical nodules)

Conclusions

- 1) ACR TI-RADS scoring correctly ranks relative malignancy risk in this subset: both cytology and surgical pathology outcomes increased in step with TI-RADS category
- 2) Nearly half (49.2%) of TR4 nodules taken to surgery were ultimately benign, indicating over-classification at the TR4 threshold
- 3) TIRADS stratifies malignancy risk within Bethesda IV cytology (35.3%→60.9% from TR3 to TR5) but not within Bethesda III
- 4) Findings support the hypothesis that subjective interpretation of TI-RADS features may inflate scores and drive unnecessary biopsy/surgery, contributing to the local biopsy backlog
- 5) Findings support the need for refined TI-RADS feature characterization and/or structured triage to reduce unnecessary procedures

Future Direction

- 1) Extend analysis to the full non-surgical biopsy population performed in Regina since 2018, to get true population-level over-classification rates (surgical subset likely overestimates malignancy yield)
- 2) Launch a prospective QI triage arm on the > 750 pending referrals, tracking monthly biopsy volume, ND/AUS rates, malignancy yield, and backlog size
- 3) Run an interobserver variability study (200 nodules, blinded re-read by two radiologists) to quantify TI-RADS feature agreement locally
- 4) Use findings to refine TI-RADS feature characterization and inform structured referral triage protocols aimed at reducing the biopsy backlog

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Kathan Choksi (Dr. Jordan Buchko)

Nearly One in Three Hip and Knee MRIs May Be Inappropriate: A Retrospective Study of 3,139 MRIs in Regina

Background: High demand and prolonged MRI wait times in Saskatchewan make it important to identify potentially unnecessary scans. This study investigated and quantified potentially inappropriate hip and knee MRIs.

Methods: We retrospectively reviewed 3,139 MRIs performed in Regina from 2023–2025. MRIs were deemed potentially inappropriate when prior plain radiography was absent, completed more than 18 months prior to MRI, performed same-day or post-MRI, or when the prior radiograph demonstrated advanced osteoarthritis (Kellgren-Lawrence grade 3–4).

Results: Overall, 948 MRIs (30.2%) met criteria for being potentially inappropriate. Among these, 59.5% lacked an appropriate X-ray prior to MRI: 39.1% had no valid X-ray within the 18-month window, and 20.4% had same-day radiography. Advanced osteoarthritis on prior X-ray was present in 43.0% of cases. Inappropriate rates were higher for hip than knee MRI (44.0% vs 27.8%). Urban Family Medicine, Rural Family Medicine, and Orthopaedics accounted for 81.7% of MRI referrals and 81.4% of potentially inappropriate MRIs.

Conclusion: Nearly one in three MRIs met predefined criteria for being potentially inappropriate. Encouraging prior X-ray use to aid diagnosis and avoid unnecessary MRI scans, and targeting high-volume referral pathways could serve as avenues for prospective quality-improvement interventions.

Nearly One in Three Hip and Knee MRIs Met Study-Defined Criteria for Potential Inappropriateness

A Retrospective Study of 3,139 Hip and Knee MRIs in Regina, Saskatchewan

Kathan Choksi, MPH¹; Kirat Shukla, PhD²; Brian Le, MD, FRCPC^{1,2}; Patricia Jo, MD, FRCPC^{1,2}; Jordan Z. Buchko, MD, FRCSC^{1,2}

¹ College of Medicine, University of Saskatchewan; ² Research Department, Saskatchewan Health Authority



BACKGROUND

Hip and knee MRI is valuable for investigating musculoskeletal pathology; however, it may provide limited additional information when appropriate radiographs have not first been obtained or when radiographs already demonstrate advanced osteoarthritis (OA).

Current imaging guidance supports a radiograph-first approach for many patients with hip or knee pain and discourages routine MRI when radiographs already demonstrate significant osteoarthritis^{1,2} (unless additional imaging is expected to change management³).

Potentially low-value MRI may consume limited imaging capacity and contribute to longer wait times for patients more likely to benefit from an MRI.

Local data are needed to quantify potentially low-value MRI use and identify actionable targets for quality improvement.

OBJECTIVE

Primary Objective

To determine the proportion and patterns of hip and knee MRIs being potentially inappropriate in Regina.

Secondary Objectives

To identify actionable targets for improving imaging utilization; examine variation by joint and referring specialty; characterize the pathways leading to potentially inappropriate MRI; and determine how changing the prior-radiograph validity window from 12 to 18 months affects classification.

METHODS

Study Design & Setting

Retrospective observational study of 3,139 hip and knee MRI examinations performed in Regina between 2023 and 2025. Eligible examinations were identified through Saskatchewan Health Authority medical imaging systems. Imaging and radiology reports were reviewed through PACS, and study data were entered into REDCap. Research ethics approval was obtained from the University of Saskatchewan Biomedical Research Ethics Board.

Data Collected

For each MRI, the study captured: **Patient characteristics** (age and sex), **Imaging** (joint, MRI date and findings), **Radiographs** (presence, date, and osteoarthritis severity), **Referral information** (referring provider and specialty), **Timing** (interval between preceding radiograph and MRI)

- (same day radiographs were also recorded if there were no other prior radiographs within the last 3 years)

The final cohort consisted of 473 hip MRIs and 2,666 knee MRIs.

Radiographic OA Assessment

Osteoarthritis severity was recorded using the Kellgren-Lawrence (KL) grading system⁴, ranging from KL 0 (no radiographic OA) to KL 4 (severe OA).

Study-Defined Potential-Inappropriateness

An MRI was classified as potentially inappropriate if it met ≥ 1 of two predefined criteria. 1) Inadequate preceding radiographic assessment: defined as no valid prior X-ray within the specified validity window (including an X-ray performed after the MRI or an X-ray obtained on the same day as the MRI). No-valid-prior-X-ray and same-day imaging were treated as mutually exclusive pathways.

2) Advanced osteoarthritis: defined as a preceding radiograph demonstrating KL grade 3–4 or equivalent advanced OA within the specified validity window. These criteria identify potential-inappropriateness and do not establish that an individual MRI was clinically unjustified.

Primary & Sensitivity Definitions

Primary analysis: 18-month radiograph validity window (548 days)

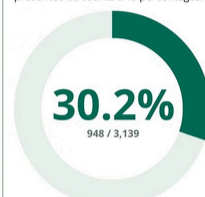
Sensitivity analysis: 12-month radiograph validity window (365 days)

The 18-month definition was selected to better account for the possibility that an appropriate radiograph obtained before MRI referral could become older than 12 months because of the delay between MRI ordering and completion.

RESULTS

Statistical Analysis

Descriptive statistics summarized the cohort and potential-inappropriateness rates by joint, referring specialty, age, and sex. Results are presented as counts and percentages.



Nearly 1 in 3

948 of 3,139 hip and knee MRIs met ≥ 1 predefined criterion for potential-inappropriateness under the primary 18-month definition.

Hip: 44.0% | Knee: 27.8%

COHORT

N = 3,139

Knee: 2,666 (84.9%) | Hip: 473 (15.1%)
Mean age: 48.5 $\pm$ 16.1 years | Age range: 17–93 years
Female: 1,567 (49.9%) Male: 1,572 (50.1%)

The sample was nearly equally distributed by sex, with knee imaging comprising the majority of examinations.

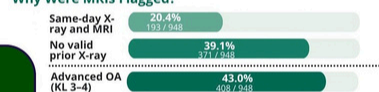
Potential-inappropriateness by joint



Potentially inappropriate MRI rates were higher for hips (44.0%) than knees (27.8%).

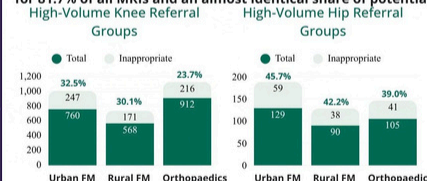
This suggests that the drivers of potentially low-value imaging—and future interventions—may differ between hip and knee pathways.

Why Were MRIs Flagged?



Among the 948 potentially inappropriate MRIs, 408 (43.0%) had advanced OA, 371 (39.1%) had no valid prior X-ray, and 193 (20.4%) had a same-day X-ray and MRI. Advanced OA could overlap with either radiographic-assessment pathway.

Urban Family Medicine (FM), Rural Family Medicine, and Orthopaedics together accounted for 81.7% of all MRIs and an almost identical share of potentially inappropriate MRIs: 81.4%.



Their contribution to potentially inappropriate MRI volume therefore closely reflected their overall referral volume, suggesting that high-volume clinical pathways may offer the greatest opportunity for system-level quality improvement.

Additional Findings: Age Patterns

Potential-inappropriateness rates showed different age patterns by joint. For knee MRI, rates increased from 19.8% in patients <40 to 50.0% in those ≥ 80 . In contrast, hip MRI did not show the same age-related trend, with the highest rate observed among patients <40 (51.5%).

DEFINITION MATTERS

12-month definition: 37.3% (1,172/3,139)

18-month definition: 30.2% (948/3,139)

Extending the radiograph-validity window to 18 months resulted in 224 MRIs no longer meeting the study-defined criteria. The change was greater for knee MRI (35.4% $\rightarrow$ 27.8%) than hip MRI (48.0% $\rightarrow$ 44.0%).

Classification was sensitive to the radiograph-validity window, highlighting the importance of imaging timing and local access context when evaluating appropriateness.

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WHAT DO THESE FINDINGS MEAN?

Potentially inappropriate MRI use was common

Nearly 1 in 3 MRIs (30.2%) met at least one study-defined criterion for being potentially inappropriate.

Hip and knee pathways may differ

Potential inappropriateness was higher for hip MRI (44.0%) than knee MRI (27.8%), suggesting that future interventions may need to be joint-specific.

Radiographic assessment is a practical target

Inadequate preceding radiographic assessment occurred in 59.5% of flagged MRIs, while advanced OA was identified in 43.0%. Radiograph-first pathways therefore represent a practical quality-improvement target.

High-volume pathways offer the greatest system-level opportunity

Urban Family Medicine, Rural Family Medicine, and Orthopaedics generated most overall and potentially inappropriate MRI volume. Targeting high-volume pathways could therefore produce the greatest absolute impact.

Appropriateness depends on context

Changing the radiograph-validity window from 12 to 18 months reduced the estimated rate from 37.3% to 30.2%, showing that imaging timing and local access context can affect classification.

LIMITATIONS

Retrospective design

Depended on available imaging records and radiology reports.

Study-defined criteria

A flagged MRI was potentially, not necessarily, clinically inappropriate.

Limited clinical context

Symptoms, examination findings, prior treatment, and surgical indications were not consistently available.

Report-based OA grading

Severity was based on radiology reports rather than independent re-grading.

Single-region study

Findings may not generalize to areas with different referral patterns or MRI wait times.

NEXT STEPS

Validate the criteria prospectively using more complete clinical information.

Target high-volume referral pathways with radiograph-first guidance and decision support.

Evaluate hip-specific ordering patterns given the higher potential-inappropriateness rate.

Reassess MRI utilization after intervention to measure improvement.

CONCLUSION

Nearly 1 in 3 hip and knee MRIs (30.2%) met study-defined criteria for being potentially inappropriate, with higher rates for hip (44.0%) than knee MRI (27.8%).

These findings identify prior radiographic assessment and high-volume referral pathways as practical targets for quality improvement.

The difference between the 12- and 18-month definitions also highlights the importance of considering imaging timing and local access context when evaluating appropriateness.

Targeted, context-specific imaging pathways may reduce low-value MRI use while preserving access for patients most likely to benefit.

Acknowledgements

Supported by the University of Saskatchewan College of Medicine Dean's Summer Research Project.

Thank you for your interest! :)

Shannon Dallaire (Dr. Andrea Lavoie)

Mechanisms and Imaging Correlates of Coronary Microvascular Dysfunction

Coronary microvascular dysfunction (CMD) is an underrecognized cause of myocardial ischemia. The microvasculature impairments frequently escape routine imaging and diagnostic protocols, leading to underdiagnosis and increased risk of major adverse cardiovascular outcomes. This study evaluated the clinical characteristics, cardiovascular risk factors, and 1-month and 1-year clinical outcomes of patients with CMD identified by coronary reactivity testing (CRT). A retrospective chart review was conducted for 53 patients presenting to Regina General Hospital from January 2020 to May 2026 with angina that were diagnosed with CMD. Out of 53 patients, the majority were females (77.4%), and presented with angina, hypertension, diabetes mellitus, dyslipidemia, and autoimmune disorders. About 81.1% were reported to be current or past smokers. Coronary microvascular dysfunction was clinically reported in 58.5% patients as a functional abnormality with CRT. CMD patients had frequent emergency visits due to the cardiac causes (9.4% patients within 1 month and 18.96% within 1 year), and high re-hospitalization rate due to cardiac causes (6.89%) at 1 year. Exercise intolerance during the stress test was significantly associated with cardiac-related ED visits at 1 year ($p = 0.043$). Further prospective studies are warranted to better define the relationship between coronary microvascular dysfunction, clinical characteristics, and long-term outcomes

Mechanisms and Demographic Correlates of Coronary Microvascular Dysfunction

Shannon Dallaire¹, Neha Mehta², Andrea Lavoie^{1,3}

¹College of Medicine, University of Saskatchewan, Regina, Canada; ²Research Department, Saskatchewan Health Authority, Regina, Canada; ³Department of Cardiology, Saskatchewan Health Authority, Regina, Canada

INTRODUCTION

- Coronary microvascular dysfunction (CMD) is an underrecognized cause of angina and myocardial ischemia (1).
- The functional or structural impairments causing this dysfunction frequently escape imaging and diagnostic protocols, leading to underdiagnosis and increased risk of major adverse cardiovascular outcomes (2).
- Past research has shown CMD to be more common in women and to be associated with increased emergency department (ED) visits (3,4).
- Characterizing CMD and its pathogenesis will improve understanding of this condition to address this diagnostic gap and improve long term prognosis.

OBJECTIVES

- To characterize the clinical profile and outcomes of patients with CMD by examining presentation, cardiovascular risk factors, comorbidities, medications, and functional assessments.
- To explore the clinical outcomes associated with these factors.

METHODS

- 53 patients presenting to Regina General Hospital with angina due to microvascular causes between January 2020 and May 2026 were selected for a retrospective chart review.
- Patients must have <50% stenosis in any major epicardial vessel and have a coronary reactivity test (CRT) performed.
- Data collected:
 - Demographics
 - Cardiovascular risk factors, past cardiac medical history, medications
 - EST and CRT results
 - Outcomes at 30 days and 1 year post CRT

RESULTS

	Clinical Features	N (%)
Sex	Female	41 (77.4%)
	Male	12 (22.6%)
Co-morbidities	Diabetes Mellitus	11 (20.8%)
	Hypertension	32 (60.4%)
	Dyslipidemia	35 (66.0%)
	Angina	53 (100%)
	Chronic kidney disease	2 (3.8%)
	Autoimmune disorders	5 (9.4%)
Smoking	Current or past	81.1%
Medications	ACEi/ARB	31 (58.5%)
	Statin	38 (71.7%)
	Beta-blocker	25 (47.2%)
	Anti-platelet	30 (56.6%)
	Anti-coagulant	5 (9.4%)
	Calcium Channel Blocker	40 (75.5%)
	Transdermal Nitrates	22 (41.5%)
	Spray Nitrates	32 (60.4%)

Table 1. Demographic and clinical profile of CMD patients.

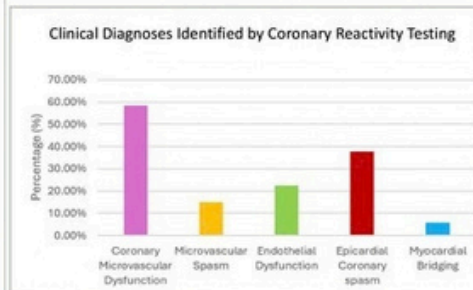


Figure 1. Clinical diagnoses identified by coronary reactivity testing. Physician-determined diagnoses among patients undergoing CRT (N=53). Values are presented as %. Diagnoses were not mutually exclusive, and patients could have more than one diagnosis.

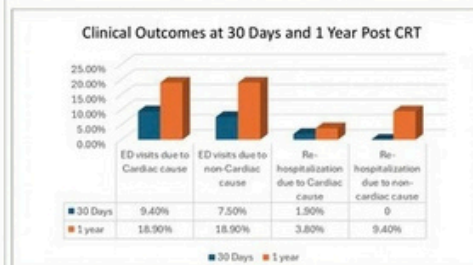


Figure 2. Clinical outcomes following coronary reactivity testing in 53 patients. Cardiac and non-cardiac emergency department visits and re-hospitalizations were observed during follow-up at 30 days and 1 year.

RESULTS

- During EST, most CMD patients with non-obstructive coronary artery disease demonstrated the appearance of either chest discomfort (47.2%), ischemic ECG changes (30.2%) and exercise intolerance (17 %).
- Consistent with the literature, high rates of cardiac and non-cardiac ED visits and re-hospitalizations were observed in CMD patients.
- In the logistic regression analysis, exercise intolerance during EST was significantly associated with cardiac-related ED visits at 1 year (OR 5.07, 95% CI 1.05–24.39; p = 0.043).

CONCLUSION

- Demographics of our patient population corresponds with existing literature.
- The association of exercise intolerance and ED visits highlights the need for improved diagnostic methods for identifying patients at greater risk of adverse clinical outcomes.
- Further prospective studies with a larger population are warranted to better define the relationship between CMD, clinical characteristics, and long-term outcomes.

ACKNOWLEDGMENTS

I would like to thank the University of Saskatchewan, College of Medicine, for funding this project. I would also like to thank my supervisor, Dr. Lavoie, for her guidance on this project.

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Abdu Etagiuri (Dr. Haron Obaid)*Diagnostic Reliability of the Radiographic Features of Acetabular Retroversion*

Objectives: Acetabular retroversion is associated with femoroacetabular impingement and hip osteoarthritis. This study assessed the diagnostic reliability of established radiographic signs of acetabular retroversion (crossover, ischial spine, posterior wall), externally validated a newly proposed elephant ear sign, and determined which individual or combined findings provide the highest diagnostic accuracy against CT

Methods: This retrospective research study will include 350 patients with pelvic radiographs and corresponding cross-sectional imaging. Each radiograph will be independently evaluated for the presence of the crossover, ischial spine, posterior wall, and elephant ear signs. CT imaging will serve as the gold standard for validation by measuring acetabular version, tonnis and lateral femoral centre edge angles. Statistical analysis will assess the sensitivity, specificity, and diagnostic accuracy of individual and combined radiographic findings.

Results: Crossover and ischial spine signs showed high specificity (86.5–89.9%) but low sensitivity (28.7–34.3%). Posterior wall sign was more balanced (sensitivity 52.5–55.3%, specificity 73.4–75.0%). Elephant ear sign performed worst (accuracy 50.6–55.1% and not significant on the right, $p=0.058$). Ischial spine or posterior wall combined gave the highest accuracy (62.9–64.9%).

Conclusion: Posterior wall sign is the strongest single classic sign, while crossover and ischial spine are highly specific but poorly sensitive. The elephant ear sign did not validate as diagnostically useful. Combining ischial spine and posterior wall signs improves accuracy over any individual sign.

INTRODUCTION

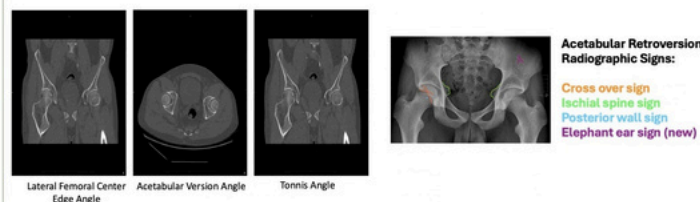
- Acetabular retroversion is defined as a malorientation of the acetabulum in which the acetabular opening is oriented more posteriorly than normal
- Reported in 5-20% of retrospective research, and markedly more common in dysplasia, Legg-Calvé-Perthes disease, and SCFE
- It has also been associated with higher rates of femoroacetabular impingement and hip osteoarthritis.
- Early diagnosis of acetabular retroversion can better long-term patient outcomes
- Diagnosis relies heavily on AP pelvic radiographs.
- Three classic signs are used: crossover sign, posterior wall sign, and ischial spine sign
- External validation is done through cross-sectional imaging such as CT or MRI
- Interobserver reliability of these signs is only moderate and depends on rater's experience
- A new "elephant's ear" sign (iliac wing flaring) was recently proposed as an additional marker for acetabular retroversion
- The elephant ear sign has not yet been validated across imaging modalities.

OBJECTIVES

- Assess the diagnostic reliability of established radiographic signs of acetabular retroversion, including the cross-over sign, ischial spine sign, and posterior wall sign
- Externally validate the elephant's ear sign
- Determine which individual or combined radiographic findings provide the highest diagnostic accuracy when compared against cross-sectional imaging (CT)

MATERIAL & METHODS

- Retrospective cohort: 350 patients (700 hips) with paired AP pelvic radiographs and CT
- Four radiographic signs scored as present/absent per hip: crossover sign, posterior wall sign, ischial spine sign, and elephant's ear sign
- For each hip, CT acetabular version, tonnis, and lateral femoral center edge angles were measured
- The complete dataset (n=350) was initially reviewed by a skilled MSK radiologist. Subsequently, a randomly selected subset of 50 cases is currently under review by another MSK radiologist
- Data was primarily analyzed by a statistician using SAS software. Each radiographic sign, individually and in combination, was compared against CT-defined retroversion using chi-square and Fisher's exact tests, with sensitivity, specificity, PPV, NPV, and accuracy calculated for each. Right and left hips were analyzed separately.



RESULTS

Individual signs:

- Crossover sign: specificity 89.86% (R) / 89.94% (L), sensitivity only 28.71% (R) / 29.83% (L), accuracy 54.57% (R) / 58.86% (L)
- Ischial spine sign: specificity 86.49% (R) / 89.94% (L), sensitivity 29.21% (R) / 34.25% (L), accuracy 53.43% (R) / 61.14% (L)
- Posterior wall sign: specificity 75.00% (R) / 73.37% (L), sensitivity 52.48% (R) / 55.25% (L), accuracy 62.00% (R) / 64.00% (L)

Elephant ear sign:

- Right: Sensitivity 29.21%, Specificity 79.73%, PPV 66.29%, NPV 45.21%, Accuracy 50.57%
- Left: Sensitivity 30.94%, Specificity 81.07%, PPV 63.64%, NPV 52.29%, Accuracy 55.14%

Combined signs:

- Ischial spine sign and the posterior wall sign gave the highest accuracy of all combinations
- Right: Sensitivity 54.95%, Specificity 73.65%, PPV 74.00%, NPV 54.50%, Accuracy 62.86%
- Left: Sensitivity 58.01%, Specificity 72.19%, PPV 69.08%, NPV 61.62%, Accuracy 64.86%

CONCLUSION

- Crossover and ischial spine are highly specific but poorly sensitive
- Posterior wall sign is more balanced and is the strongest single classic sign
- Elephant ear sign had the lowest accuracy of the signs, was not statistically significant on the right side, and reduced accuracy whenever added to a combination.
- Best diagnostic accuracy is the posterior wall sign and the ischial spine sign

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ACKNOWLEDGMENTS & CONTACTS

Radiographic review was conducted by Dr. Obaid and Dr. Vassos. Statistical analysis was performed by Dr. Prosanta. No external funding was received for this study.
Contact: Abdu Etagiuri, aac682@usask.ca

Aidan Hydomako (Dr. Amit Persad)

Quantifying Resection and Ablation Extent in Mesial Temporal Epilepsy Surgery: A Scoping Review of Methods, Anatomy, and Outcomes

Objective: To examine how surgical extent is measured in mesial temporal lobe epilepsy (mTLE) and its associations with seizure and neuropsychological outcomes.

Methods: MEDLINE and Embase were searched for adult studies reporting quantitative or semi-quantitative surgical extent values. Measurement methods, anatomical targets, seizure outcomes, and neuropsychological outcomes were extracted.

Results: 61 publications were eligible. We found extent assessment has evolved from linear and anatomical-landmark approaches toward quantitative MRI, automated segmentation, and recently, voxel-wise spatial methods. MRI-based volumetric studies of resective surgeries predominantly found no association between greater amygdalohippocampal extent and seizure freedom. Conversely, 8/11 publications evaluating piriform cortex extent reported favourable seizure associations. Laser interstitial thermal therapy (LiTT) studies similarly showed predominantly null findings for gross ablation volume and conventional hippocampal/amygdala extent. In contrast, smaller subregional, spatial, and biologically defined targets with LiTT showed more favourable associations. Neuropsychological evidence was heterogeneous and dependent on anatomical targets, laterality, and domain with evidence concentrated around hippocampal extent and memory.

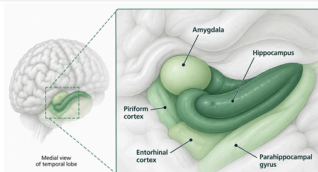
Significance: Current evidence has not identified a consensus surgical extent target that consistently predicts superior seizure outcomes. Rather, it supports a shift from maximal treatment extent toward identifying precise spatial and anatomical targets, with individual seizure-network characterization being an important area of investigation.

Quantifying Resection and Ablation Extent in Mesial Temporal Lobe Epilepsy Surgery: A Scoping Review of Methods, Anatomy, and Outcomes

Aidan Hydromako, Dr. Amit Persad

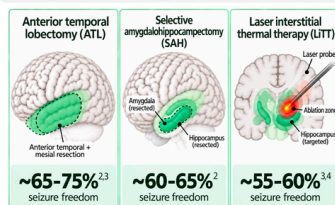
Background

- ❖ Mesial temporal lobe epilepsy (mTLE) is a focal epilepsy arising from interconnected mesial temporal structures and networks



- Mesial temporal sclerosis (MTS) is the most common underlying pathology¹
- ~75% of patients with mTLE-HS remain drug-resistant despite antiseizure medications¹

- ❖ Surgical treatment for mTLE can be curative



- ❖ Optimal extent and distribution of treatment remains uncertain

Surgical extent and anatomical distribution



Seizure control Neuropsychological outcomes

- "Extent" is defined and quantified inconsistently across the literature

How much tissue should be treated – and does where matter more than how much?

Objective

To characterize how surgical extent has been quantified in mTLE and synthesize associations between resection or ablation extent and seizure and neuropsychological outcomes.

Materials & Methods

- ❖ Study Eligibility

Population: Adults with refractory mTLE

Intervention: resection (ATL, SAH) or ablation (LITT)

Comparator: quantified extent of treatment

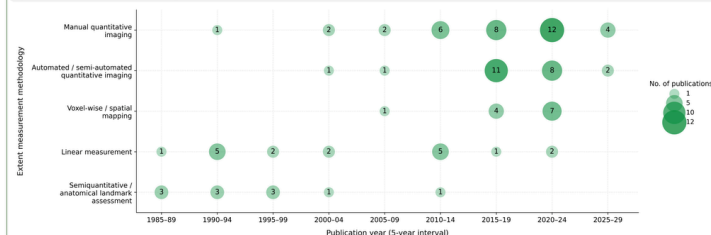
Outcome: seizure and/or neuropsychological outcome

- ❖ Search & Screening

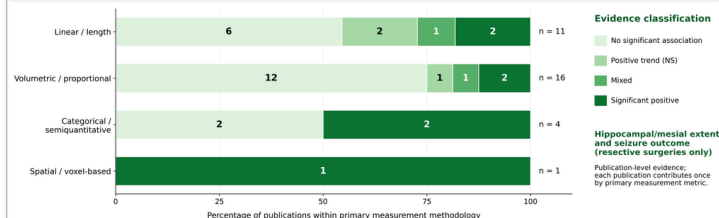


Results

- 1) Measurement of surgical extent in mTLE has evolved



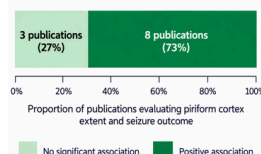
- 2) Greater mesial temporal resection extent is not consistently associated with better seizure control



- 3) Emerging evidence suggests treatment location may matter more than gross extent

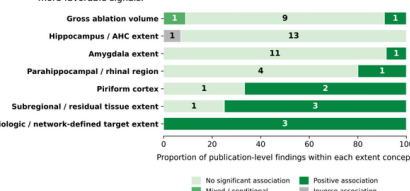
Piriform cortex

Greater piriform cortex extent is associated with better seizure outcome



LITT: Extent-seizure outcome evidence by concept

Conventional extent measures show predominantly null associations, whereas subregional and biologic/network-informed targeting show more favorable signals.



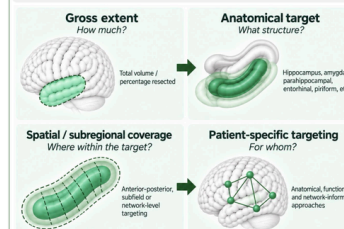
Conclusions & Next Steps

The current literature does not support a single surgical extent threshold that consistently predicts seizure outcome.

Evidence supports a shift from maximizing treatment extent toward identifying anatomically and spatially relevant targets.

Cognitive effects remain incompletely characterized and are anatomy and domain-dependent.

- ❖ Evolving concept of surgical extent



- ❖ Next steps – local translation

Scoping review

What does the literature show?

USask ATL retrospective cohort
Does residual hippocampus or treatment of extra-hippocampal structures relate to seizure outcome in our patients?

~90 patients who underwent ATL at RUH

Future directions

Can surgical targeting better balance seizure control with cognitive preservation?

Can patient-specific biologic/network-informed targeting outperform standardized operations?

Acknowledgments

This research project was supported by the Dean's Summer Research Project Initiative offered by the University of Saskatchewan College of Medicine, Office of the Vice-Dean Research (OVDR).

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Scan for full references



Benjamin Katz (Dr. Uzair Ahmed)

Super Large-Bore Aspiration in Acute Ischemic Stroke: Developing a Vessel–Device Geometry Database to Predict First-Pass Effect and Clinical Outcomes

Background: First-pass effect (FPE) during mechanical thrombectomy is associated with improved procedural and clinical outcomes, yet remains inconsistently achieved despite advances in large-bore aspiration technology. Patient-specific vascular anatomy and device–vessel geometry may contribute to this variability.

Methods: We developed a retrospective observational study of adults undergoing aspiration-first thrombectomy for anterior circulation large-vessel occlusion at the Saskatchewan Cerebrovascular Centre between January 2024 and December 2025. Literature reviews evaluating predictors of FPE and methods of quantifying vascular tortuosity informed development of a standardized vessel–device geometry framework. A REDCap registry was constructed integrating clinical characteristics, CTA-derived vascular anatomy, catheter dimensions, procedural geometry, and clinical outcomes. Key parameters include catheter-to-vessel ratio, lumen coverage ratio, guide catheter positioning, vessel diameter, and segmental tortuosity. Standardized imaging procedures and inter-rater reliability testing were incorporated to improve measurement reproducibility.

Results: Study infrastructure, literature reviews, imaging methodology, REDCap architecture, and regulatory approvals were completed. The framework preserves raw anatomical measurements, enabling evaluation of multiple geometric models during subsequent analysis.

Conclusion: This study establishes a standardized framework for investigating vessel–device interactions during aspiration thrombectomy. Identifying geometric predictors of FPE may ultimately enable pre-procedural CTA-based individualized device selection and improve first-pass reperfusion.

Tasin Obi (Dr. Lissa Ogieglo)

Temporal FTIR Imaging of Biochemical Changes Following Intracerebral Hemorrhage

Intracerebral hemorrhage (ICH) causes blood to accumulate within brain tissue. This can lead to inflammation, oxidative stress, and secondary tissue injury. The timing and spatial progression of oxidative injury after ICH remain unclear. This study examined biochemical changes following ICH using Fourier transform infrared (FTIR) microscopy imaging. A collagenase-based ICH model was used to induce hemorrhage in mice. Brain tissue was collected at different time points following hemorrhage. FTIR imaging was used to map lipids, proteins, lactate, and oxidized lipid products within the brain. Tissue regions were identified using unsupervised clustering. Lipid intensity and the $1718/1740\text{ cm}^{-1}$ ratio were examined as markers of lipid content and oxidation. FTIR imaging identified distinct biochemical patterns within hemorrhagic brain tissue. Lipid intensity changed across the measured time points. The $1718/1740\text{ cm}^{-1}$ ratio was also examined to assess lipid oxidation. However, this ratio showed limitations due to weak oxidation signals and background effects. Tissue masking was therefore used to reduce off-sample artifacts. These findings demonstrate the potential of FTIR imaging to characterize spatial and temporal biochemical changes following ICH.

Temporal FTIR Imaging of Biochemical Changes Following Intracerebral Hemorrhage

By Tasin Obi, Nicole Coote, Nicole Sylvain, and Huishu Hou.

Supervisors: Dr. Jake Pushie, Dr. Lisa Ogieglo

Abstract

Intracerebral hemorrhage (ICH) causes blood to accumulate within brain tissue and can lead to oxidative stress and secondary injury. The timing and spatial progression of these changes remain unclear. This study used Fourier transform infrared (FTIR) imaging to characterize biochemical changes following ICH in mice. Lipid, protein, and lactate signals were mapped across brain tissue at different time points after hemorrhage. Lipid intensity and the 1718/1740 cm^{-1} ratio were also examined as markers of lipid content and oxidation. FTIR imaging identified changes in biochemical signals within hemorrhagic tissue over time. These findings demonstrate the potential of FTIR imaging to track spatial and temporal biochemical changes following ICH.

Objectives

Characterize spatial and temporal biochemical changes in brain tissue following intracerebral hemorrhage (ICH) using FTIR imaging.

Evaluate changes in lipid content and lipid oxidation following hemorrhage.

Assess changes in lipid-associated metabolites and biochemical markers, including lactate and proteins.

Identify spatial patterns and differences in biochemical signals across brain regions and time points.

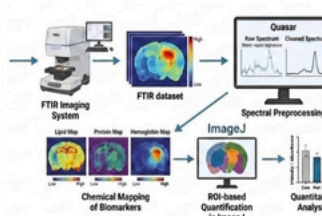
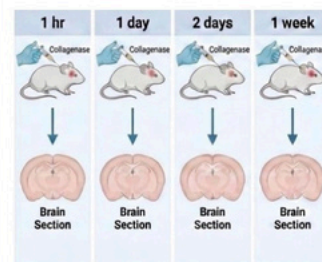
Methods

Animal Model & ICH Induction: Collagenase was used to induce intracerebral hemorrhage (ICH) in mice. Brain tissue was collected at defined time points following hemorrhage.

Tissue Preparation: Brain tissue was sectioned and prepared for FTIR imaging. Regions of interest were identified across hemorrhagic and surrounding brain tissue.

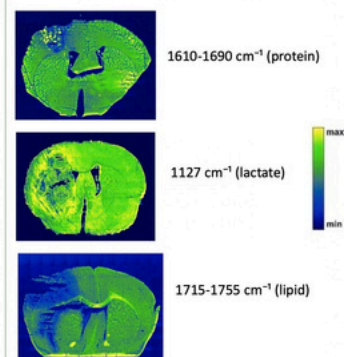
FTIR Imaging: Fourier transform infrared (FTIR) microscopy was used to measure biochemical signatures within brain tissue. Spectral regions associated with lipids, proteins, lactate, and other metabolites were analyzed. Lipid-associated peaks were examined to assess changes in lipid composition and abundance. The 1715–1755 cm^{-1} region was examined for signals associated with lipid oxidation.

Spectral & Spatial Analysis: Unsupervised clustering was used to identify regions with distinct biochemical profiles. Lipid intensity and the 1718/1740 cm^{-1} ratio were evaluated across time points. Tissue masking was applied to minimize background and off-tissue signals. Changes in biochemical signatures were compared across brain regions and time points.

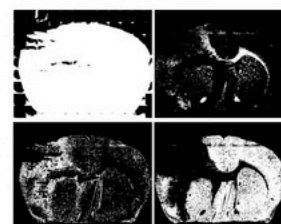


Results

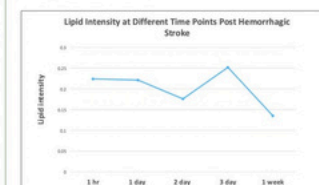
Spectral signature of hemorrhage:



Unsupervised clustering identifies distinct tissue regions in hemorrhage:



Total Lipid Intensity in Hemorrhage Region (n=1):



Discussion and Conclusion

FTIR imaging identified spatial and temporal changes in biochemical signatures following ICH. Changes in lipid signals suggest alterations in lipid metabolism following hemorrhage. Lactate and other metabolic signals also varied across brain regions and time points, reflecting changes in tissue metabolism after ICH. Clustering identified distinct biochemical regions within hemorrhagic brain tissue.

The 1718/1740 cm^{-1} ratio showed potential for assessing lipid oxidation, but interpretation was limited by weak oxidation signals and background effects. Tissue masking improved analysis by reducing signals from areas outside the brain tissue.

Changes in lipids, lactate, proteins, and lipid-associated signals demonstrate the complex metabolic response to hemorrhagic injury. FTIR may provide a useful approach for studying biochemical changes that occur during the progression of ICH. Further optimization of lipid oxidation measurements and validation with complementary methods is needed to better define the role of oxidative damage following ICH.

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Maxwell Pally (Dr. Michael Kelly)

Chemically specific X-ray fluorescence imaging of phosphorus

Phosphorus is an important component in multiple molecules involved in stroke. Conventional X-ray fluorescence imaging (XFI) can tell us where phosphorus is located, but not its chemical form. We investigated whether phosphorus K-edge X-ray absorption spectroscopy (XAS) and XFI at multiple energies could distinguish chemical forms of phosphorus in mouse brain tissue after stroke. A reference library of known phosphorus compounds was used in linear combination fitting of a prepared mixture, tissue spectra, and multi-energy maps. Fitting identified the compounds in the mixture but inaccurately estimated their proportions. Correcting for self-absorption, where a sample reabsorbs some of its own fluorescence, improved these estimates. Bone and some lesion hotspots showed spectral features resembling apatite, and fitting assigned substantial contributions to the apatite reference, supporting the presence of calcium phosphate. Three separate pixelwise fits, each pairing inorganic phosphate with ATP, polyphosphate, or pyrophosphate, consistently fit a lower relative contribution from the high-energy phosphate in the lesion than in surrounding tissue. These results suggest that XAS and multi-energy XFI can reveal differences in phosphorus chemistry after stroke, although similarities in reference spectra make fitting sensitive to self-absorption.

Chemically Specific X-Ray Fluorescence Imaging of Phosphorus

Max Pally, Dr. Jake Pushie, Dr. Michael Kelly

INTRODUCTION

Phosphorus is an important component in multiple molecules involved in stroke. Conventional X-ray fluorescence imaging (XFI) can tell us where phosphorus is located, but not its chemical form. We investigated whether phosphorus K-edge X-ray absorption spectroscopy (XAS) and XFI at multiple energies could distinguish chemical forms of phosphorus in mouse brain tissue after stroke.

METHODS

X-ray fluorescence imaging (XFI)

XFI records fluorescence as an X-ray beam scans across a sample, producing a map of elemental distribution.

X-ray absorption spectroscopy (XAS)

XAS records fluorescence at a single point while varying the energy of an incident X-ray beam. The resulting spectrum reflects chemical form.

Spectra of multiple chemical forms of phosphorus were collected to create a reference library.

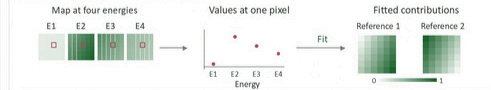
Linear combination fitting

The combination of reference spectra which best fit the spectrum produced by a mixture can identify the components of that mixture.

Multi-energy maps

Multi-energy maps combine XFI with XAS by recording fluorescence across a sample at more than one incident X-ray energy. The result is a map containing a partial spectrum at each pixel, theoretically allowing linear combination fitting to determine the chemical forms present at each pixel.

Pixelwise fitting of multi-energy maps



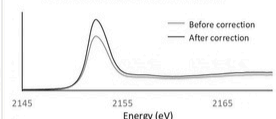
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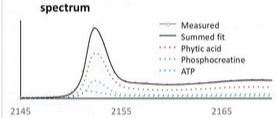
RESULTS

1. Linear combination fitting of a prepared mixture reveals sensitivity to self-absorption

1A Spectrum collected from mixture before and after correcting for self-absorption



1B Fitting self-absorption corrected spectrum



1C Fit proportions before and after correcting for self-absorption

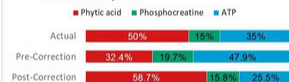
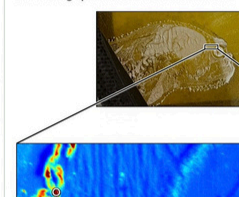


Figure 1. Linear combination fitting of a prepared phosphorus mixture. **A.** Measured spectrum before and after correcting for the reabsorption of fluorescence by the sample. **B.** Corrected spectrum, summed fit, and weighted contributions from phytic acid, phosphocreatine, and ATP. **C.** Known and fitted proportions of total phosphorus before and after correction.

2. Spectra from bone and lesion hotspots suggest presence of calcium phosphates

2A Fitting spectrum collected from bone



2B Fitting spectrum collected from stroke lesion hotspot

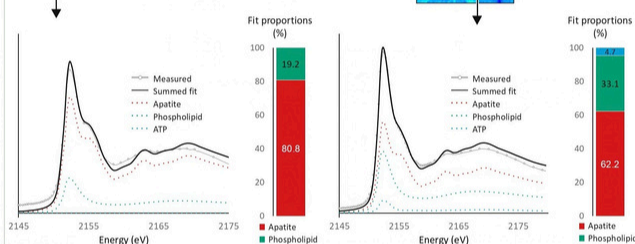
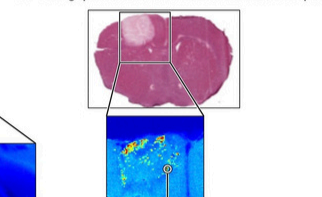
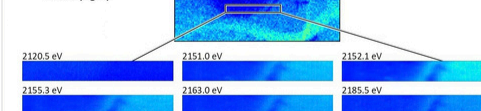


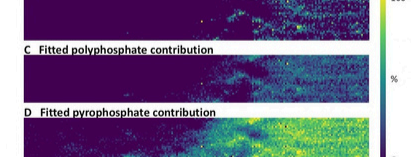
Figure 2. Linear combination fits for **A.** bone and **B.** a stroke lesion hotspot. Optical images locate XFI maps, and arrows link circled measurement sites to their phosphorus K-edge XAS spectra. Plots show the measured spectrum, summed fit, and weighted reference contributions from apatite, phospholipid, and ATP. Stacked bars show the relative fitted proportions of each phosphorus species.

3. Linear combination fitting of a multi-energy map suggests fewer high-energy phosphates in stroke lesion

3A A multi-energy map spanning stroke lesion (left) and surrounding tissue (right)



B Fitted ATP contribution



C Fitted polyphosphate contribution



D Fitted pyrophosphate contribution



Figure 3. Fitting of a multi-energy XFI map. **A.** Overview XFI map with scan region outlined and maps collected at six incident energies shown below. **B-D.** Results of three separate pixelwise linear combination fits. Each fit uses inorganic phosphate paired with one high-energy phosphate reference: **B.** ATP, **C.** polyphosphate, **D.** pyrophosphate. Colours indicate the relative contribution of the high-energy phosphate reference.

CONCLUSIONS

Spectral similarity of phosphorus species and resulting sensitivity to self-absorption limit confidence in linear combination fits. However, distinctive spectral features support the presence of calcium phosphate in bone and some stroke lesion hotspots. And linear combination fitting of multi-energy maps using inorganic phosphate paired with a high-energy phosphate suggests a lower relative contribution from high-energy phosphates in lesions than in surrounding tissue.

ACKNOWLEDGEMENTS

I'd like to thank Dr. Jake Pushie, Nicole Sylvain, Huishu Hou, Dr. Michael Kelly, and the rest of the Kelly lab for all of their support and guidance. This project was funded by the NSERC USRA and Biomedical Summer Research Award.

Obstetrics & Gynecology





Jordan Reekie (Dr. Garson Chan)

Predictive Value of Asymptomatic Bacteriuria in Pregnancy for Recurrent Urinary Tract Infection During Pregnancy and Postpartum

Objective: Asymptomatic bacteriuria (ASB) is a common condition in pregnancy, defined as the presence of $\geq 100\,000$ colony forming units of bacteria/mL of urine in the absence of symptoms. ASB is screened in pregnancy due to it potentially increasing the risk of pyelonephritis, a severe complication that risks both the mother and fetus. However, ASB's association with subsequent symptomatic urinary tract infections (UTI) remains largely under-investigated.

Methods: A retrospective chart review of 10 063 pregnant patients found 1082 mothers were screened for ASB in Jim Pattison Children's Hospital from June 2025 – June 2026, inclusive (Table 1 demographics). We investigated how ASB, along with associated factors such as age and parity, influenced the occurrence of symptomatic UTI later in pregnancy and in the post-partum period (< 6 months). Results were analyzed using a multivariable logistic regression model.

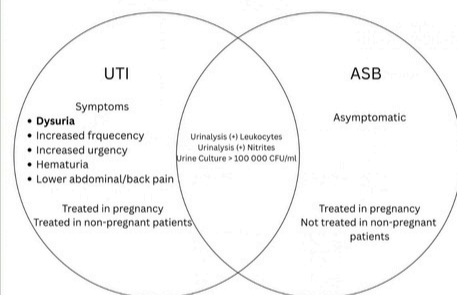
Results: Women with ASB were 192% more likely to have symptomatic UTI later in pregnancy or post-partum compared to women without ASB (OR 2.92, CI 1.66–5.13). Age and previous pregnancy also affect the odds of having UTI in pregnancy as independent variables. This information can provide guidance to determine appropriate screening, treatment, and follow-up guidelines regarding ASB in pregnancy.

Predictive Value of Asymptomatic Bacteriuria in Pregnancy for Recurrent Urinary Tract Infection During Pregnancy and Postpartum

Reekie J, Zhou A, Chan G

INTRODUCTION

- **Asymptomatic bacteriuria (ASB)** is a condition commonly screened for in pregnancy via urinalysis and urine culture (1)
- Current guidelines suggest treatment of a positive result via antibiotics to minimize the risk of developing pyelonephritis (2)
- Both ASB and symptomatic urinary tract infections (UTIs) are common in pregnancy, with recurrent UTIs affecting some women, but remain largely under researched (3)
- Independent risk factors for bacteriuria include slowed urine flow and reduced immune function, factors that are especially prevalent during pregnancy (4)



There is current no universally accepted screening, treatment, and follow-up regimen for ASB in pregnancy.

OBJECTIVES

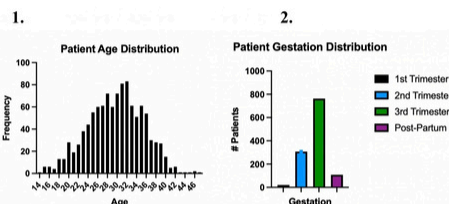
Hypothesis: pregnant patients with ASB are at a higher risk of developing recurrent symptomatic UTIs later in pregnancy or within 6 months postpartum compared to those without ASB. Clinical risk factors such as parity, age, and gestational diabetes will independently predict recurrence.

Primary objective – quantify risk of recurrent UTI in patients with ASB versus those without ASB.

Secondary objective – identify independent clinical risk factors for the development of ASB and/or recurrent UTI such as age, parity, gestation, and gestational diabetes.

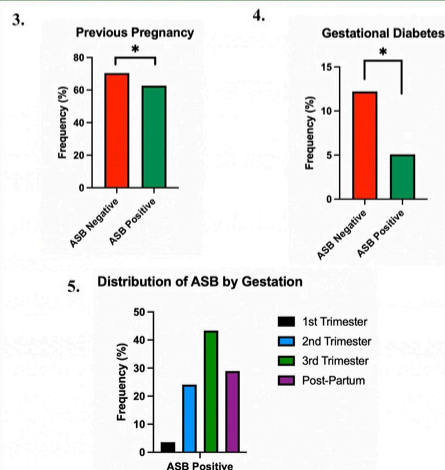
MATERIALS & METHODS

- **Population:** Pregnant patients screened for bacteriuria at JCPH over June 2025 until June 2026 inclusive
- **Data collection:** Retrospective chart review of urinalysis / urine culture results, symptoms, and treatment plans. Total charts included in analysis = 1082 (out of 10 063)
- **Analysis:** multivariable logistical regression using SAS 9.4



Demographic Data: (1) Mean age is 27.9 years old (St. Dev 5.65). (2) Gestation distribution at time of ASB screening – 1.67% 1st trimester, 25.62% 2nd trimester, 63.69% 3rd trimester, 9.02% postpartum

RESULTS



Analyzed by Chi-Square test. (3) ASB is found to be negatively associated with having had at least one previous pregnancy (p-value = 0.0425). (4) ASB is found to be negatively associated with gestational diabetes (p-value = 0.006). (5) Women were found to have ASB most often in the 3rd trimester (3.61% 1st trimester, 24.10% 2nd trimester, 43.47% 3rd trimester, and 28.92% postpartum)

DISCUSSION

- **Odds of having a UTI were significantly higher (92%) among women with ASB positive compared to ASB negative (OR=2.92, 95% CI: 1.66-5.13, p-value=0.0002)**
- Chance of UTI was significantly higher:
 - Women with previous pregnancy (OR=1.37, 95% CI 1.03-1.82, P = 0.02)
 - 3rd trimester (OR=5.24, 95% CI 1.17-23.43, P=0.03)
 - Postpartum (OR=17.84, 95% CI 3.78-84.21, P=0.0002)
- **Limitations:**
 - Only 47.46% of patients with ASB received antibiotics
 - Only 25.41% of patients had a repeat urinalysis and urine culture

CONCLUSIONS

- ASB in pregnancy increases the risk of developing UTIs throughout pregnancy and the postpartum period. Additionally, parity and gestation appear to be independent risk factors for developing a UTI.
- The inconsistency of treatment and follow-up surveillance provides insight into future changes to clinical practice.
- These findings provide more information about the potential causes of recurrent UTIs in pregnancy. Using this data, guidelines for screening and treatment of ASB in pregnancy can be targeted to mitigate the risk of the development of recurrent UTI.
- Further study of this topic will include the association of bacterial pathogens with recurrent UTIs, as well as the difference in outcomes between antibiotic therapies.
- This population excluded those seeking care and screening through primary care and did not allow access to follow up through these avenues, which could result in an unrepresentative population.
- Some women received urinalysis without urine culture, decreasing our sample size, yet proving the non-universal approach to ASB screening.

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ACKNOWLEDGEMENTS

Thank you to Dr. Garson Chan, and Dr. Amy Zhou for your guidance and support throughout the project! Thank you to the University of Saskatchewan Clinical Research Support Unit for the assistance with statistical analysis. Thank you to the Office of the Vice-Dean Research for the opportunity to participate in the Dean's Summer Research Program.

OA-UofS-5953



Aluk Geu (Dr. Sarah Smith)

Assessing Multidimensional Postpartum Recovery Among Women in Saskatchewan

Postpartum recovery has traditionally been defined by physical healing within six weeks of childbirth. Current professional guidelines for postpartum care from the American College of Obstetricians and Gynecologists (ACOG) and the World Health Organization (WHO) recommend a comprehensive assessment. The aim of this study is to determine the proportion of women in Saskatchewan who have fully recovered by 3–6 months postpartum and identify factors influencing recovery, providing evidence to tailor care, optimize support, and inform extended postpartum follow-up.

A cross-sectional survey assessed the full recovery of postpartum women 3–6 months after childbirth across four domains (physical, mental, sexual, functional). At the time of this interim analysis, data was available for 43 participants (N=43). The proportion of women achieving full recovery was estimated using descriptive statistics, Pearson's chi-square tests, Fisher's exact test, t-tests, and multivariable logistic regression.

Full recovery across all four domains was uncommon in this interim sample (13.95%). Functional recovery was the most achieved outcome (88.37%), whereas sexual (39.53%) and physical (53.49%) recovery were less frequently reported. Mental recovery was reported by 24 participants (55.81%). Higher anxiety and depressive symptom scores and lower perceived social support were associated with lower likelihood of being classified as fully recovered.

Assessing Multidimensional Postpartum Recovery

Among Women in Saskatchewan

Aluk Geu, Sarah Naden Smith, Shirmin Kader

INTRODUCTION

- Postpartum recovery has traditionally been defined by physical healing within six weeks of childbirth
- Current professional guidelines for postpartum care from the American College of Obstetricians and Gynecologists (ACOG) and the World Health Organization (WHO) recommend a comprehensive assessment



Figure 1. The four domains of recovery recommended by the literature.

- The aim of this study is to determine the proportion of women in Saskatchewan who have fully recovered by 3–6 months postpartum
- The aim of this study is to identify factors influencing recovery, providing evidence to tailor care, optimize support, and inform extended postpartum follow-up

MATERIALS & METHODS

Postpartum Recovery Survey

- Fatigue and Pain
- Resumption of sexual activity
- Presence and severity of pain during sexual intercourse
- Independently perform routine daily activities
- Independently care for newborn
- Confidence in Newborn Caregiving
- Return to usual emotional state
- Edinburgh Postnatal Depression Scale (EPDS)
- History of previous mental health conditions

- Which week the recovery was achieved

MATERIALS & METHODS

Statistical Analysis

- Analyses were conducted using R version 4.4.3.

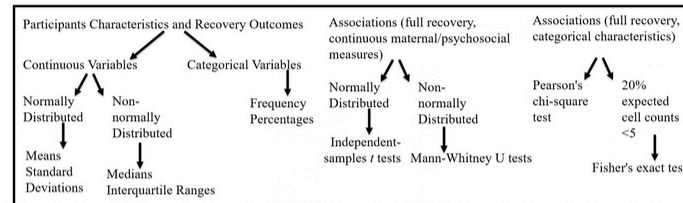


Figure 2. Summary of statistical analyses work flow. (a) Descriptive statistics of participants characteristics and recovery outcomes. (b) Inferential statistics of the association between full recovery and continuous maternal or psychosocial measures. (c) Inferential statistics of the associations between full recovery and categorical characteristics.

RESULTS

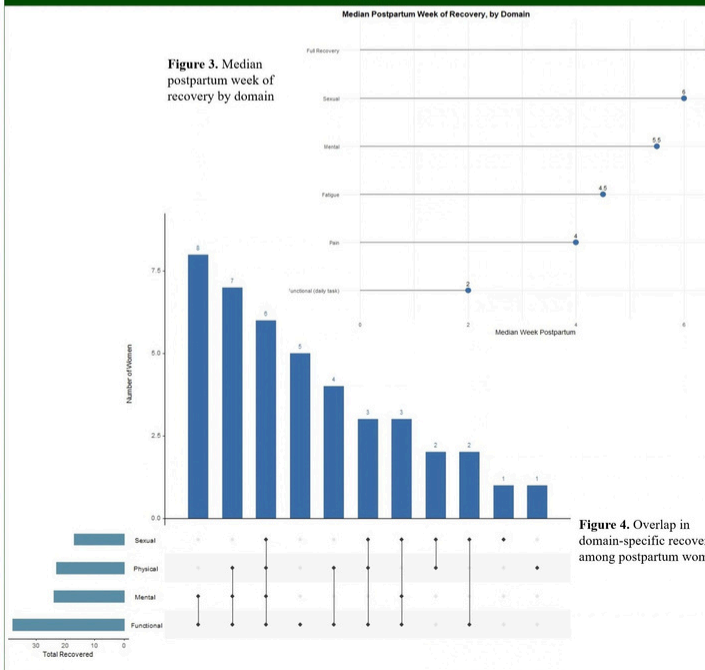


Figure 3. Median postpartum week of recovery by domain

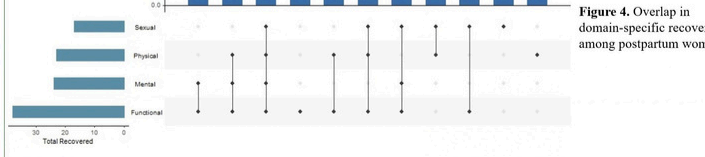


Figure 4. Overlap in domain-specific recovery among postpartum women

DISCUSSION & CONCLUSION

- Full recovery across all four domains was uncommon in this interim sample (13.95%)
- Functional recovery (88.37%)
- Sexual recovery (39.53%)
- Physical recovery (53.49%)
- Mental recovery (55.81%)
- Higher anxiety and depressive symptom scores and lower perceived social support were associated with lower likelihood of being classified as fully recovered
- Interim analysis suggests greater social support are associated with better full recovery
- Plan to explore these associations further with regression analysis

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ACKNOWLEDGEMENT

This project was supported by the 2026 College of Medicine Dean's Project Program



Sharon Jacob (Dr. Peter Thiel)

Accuracy and Quality of AI-Generated Documentation in Gynecology: A Prospective Paired Comparison Using Standardized Patient Encounter

Objective: To compare the quality and accuracy of physician- and AI-generated gynecologic consultation notes.

Methods: This paired-comparison study used standardized patient encounters. Four gynecologists and two senior residents each completed three encounters drawn from six scripted cases (18 encounters, 54 notes). Each encounter generated a physician note, a raw AI note, and a physician-edited AI note. Blinded raters scored quality with a modified Physician Documentation Quality Instrument-9 (mPDQI-9, range 8-40) and accuracy against a reference transcript using a 36-item checklist. Documentation time was recorded. Analysis was completed using repeated-measures ANOVA.

Results: PDQI-9 scores were similar across conditions (physician 31.5 ± 5.5 , raw AI 34.2 ± 3.8 , edited AI 33.7 ± 3.8 , $p = 0.12$). The physician versus raw AI difference was -2.7 points (95% CI -5.4 to 0.1), favoring the AI note. Errors per note were equivalent, and 62 of 69 errors were omissions, with no incorrect statements or clinically important errors in any note. Editing the AI note took 3.1 ± 2.8 minutes versus 9.7 ± 4.1 minutes to document independently, saving 6.6 minutes (95% CI 4.6–8.5, $p < 0.001$).

Conclusions: AI-generated notes matched physician notes in quality and accuracy, with no fabrication and reduced documentation time.



Accuracy and Quality of AI-Generated Documentation in Gynecology: A Prospective Paired Comparison Using Standardized Patient Encounter

Sharon Jacob, Asya Dinh, Darrien Rattray, Tanner Adams-White, Peter Thiel
College of Medicine, University of Saskatchewan

BACKGROUND

Clinical documentation is a growing driver of physician workload and burnout [1]. AI scribes, which use speech recognition and natural language processing to draft notes from patient-physician encounters, are being rapidly adopted [2]. Early work suggests AI scribes reduce documentation time and improve workflow efficiency [3]. However, concerns persist about what those notes contain [3]. Reported limitations include omitting clinically important detail and generating inaccurate or fabricated content [3]. Studies comparing AI-generated and clinician-written notes have found broad similarity, but findings remain inconsistent [4].

The objective of this study was to compare the quality and accuracy of AI-generated with physician-generated consult notes during standardized gynecologic patient encounters

METHODOLOGY

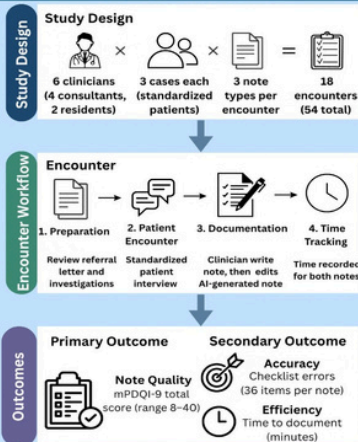


Figure 1: Study Design, Encounter Workflow, and Outcome Measures
Six clinicians each completed three standardized patient encounters, generating physician-written, raw AI-generated, and physician-edited AI notes. Note quality was assessed using mPDQI-9, while secondary outcomes included checklist-based accuracy and documentation time.

ANALYSIS

Note quality (mPDQI-9): repeated measures ANOVA with 3 prespecified pairwise comparisons (Bonferroni corrected, adjusted $\alpha = 0.017$)

1. Physician vs raw AI
2. Raw AI vs edited AI
3. Physician vs edited AI

Note accuracy: Friedman test with same three comparisons

Documentation time: paired t-test, write note vs editing the AI note

RESULTS

QUALITY

Eighteen encounters were completed by six physicians, yielding 54 notes.

Table 1. Note quality, mPDQI-9 TOTAL (out of 40)

Note type	Mean (SD)	Median	Range
Physician	31.5 (5.5)	31.5	20-40
Raw AI	34.2 (3.8)	34.0	28-40
Edited AI	33.7 (3.8)	34.0	35-40

Table 1: Mean mPDQI-9 scores were comparable across physician-written, raw AI-generated, and physician-edited AI notes, with no significant overall difference between conditions.

Table 2. Pairwise Comparison of mPDQI-9 Scores by Note Type

Comparison	Mean Diff.	95% CI	p
Physician / raw AI	-2.7	-5.4 to 0.1	0.06
Raw AI / unedited AI	0.5	-1.9 to 2.9	0.67
Physician / edited	-2.2	-5.4 to 1.1	0.17

Table 2: Pairwise comparisons of mPDQI-9 scores between documentation conditions. Mean paired differences, 95% confidence intervals, and unadjusted p-values are shown. No pairwise comparison reached statistical significance.

No significant difference
Physician 31.5 → Raw AI 34.2
 $p = 0.17$

NOTE ACCURACY

Table 3. Accuracy and errors across note types

Note type	Errors/note (SD)	Mean accuracy	Error free notes (/18)
Physician	1.33 (1.41)	96.3%	7
Raw AI	1.33 (1.08)	96.3%	4
Edited AI	1.17 (0.92)	96.8%	5

Table 3: Error rates were similar across note types ($p = 0.47$). Of 69 errors, 62 were omissions and 7 unsupported additions; none contradicted the transcript.

~96% accuracy across documentation methods



Figure 2: Checklist errors by documentation condition. Distribution of errors per note across 18 notes per condition. No significant difference in error counts was observed.

DOCUMENTATION TIME

Figure 3. Documentation time by method. Paired documentation times for writing a physician note versus reviewing and editing an AI-generated note across 18 encounters.

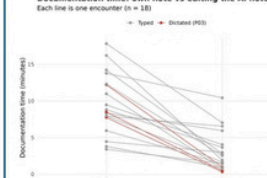


Figure 3: Documentation time by method. Paired documentation times for writing a physician note versus reviewing and editing an AI-generated note across 18 encounters.

Table 4: Documentation time and time saving

	Mean min. (SD)	Range
Writing physician note	9.7 (4.1)	3.4 to 17.9
Reviewing/editing AI note	3.1 (2.8)	0.3 to 10.4

Table 4: Reviewing and editing AI-generated notes reduced documentation time by a mean of 6.6 minutes per encounter (95% CI 4.6-8.5; $p < 0.001$).

Average time savings per note

6.6 min
95% CI, 4.6 – 8.5, $p < 0.001$

DISCUSSION

Quality

AI-generated notes demonstrated comparable quality to physician-generated notes. mPDQI-9 scores were similar across all note types, with no significant differences between any paired comparison.

Accuracy

Accuracy was excellent in physician and AI notes with overall accuracy above 96%. More importantly, there were no clinically important errors identified across 54 notes.

Substantial Time Savings

AI-assisted documentation significantly reduced documentation time. On average, physicians saved 6.6 min reviewing and editing AI-notes when compared to typing their own for a given encounter.

CONCLUSION

In simulated gynecologic consultations, AI-generated notes matched physician notes on quality and accuracy, contained no fabricated content, and took roughly a quarter of the time to produce.

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Please direct any questions to Sharon Jacob @ shj144@usask.ca.

ACKNOWLEDGEMENTS

We thank the College of Medicine for a Dean's Summer Studentship. Thank you, Dr. Peter Thiel. We acknowledge that this research was conducted on Treaty 6 territory and the Homeland of the Métis. We pay our respect to the First Nations and Métis ancestors here and reaffirm our relationship with one another.





Carlie Klatt (Dr. Sarah Smith)

Postpartum Depression and Sleep Quality in Saskatchewan

Background: Physiological and lifestyle changes in the postpartum period can contribute to the development of postpartum depression. In Canada, rates of postpartum depression have been reported to be as high as 23%. Research about specific factors which predispose people to postpartum depression are largely conflicting. Despite evidence that poor sleep quality contributes to depressive symptoms in the general population, this link has not been solidified in the postpartum period.

Methods: Validated self-reported questionnaires were used to quantify sleep quality, depressive symptoms, anxiety symptoms, and perceived social support in Saskatchewan residents 3-6 months postpartum. Statistical analysis identified correlations and associations between variables. Measures of sociodemographic and obstetric variables were also analyzed.

Results: The results of this preliminary analysis show that majority (81.25%) of those postpartum reported having poor sleep quality. Those with poor sleep quality had higher median scores of depressive and anxiety symptoms, although this was not statistically significant. Those with poor sleep quality reported lower levels of social support ($p=0.057$).

Conclusions: While the results of this study did not reach statistical significance, this is likely due to the small sample size. As enrollment in the study increases, it will provide an important dataset for Saskatchewan physicians treating postpartum people.

INTRODUCTION

The physiological and lifestyle changes that occur following giving birth can predispose people to poor mental health and poor sleep quality. The worldwide prevalence of postpartum depression (PPD) is estimated to be 14%, with significantly higher rates in developing countries¹. In Canada, rates may be as high as 23% as reported by Statistics Canada and the Public Health Agency of Canada in 2019². Poor sleep quality is the number one concern reported by those postpartum^{3,4}. Despite the known link between poor sleep quality and depression in the general population, the link between these factors in the postpartum period is elusive.



OBJECTIVES

This study aims increase the understanding of the intersection of postpartum mental health, sleep quality, and social support in Saskatchewan through the following objectives:

1. Quantify sleep quality, symptoms of depression and anxiety, and perceived social support among those postpartum.
2. Analyze associations between sleep quality and symptoms of depression and anxiety and perceived social support.
3. Evaluate how sociodemographic and obstetric covariates influence sleep quality and mental health outcomes.

METHODS

Study Design: This is a cross-sectional analysis utilizing data from an ongoing PPD study.

Participants: Postpartum people within 6 months following childbirth who voluntarily completed validated self-reported questionnaires to assess sleep quality, symptoms of anxiety and depression, and perceived social support.

Sample Size: This study is a preliminary analysis which represents current study enrollment (N=43). Re-analysis of the data will be done when the full enrollment target is reached.

Measurements: Validated self-reported questionnaires were utilized to collect data. These included the Pittsburgh Sleep Quality Index (PSQI), Edinburgh Postnatal Depression Scale (EPDS), Generalized Anxiety Disorder Scale (GAD-7), and the Functional Social Support Questionnaire (FSSQ). Sociodemographic and obstetric covariates were also statistically analyzed, including maternal age, parity, number of living children, ethnicity, immigration status, highest education level, marital status, and number of antenatal checkups.

Statistical Analysis: Bivariate associations between poor sleep quality (dichotomized PSQI) and continuous variables were assessed using independent-samples t-tests for normally distributed variables (age, parity, number of children) and Mann-Whitney U tests for non-normally distributed variables (EPDS, GAD, and FSSQ scores), with results presented as mean (SD) or median (IQR) by group as appropriate. Associations between poor sleep quality and categorical variables (PPD screen status, ethnicity, immigration status, education, marital status, antenatal checkup frequency) were assessed using chi-square tests, with Fisher's exact test substituted automatically when more than 20% of expected cell counts were below 5. A two-sided p-value <0.05 was considered statistically significant. All analyses were conducted in R (version 4.4.3).

RESULTS

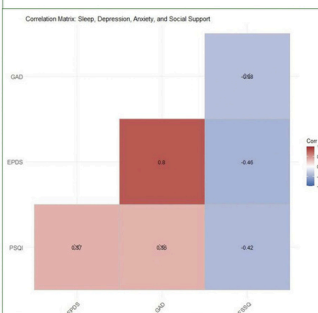


Figure 1: Correlation matrix showing positive correlation of higher GAD and EPDS scores and negative correlation of high FSSQ scores with low PSQI and high EPDS scores.



Figure 2: Bar graphs showing percentage of participants with depressive symptoms (≥ 13 on the EPDS), sorted by sleep quality according to PSQI (poor sleep quality being a score > 5). 19% of participants with poor sleep report depressive symptoms.

CONCLUSIONS

This preliminary data suggests that majority of those in the postpartum period experience poor sleep quality. Furthermore, those with poor sleep may be more likely to have elevated depressive symptoms.

Correlation studies reveal that symptoms of anxiety and depression are positively correlated, while increased perceived social support is negatively correlated with depressive symptoms and poor sleep quality.

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ACKNOWLEDGEMENTS

We thank the Dean's Summer Research Project, the College of Medicine Research Award, and the Saskatchewan Health Authority Research Department for funding this project. I would like to thank Dr. Sarah Smith for supervising this project.



Sarah Power (Dr. Maria Giroux)

Reoperation Rates After Primary Repair of Obstetric Anal Sphincter Injuries (OASIs): Insights from a Canadian Tertiary Centre

Introduction: Obstetric anal sphincter injuries (OASIs) may require surgery, but Canadian reoperation data are limited. This study aimed to determine the 2-year reoperation rate after primary OASI repair and characterize indications, procedures, and exploratory associations.

Methods: A single-centre retrospective cohort included patients undergoing primary OASI repair at Regina General Hospital between January 1, 2019, and December 31, 2023. Provincial records identified reoperations within 2 years postpartum. Associations among reoperated patients were assessed using Fisher's exact tests.

Results: Of 848 patients, 19 underwent reoperation (2.24%, 95% CI, 1.35-3.48) with a mean of 51.5 days postpartum (range 6-290). Non-mutually exclusive indications were wound dehiscence, and retained products of conception (each 7/19, 36.8%); surgical-site infection (5/19, 26.3%); persistent pain, and granulation tissue (each 4/19, 21.1%). Procedures included perineal wound revision (11/19, 57.9%); secondary anal sphincter repair, dilation and curettage, and hysteroscopy (each 5/19, 26.3%). Within the reoperation subgroup, absence of antibiotic prophylaxis was associated with wound infection (4/6 vs 1/13, $p=.017$) and perineal wound revision (6/6 vs 5/13, $p=.018$).

Conclusion: Reoperation after primary OASI repair was uncommon, although wound complications imposed a substantial surgical burden. The observed association between absence of antibiotic prophylaxis and wound morbidity warrants evaluation in the full OASI cohort.

Two-Year Reoperation Rate Among Patients With Obstetric Anal Sphincter Injuries (OASIs): A Canadian Tertiary-Centre Cohort

Power S.,¹ Sultana S.,² Giroux M.^{1,2,3}

¹College of Medicine, University of Saskatchewan, Regina, Canada; ²Research Department, Saskatchewan Health Authority, Regina, Canada; ³Department of Obstetrics and Gynecology, Saskatchewan Health Authority, Regina, Canada

Introduction

- Obstetric anal sphincter injuries (OASIs) are third- and fourth- degree perineal lacerations affecting 5.37% of vaginal deliveries at Regina General Hospital (RGH) (1).
- OASIs can cause short- and long-term morbidity, including anal incontinence, pain, dyspareunia, and psychological distress (2-7).
- Patients with OASIs may require postpartum reoperation for wound complications and other indications (8).
- Reported international reoperation rates range from 1.16% to 2.1%, but Canadian data are lacking (9-10).
- Hypothesis:** The 2-year reoperation rate at RGH would be similar in magnitude to the rates reported by international tertiary centres.

Objectives

Primary objective: Determine the rate of any reoperation within 2 years postpartum among patients who underwent primary OASI repair at RGH. **Secondary objectives:** Characterize the indications, procedures, and timing of reoperation and explore associations within the reoperation subgroup.

Materials and Methods

- This single-centre retrospective cohort included Saskatchewan residents aged ≥ 18 years who underwent primary OASI repair at RGH between January 1, 2019, and December 31, 2023.
- Research Ethics Board approval (REB 26-12) and Operational Approvals (OA-SHA-26-12) were obtained prior to data collection.
- OASI cases were identified using CIHI diagnostic codes linked to medical record numbers. Cases with incomplete records were excluded.
- A review of provincial health records identified any reoperation within 2 years postpartum performed in Saskatchewan.
- Extracted variables included demographics, delivery and primary repair characteristics, postpartum care, indications for reoperation, and procedures performed.
- The 2-year reoperation rate was reported with an exact binomial 95% confidence interval.
- Exploratory associations among reoperated patients were assessed using two-sided Fisher's exact tests.

Results

- Primary outcome:** Of 848 patients who underwent primary OASI repair, **19 underwent reoperation within 2 years postpartum (2.24%, exact 95% CI 1.35%–3.48%)**. Mean time to reoperation was **51.5 days** (range 6–290).
- Excluding reoperations attributable to retained products of conception (RPOC), the reoperation rate was 1.42% (12/848; exact 95% CI 0.73–2.46%).
- Reoperated cohort:** Mean age was 31.6 ± 4.6 years, mean BMI at term was 31.7 ± 6.3 kg/m², and 15/19 (78.9%) were primiparous.
- Delivery:** Spontaneous vaginal delivery occurred in 3/19 (15.8%). Operative vaginal delivery occurred in 16/19 patients (84.2%): forceps in 6/19 (31.6%), vacuum in 5/19 (26.3%), and a combination of vacuum and forceps in 5/19 (26.3%).
- Antibiotic prophylaxis:** Antibiotics were administered at delivery to 13/19 patients (68.4%).
- Indications:** Wound dehiscence and retained products of conception were the most common indications, each occurring in 7/19 patients (36.8%).
- Procedures:** Perineal wound revision was the most common procedure, performed in 11/19 patients (57.9%).
- Exploratory subgroup analysis:** Among reoperated patients, absence of antibiotic prophylaxis was associated with surgical-site infection (4/6 (66.7%) vs 1/13 (7.7%), $p=.017$) and perineal wound revision (6/6 (100%) vs 5/13 (38.5%), $p=.018$).

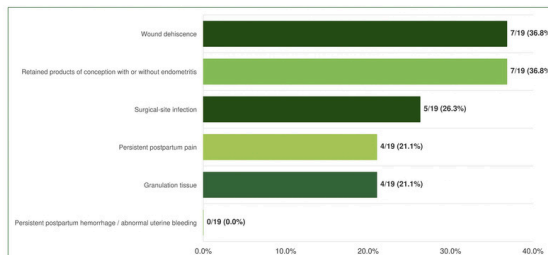


Figure 1: Indications for reoperation among reoperated patients (n=19).

Percentages do not sum to 100% because categories were non-mutually exclusive.

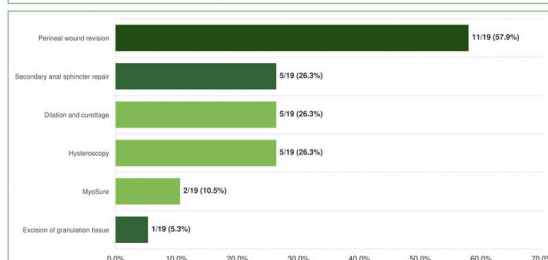


Figure 2: Procedures performed at reoperation (n=19).

Percentages do not sum to 100% because categories were non-mutually exclusive.

Discussion

- To authors' knowledge, this is the first Canadian study of 2-year reoperation after primary OASI repair. The 2.24% all-cause reoperation rate was similar in magnitude to international reports.
- Perineal wound complications represented the greatest OASI-related surgical burden, with wound revision most commonly performed procedure.
- RPOC contributed substantially to all-cause reoperation but is not OASI-specific; after excluding reoperations attributable to RPOC, the rate was 1.42%.
- Among reoperated patients, absence of antibiotic prophylaxis was associated with surgical-site infection and wound revision. These exploratory findings are hypothesis-generating and require validation in the full OASI cohort.
- Reoperations occurred 6–290 days postpartum, supporting continued postpartum surveillance. Limitations include the single-centre retrospective design and small reoperation subgroup (n=19).

Conclusion

- Reoperation after primary OASI repair was uncommon: 2.24% overall and 1.42% after excluding RPOC-related reoperations.
- Perineal wound complications accounted for the greatest OASI-related surgical burden.
- This study provides Canadian benchmark data for reoperation rate after OASI repair and supports attention to infection prevention and postpartum wound surveillance.

Acknowledgements

This study was supported through the 2025–2027 Clinician Research Support Program (CRSP) and Dean's Project Awards. The authors gratefully acknowledge research support provided by the Saskatchewan Health Authority Research Department.

References





Ayesha Shafiq (Dr. Ryan Lett)

Clinical Validation of NiADA (Non-invasive Anemia Detection with Artificial Intelligence) for Screening of Hemoglobin in Postpartum Women

Introduction: Postpartum anemia is associated with impaired recovery, reduced breastfeeding success, and postpartum depression. We evaluated the accuracy of an artificial intelligence-based smartphone application that estimates hemoglobin (Hb) from palpebral conjunctival images.

Methods: In this prospective observational validation study, 201 postpartum women aged ≥ 18 years undergoing a day-1 complete blood count within four hours of imaging were included. Trained personnel acquired images. Agreement was assessed using bias, error measures, Bland–Altman analysis, intraclass correlation coefficient (ICC), and accuracy thresholds.

Results: Paired measurements were available for 201 participants. Mean laboratory and app-estimated Hb were 10.9 ± 1.53 and 13.5 ± 1.06 g/dL, respectively. The application overestimated Hb, with a mean bias of $+2.56$ g/dL (95% CI, 2.34–2.79), mean absolute error of 2.61 g/dL, and limits of agreement of -0.62 to $+5.75$ g/dL. Only 8.5% of estimates were within $\pm 5\%$ and 14.9% within ± 1 g/dL of laboratory Hb. Absolute agreement was low (ICC, 0.081). Bias increased as laboratory Hb decreased ($p < 0.001$), reaching $+6.19$ g/dL when Hb was < 8 g/dL, but did not differ by Fitzpatrick skin type or operator.

Conclusion: The application substantially overestimated Hb, particularly at lower concentrations, and cannot yet replace laboratory screening without further algorithm refinement and validation.

Clinical Validation of Non-Invasive Hemoglobin Screening in Postpartum Women

SANSKRITI SHRESTHA¹, AYESHA SHAFIQ¹, DAVID WEI¹, SABIHA SULTANA², CHRISTINE LETT^{1,3}, RYAN LETT^{1,4}

¹University of Saskatchewan College of Medicine; ²SHA Research Department; ³University of Saskatchewan Department of Obstetrics and Gynecology; ⁴University of Saskatchewan Department of Anesthesiology

INTRODUCTION

- Postpartum anemia affects **30–50% of women in developed countries** and up to **80% worldwide**.¹
- It is associated with impaired recovery, reduced breastfeeding success, poorer maternal–infant bonding, and postpartum depression.^{2,3}
- Screening typically relies on venous CBC testing, which is invasive and may be delayed.
- Smartphone-based artificial intelligence (AI) estimation of hemoglobin (Hb) from palpebral conjunctival images offers a potential rapid, non-invasive alternative.

OBJECTIVE

- To assess agreement between smartphone-based Hb estimation and laboratory Hb in postpartum women.
- To identify screening factors associated with measurement error.

MATERIALS AND METHODS

- Prospective validation study of 201 postpartum women.
- Participants received routine postpartum care and day 1 CBC testing.
- Trained personnel captured palpebral conjunctival images using the NiADA smartphone application.
- Laboratory Hb within 4 hours served as the reference standard.
- Clinical variables included BMI, Fitzpatrick skin type, blood loss, transfusion, iron use, and delivery mode.
- Agreement was assessed using bias, MAE, RMSE, Bland–Altman analysis, ICC, and predefined accuracy thresholds.

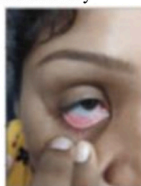


Figure 1. Eyelid and sclera segmentation from raw image. <https://pubmed.ncbi.nlm.nih.gov/39071070/>

RESULTS

➤ *The application consistently overestimated Hb, with greater error at lower Hb levels.*

Measure	Result	Measure	Result
Participants analyzed	201	MAE	2.61 g/dL
Mean lab Hb	10.9 ± 1.53 g/dL	RMSE	3.03 g/dL
Mean app-estimated Hb	13.5 ± 1.06 g/dL	ICC	0.081
Mean bias	+2.56 g/dL (95% CI 23.4–27.9)	within ±5%	8.5%
		within ±10%	14.9%

Table 1. Summary of the Application Performance and Agreement With Laboratory Hemoglobin.

➤ *Bland–Altman limits of agreement were wide (–0.62 to +5.75 g/dL).*

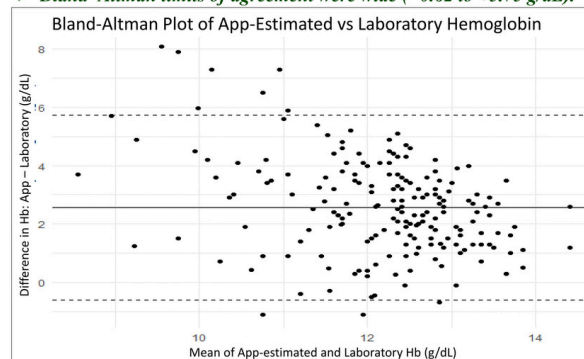


Figure 2. Bland–Altman Agreement Between App-Estimated and Laboratory Hb.

➤ *Application overestimation increased significantly as laboratory Hb decreased ($p < 0.001$)*

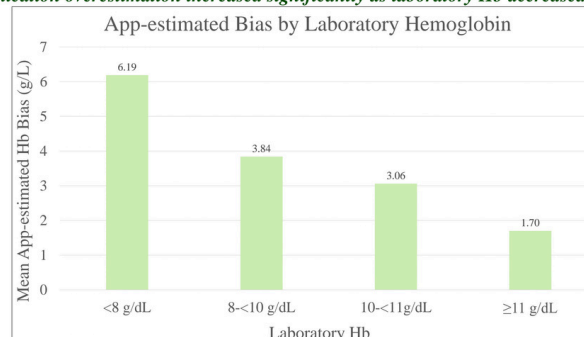


Figure 3. Mean App-Estimated Bias by Laboratory Hb Concentration

DISCUSSION

- The application systematically overestimated Hb, with greater bias at lower laboratory Hb concentrations.
- Wide limits of agreement and a low ICC demonstrated poor agreement between methods.
- Bias was not significantly associated with Fitzpatrick skin type or image operator.
- Greater error at low Hb levels may limit detection of clinically important postpartum anemia.^{1,3}

CONCLUSION

- The application is not currently accurate enough to replace laboratory Hb testing for postpartum anemia screening.
- Algorithm refinement should prioritize lower Hb concentrations.
- Future studies should assess whether the application can reliably track within-person Hb changes and validate the refined algorithm in larger, more diverse postpartum populations.

REFERENCES



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ACKNOWLEDGEMENTS

We thank Dr. Lett for his guidance, Monere for providing access to the application, and the Saskatchewan Health Authority Research Department for study support.

Oncology





Samantha Allan (Dr. Linda Chelico)

The Effect of the A3B-HUWE1 Protein-Protein Interaction on cMyc in Breast Cancer

Through affinity purification mass spectrometry APOBEC3B (A3B), a deoxycytidine deaminase, was found to interact with two proteins – PFD5 and HUWE1 – involved in the regulation of the oncogene cMyc. The Chelico lab demonstrated that A3B can indirectly regulate cMyc through its protein interaction with PFD5 in various breast cancer cell lines.¹ Following the same methods in a HEK293T cell line we showed that the A3B-HUWE1 interaction appeared to stabilize cMyc levels. To make this research more applicable, we wanted to validate these results in a breast cancer cell line using an endogenous protein system. Both HUWE1 and A3B are overexpressed in breast cancer and the effects of this interaction on cMyc have yet to be demonstrated in a breast cancer cell line.²⁻³ We aimed to discover this effect using an ER+ breast cancer cell line with doxycycline inducible A3B and short hairpin RNA targeted to HUWE1 to knock it down. Using qPCR and immunoblotting we were able to show that loss of cMyc resulted from the absence of A3B and knockdown of HUWE1, validating our findings in HEK293T cells. The results of this research indicate that the A3B-HUWE1 interaction could be a potential therapeutic target as stabilized cMyc could lead to uncontrolled cell replication and tumor development.

The Effect of the A3B-HUWE1 Protein-Protein Interaction on cMyc in Breast Cancer

Samantha Allan¹, Linda Chelico¹

Department of Biochemistry, Microbiology, and Immunology, University of Saskatchewan¹

INTRODUCTION

- The protein-protein interaction map generated by the Chelico & Krogan Labs demonstrated that APOBEC3B (A3B) interacts with two proteins - PFD5 and HUWE1 - involved in the regulation of cMyc.¹



- A3B was found to indirectly regulate cMyc through its protein interaction with PFD5.¹
- HUWE1 regulates cMyc through either K63 or K48 ubiquitin linkages in various cancers.²⁻⁴
- We previously showed in HEK293T cells through a transfection-based system that the A3B-HUWE1 interaction appears to stabilize cMyc levels.
- Both HUWE1 and A3B are highly expressed in breast cancer cell lines and maintain low levels in normal breast cells.⁵⁻⁶
- A3B is associated with poor survival in ER+ breast cancer.⁷

OBJECTIVES

- Use ER+ MCF7 doxycycline inducible A3B cell line to examine the A3B-HUWE1 interaction.
- Determine which ubiquitin linkage HUWE1 uses in an ER+ breast cancer cell line.

METHODS

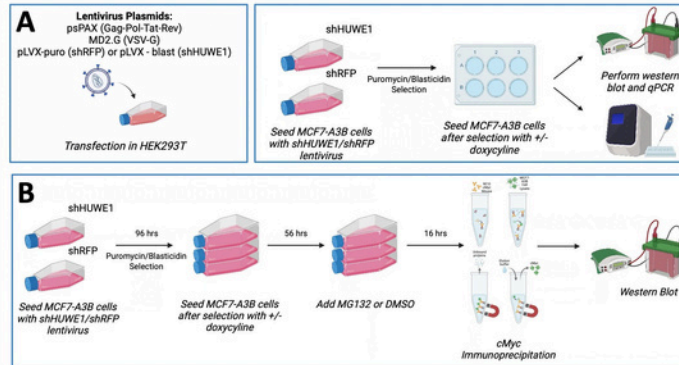


Figure 1. Experimental Methodology followed
A. Method followed for MCF7-A3B HUWE1 knockdown and A3B doxycycline induction B. Method developed for MCF7-A3B cMyc Immunoprecipitation

RESULTS

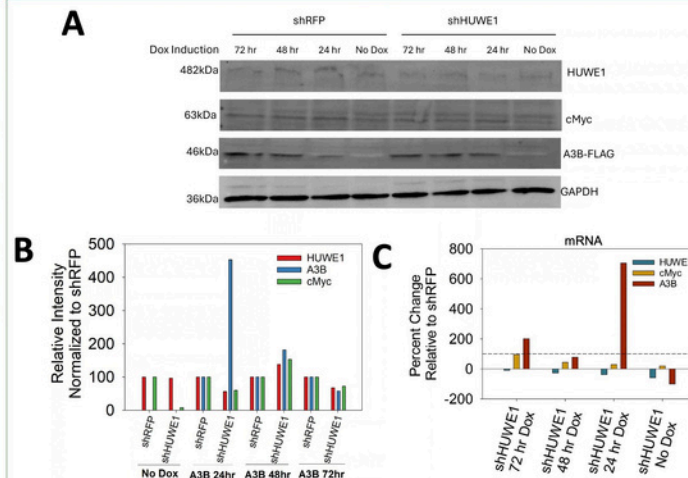


Figure 2. Loss of HUWE1 and A3B leads to loss of cMyc
A. Representative western blot showing loss of cMyc caused by HUWE1 knockdown and absence of A3B
B. Quantitative Analysis of relative HUWE1, A3B, and cMyc band intensities C. qPCR results validating western blot

CONCLUSIONS

- Loss of HUWE1 and A3B leads to loss of cMyc.
- HUWE1 has proven to be a difficult protein to work with and requires extensive optimization.
- The HUWE1-A3B interaction could be a potential therapeutic target.

FUTURE DIRECTIONS

- Optimize the immunoprecipitation protocol
- Determine which ubiquitin linkage HUWE1 tags cMyc with in breast cancer
- Determine if there is cytotoxicity in the presence of HUWE1 and A3B

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ACKNOWLEDGEMENTS

- Supervisor, Dr Linda Chelico
- Dr Ashtalakshmi Ganapathysamy
- Rhea Martin
- Chelico Lab Members



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Sarim Asim

AI model validation and utilization in skin cancer classification

Background: Melanoma is highly treatable when caught early, but lesions are often difficult to classify outside dermatology, and Saskatchewan patients wait months for referral. Artificial intelligence (AI) models can classify skin lesions accurately, but their effect on clinician decision-making remains unclear.

Methods: A computer vision model was trained on 23,648 dermoscopic and clinical images from the International Skin Imaging Collaboration (ISIC) Archive. In a paired pilot study, one physician and two medical students each classified 100 lesions (50 benign, 50 malignant) not used in training, first unaided and then with AI confidence scores and visual aids. Readers classified lesions as benign or melanoma, and decided whether to biopsy or refer. Performance was assessed using receiver operating characteristic (ROC) curves and area under the curve (AUC).

Results: AI support increased AUC for all readers: physician 0.607 to 0.909; students 0.617 to 0.831 and 0.583 to 0.735. For the physician, AI support increased accuracy from 60% to 87%, sensitivity from 46% to 82%, and specificity from 74% to 92%, compared with 89% accuracy, 82% sensitivity, and 96% specificity for AI alone.

Conclusion: AI support improved lesion classification and referral decisions across all readers. However, findings are limited by small internal sample, and a larger study involving front-line clinicians is planned.

Artificial Intelligence Model Evaluation and Utilization in Skin Cancer Classification

M. Sarim Asim, K. Mazinke, Krystal Kan, A. Sharma, T.D. Oleskiw PhD, R. Jaggi MD

Introduction

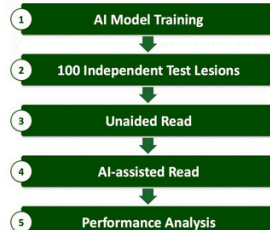
- Melanoma affects one in six Canadians, and survival depends heavily on early and accurate detection.¹
- Suspicious lesions are often first assessed in primary care, where clinicians must triage patients with limited diagnostic tools.
- In Saskatchewan, patients may face a prolonged wait for dermatology referral.
- Artificial intelligence (AI) can classify skin lesions with performance comparable to specialists,^{2,3} but its clinical value depends on how it affects clinician decision-making.
- We evaluated an AI model and its effect on clinician classification and triage.

Objectives

- To evaluate the performance of an AI model in classifying benign and malignant skin lesions.
- To assess the effect of AI support on clinician skin lesion classification and triage decisions.

Methods

- A computer vision model was trained on 23,648 dermoscopic and clinical images from the International Skin Imaging Collaboration (ISIC) Archive.
- One physician and two medical students assessed 100 randomly selected lesions (50 benign, 50 malignant) not used in training.
- Readers first assessed lesions independently and then with AI support.
- Classification and triage performance were evaluated using receiver operating characteristic (ROC) curves and area under the curve (AUC).



Results

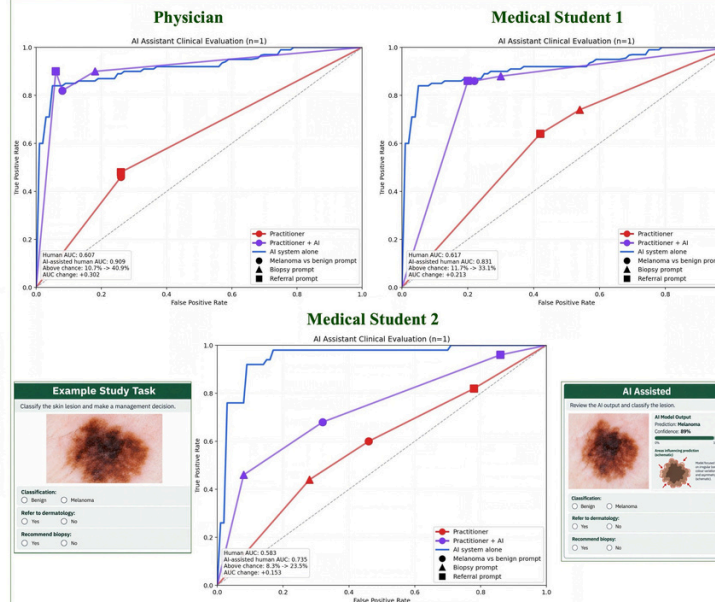


Figure 1. ROC curves and AUC for three readers (one physician, two medical students) classifying 100 lesions, unaided versus AI-assisted, with the AI model's standalone performance shown for reference.

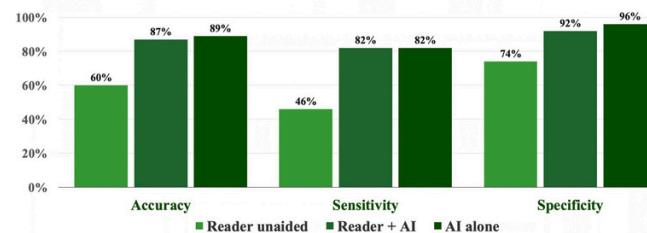


Figure 2. Diagnostic accuracy, sensitivity, and specificity for a practitioner unaided, with AI support, and the AI model alone, classifying 100 test lesions.

Discussion

- AI support was associated with improved diagnostic performance across different experience levels, consistent with larger reader studies.⁵
- Improved specificity may support more efficient referral triaging.
- AI-assisted readers approached the model's standalone performance for two readers.

Limitations

- Paired design: Repeat exposure to lesions may contribute to observed improvement.
- Small internal sample of three readers limits generalizability.
- ISIC's limited skin tone diversity may affect performance across all skin types.⁶
- Classification was limited to melanoma versus benign lesions.

Next Steps

- Recruitment of Saskatchewan family physicians, residents, and nurse practitioners for a larger study.
- Measure diagnostic accuracy, triage, and response time in a powered study
- Assess skin tone bias; extend classification to basal and squamous cell carcinoma.

Conclusions

- AI support was associated with improved lesion classification and referral performance among the three readers in this pilot study.
- Findings are limited by sample size and support further evaluation in a larger study with front-line clinicians.

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Acknowledgements

Supported by the University of Saskatchewan College of Medicine Dean's Project Program and the Mach-Gaensslen Foundation of Canada.



Jeshua Jacob (Dr. George Katselis)

Characterization of Platelet-Complement Protein-Protein Interactions Using Mass-Spectrometry Based Proteomics

Platelets and the complement system are essential homeostatic components that interact bidirectionally in the body's innate immune system. Existing research is unable to characterize protein-protein interactions between platelet and complement proteins due to the sheer number of proteins involved in the two systems and the low sensitivity of traditional methods. This project circumvents that barrier by combining mass spectrometry (MS)-based proteomics and bioinformatics to reliably identify and characterize proteins in both systems and ultimately decipher the platelet-complement crosstalk mechanisms. Blood samples were processed to isolate the platelet- and complement- associated fractions, followed by the digestion of the proteins into peptides for MS analysis. Bioinformatics validation of the identified proteins revealed a total of 269 platelet proteins and 28 complement proteins from their respective milieu. 75 of those 269 platelet proteins participated in biologically significant functions and interactions with the complement system. Differentially expressed platelet and complement proteins were mapped in STRING revealing the complex crosstalk mechanisms between the two systems. These findings establish a MS-based platform to better understand how a dysregulated platelet-complement system may contribute to the pathophysiology of a wide range of clinical disorders thereby supporting the discovery of potential therapeutic targets in future studies.



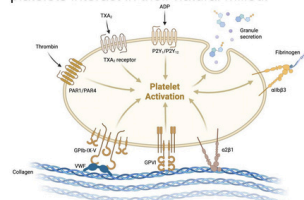
Characterization of Platelet-Complement Protein Interactions Using MS-Based Proteomics

Jeshua Jacob¹, Hadi Goubbran-Messiha², George S. Katselis^{1,3}

¹Department of Biochemistry, Microbiology & Immunology; ²Department of Oncology; ³Department of Medicine (CCRAH), College of Medicine, University of Saskatchewan

Introduction

- Platelets are tiny cell fragments produced in the bone marrow by megakaryocytes and act as the body's first line of defence through the proteins on their cell surface and in their granules [1].
- Platelets are mostly known for their role in hemostasis but are now increasingly recognized for their multifaceted roles in immunity, inflammation, and tissue repair [2].
- Recently, high-throughput techniques, such as mass spectrometry (MS), have significantly enhanced our understanding of platelet biology and its clinical implications in transfusion medicine [2].
- Platelet proteomics offers a retrospective view of physiological and pathological changes over the platelets' 7-10 day lifespan, making it a unique tool for studying cumulative biological events [2].
- Researchers often study interactions between coagulation factor proteins and platelet surface integrin proteins. Less work, however, has focused on platelet proteins and its interaction and regulation of the complement system, the third pillar of immunity, that is critical at the crossroads of inflammation, infection, immunity, and hemostasis [3].
- Combining platelet proteomics and plasma proteomics offers a wide perspective on how platelets interact in their natural milieu.

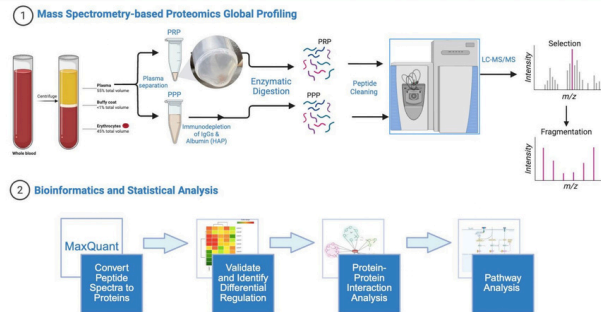


Scope of Study

Hypothesis: MS-based proteomics and bioinformatics can characterize protein-protein interactions (PPI) between platelet and complement system proteins in platelet-rich plasma (PRP) and platelet-poor plasma (PPP), respectively.

Specific objectives: 1) Use of MS global proteomics to identify a) platelet proteins from the platelet surface (integrins) and platelet contents, including alpha and dense granules, in PRP, and b) complement system proteins in PPP. 2) Use bioinformatics analysis to characterize PPI between the identified platelet and complement proteins.

Methods



Results

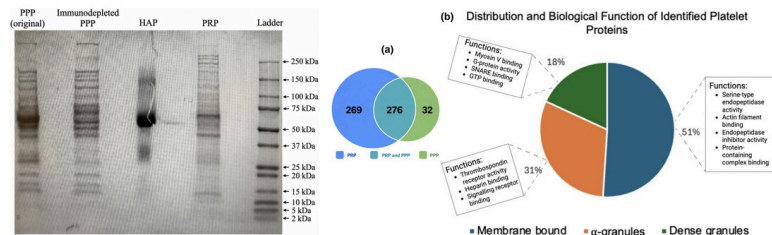


Figure 1: SDS-PAGE gel of PPP, Immunodepleted PPP, High abundant proteins (HAP) and PRP. Distinct protein patterns are observed in PPP, after immunodepletion, and in PRP.

Figure 2: (a) Venn diagram of identified proteins and (b) pie chart detailing the localization of the platelet proteins in three categories: membrane-bound, α-granules, and dense granules. A total of 577 proteins were identified in PRP and PPP, and 75 of the 269 platelet proteins were found to significantly interact with the complement proteins (38 membrane-bound; 23 α-granules, and 14 dense granules).

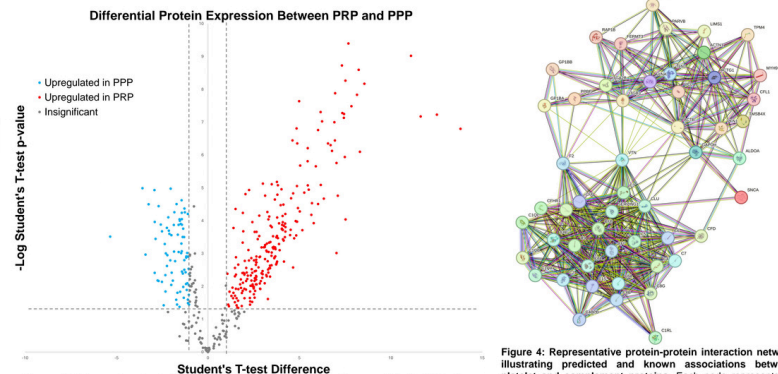


Figure 3: Volcano plot displaying differential protein expression between Platelet-Rich Plasma (PRP) and Platelet-Poor Plasma (PPP). T-test at $p \leq 0.05$ and a log₂ fold change of ≥ 1 . 240 proteins significantly upregulated in PRP compared to PPP, and 105 proteins upregulated in PPP compared to PRP.

Figure 4: Representative protein-protein interaction network illustrating predicted and known associations between platelet and complement proteins. Each node represents an individual protein and the lines connecting each node represents a physical or functional association. There are two major clusters with the complement proteins cluster at the bottom and the platelet proteins cluster at the top.

Conclusions

- In this work, we prepared platelet-rich and platelet-poor plasma fractions to characterize the platelet-complement interactome using MS-based proteomics.
- We identified and characterized 269 proteins derived from the platelet membrane, the alpha, and dense platelet granules in blood.
- We identified 28 complement proteins in the plasma belonging to three complement activation pathways (Classical, Lectin and Alternative) and demonstrated their interactions with platelet proteins.
- Bioinformatics revealed unique functions of the identified platelet and complement proteins.

Future Directions

- Establishing this platform enables its application across diverse physiological and pathological conditions, including infection, inflammation, immune disorders, malignancy, and thrombotic states.
- The technology has limitless potential when combined with plasma proteomics and other omics technologies to explore the pathophysiology of a wide range of clinical disorders.

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Acknowledgements

Katselis MS Lab for Omics Research:

Rachel Guerra; Zarlish Mubashar

Funding sources:

College of Medicine Biomedical Summer Research Project

NSERC USRA



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Morgan Johansson (Dr. Deborah Anderson)

Evaluating the anti-metastatic activity of the CLIC3 inhibitor BP370 in triple-negative breast cancer cell lines

Breast cancer is the most commonly diagnosed cancer among Canadian women, and accounts for approximately 26% of all new cancer cases. More specifically, triple negative breast cancer is known for its high mortality rate and increased risk of relapse. This is generally attributed to the lack of targetable receptors seen in other breast cancer subtypes (progesterone receptor, estrogen receptor, and HER2 receptor). Our laboratory has previously identified CLIC3 as a druggable target in triple negative breast cancers. CLIC3 is an intracellular chloride ion channel which is overexpressed in highly aggressive breast cancer cell lines. CLIC3 is a glutathione-dependant oxidoreductase. It is involved in promoting cancer migration, invasion, tumor progression, and angiogenesis through transglutaminase-2 activation and integrin signaling. Due to this, our laboratory has developed the novel small-molecule CLIC3 inhibitor BP370. To evaluate the anti-metastatic activity of BP370, several breast cancer cell lines, (BT20, BT549, HCC1806, MDA-MB-231), were treated with varying concentrations of BP370. Anti-metastatic activity was assessed via migration and invasion transwell assays. Thus far, BP370 has shown promising anti-migratory and anti-invasive activity. It has decreased both migration and invasion in cell lines of varying CLIC3 expression. Inhibitory effects are also observed in a concentration-dependant manner, further demonstrating its potential as an anti-metastatic inhibitor.

Evaluating the anti-metastatic activity of the CLIC3 inhibitor BP370 in triple-negative breast cancer cell lines

Johannson M^{1,3,4}, Mellor P⁴, Anderson D^{1,2,3,4}

¹Saskatchewan Cancer Agency, ²Department of Oncology, ³Department of Biochemistry, Microbiology, and Immunology, ⁴College of Medicine

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer among Canadian women and is the second leading cause of death (1). More specifically, triple negative breast cancer (TNBC) is known for its high mortality rate and increased risk of relapse (2). Due to the lack of clinical targets, there is an unmet need for therapeutics for TNBC cases. Intracellular chloride ion channel 3 (CLIC3) is expressed in highly aggressive cancer subtypes, including TNBC and is involved in cell invasion, migration, tumor progression, and metastasis (3). CLIC3 is a glutathione-dependant oxidoreductase which activates transglutaminase-2 and integrin signaling, helping to explaining its role in cancer metastasis (4,5,6). Due to CLIC3's potential as an anti-metastatic therapeutic target, the Anderson lab began developing small-molecule CLIC3 inhibitors. Of the inhibitors evaluated thus far, BP370 has emerged as the leading compound at a 10 μ M concentration.

OBJECTIVES

- To determine whether BP370 can inhibit cell migration at 25 μ M and 50 μ M concentrations in varying cell lines, with varying levels of CLIC3 expression.
- To determine if BP370 can inhibit cell invasion through Matrigel at 10 μ M, 25 μ M, and 50 μ M concentrations in varying cell lines, with varying levels of CLIC3 expression.

METHODS

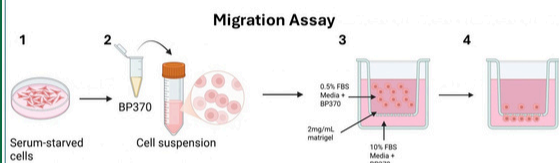


Figure 1. Workflow of the migration assay. 1: Cells are serum starved overnight in 0.5% FBS media. 2: The following day, cells are detached and resuspended at a concentration of 4×10^5 cells/mL. Cells are then pre-treated with BP370 for 2 hours. 3: 10% FBS medium is added to the bottom of a transwell plate, and Boyden chambers (8-micron filters) are placed in. Treated cells are then added to the top of the filter in 0.5% FBS media and allowed to migrate. Both the top and bottom chambers contain the same concentration of BP370, which is the same as the pretreatment. A DMSO control is also used (0.1%). 4: Following the migration period, cells on the bottom of the filter are fixed and counted.

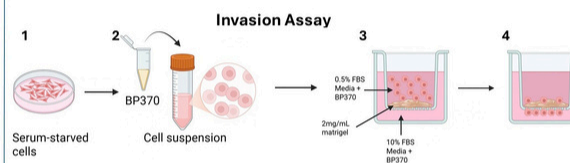


Figure 2. Workflow of the invasion assay. 1: Cells are serum starved overnight in 0.5% FBS media. 2: The following day, cells are detached and resuspended at a concentration of 4×10^5 cells/mL. BP370 is then added to the cell suspension. 3: Immediately after BP370 addition, 10% FBS medium is added to the bottom of a transwell plate, and Boyden chambers (8-micron filters), containing 2 mg/mL Matrigel (100 μ L) are placed in. Treated cells are then added to the top of the filter in 0.5% FBS media and allowed to invade through the Matrigel membrane. Both the top and bottom chambers contain the same concentration of BP370. A DMSO control is also used (0.1%). 4: Following the invasion period, cells on the bottom of the filter are fixed and counted.

RESULTS

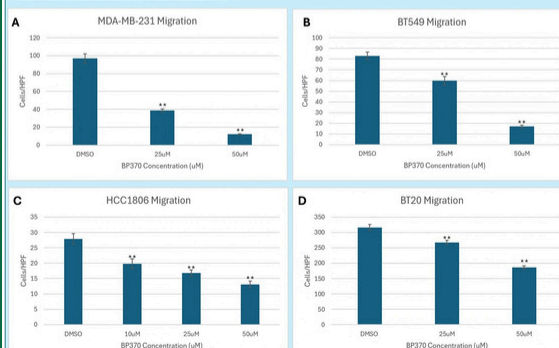


Figure 3. Migration assay cell counts in varying concentrations of BP370 treatment. Cells were seeded at 4×10^5 cells/mL for all cell lines examined. Prior to performing the migration assay, cells were incubated with inhibitor for 2 hours. Cells were then allowed to migrate for varying time periods (MDA-MB-231 – 4 hours, BT549 – 6 hours, BT20 – 8 hours, HCC1806 – 17 hours). BP370 treatment appears to successfully limit cell migration in all cell lines examined, with higher concentrations having stronger inhibitory effects. Therefore, showing BP370's strength as an anti-metastatic compound. Data is presented as mean $\pm$ SD from n = 3 independent experiments. Statistical significance versus DMSO control was determined using student t-test; *p < 0.05, **p < 0.001.

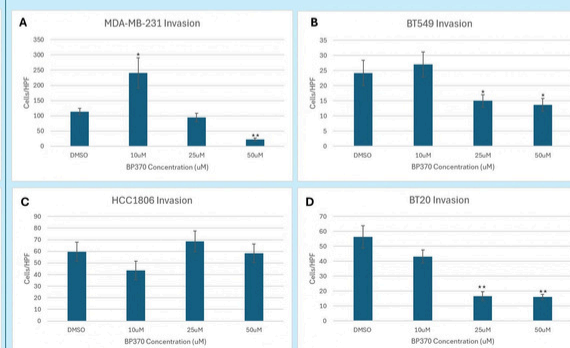


Figure 4. Invasion assay cell counts in varying concentrations of BP370 treatment. Cells were seeded at 4×10^5 cells/mL for all cell lines examined. Prior to performing the invasion assay, 100 μ L of 2 mg/mL Matrigel was added to the top of each Boyden chamber. Cells were then allowed to invade for varying time periods (MDA-MB-231 – 17 hours, BT549 – 17 hours, BT20 – 22 hours, HCC1806 – 20 hours). BP370 treatment appears to successfully limit cell invasion in all cell lines examined, with higher concentrations generally having stronger inhibitory effects. In some cases, higher concentrations of inhibitor are unsuccessful at limiting invasion (C). Overall, this shows BP370's strength as an anti-metastatic compound. Data is presented as mean $\pm$ SD from n = 3 independent experiments. Statistical significance versus DMSO control was determined using student t-test; *p < 0.05, **p < 0.001.

DISCUSSION

- The results of these experiments show BP370 demonstrates promising anti-migratory and anti-invasive activity. It can successfully inhibit both cell migration and invasion in various cell lines, which contain varying levels of CLIC3 expression. BP370 reduced cell migration in a concentration-dependent manner.
- Overall, these results demonstrate that BP370 shows promising anti-migratory and anti-invasive activity in TNBC cell lines.
- Going forward, the anti-metastatic activity of BP370 will be tested in CLIC3-knockout cell lines to evaluate specificity of the inhibitor. The compound will also be tested in mouse models of TNBC, delivered via oral gavage.

ACKNOWLEDGEMENTS

- This project was funded by the CoM Biomedical Summer Research Grant. I would like to thank all members of the Anderson lab – Dr. Deborah Anderson, Dr. Paul Mellor, and Dr. Tetiana Katiri for their mentorship and guidance throughout this project.

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Scott Jones (Dr. Osama Souied)

Retrospective Analysis of Metastatic Bladder Cancer Patient Outcomes Receiving Enfortumab Vedotin in the Province of Saskatchewan

Background: EV-301 is a global study that pioneered the future of treatment following the progression of locally advanced urothelial carcinoma following platinum-based chemotherapy and programmed cell death protein (PD-1) or programmed death ligand inhibitor (PD-L1) treatment¹.

Methods: We conducted a retrospective cohort population study on patients in Saskatchewan diagnosed with locally advanced or metastatic urothelial carcinoma that received Enfortumab Vedotin following disease progression after receiving platinum-based chemotherapy and programmed cell death protein or programmed death ligand inhibitor treatment. 56 patients were identified through the SCA Oncology Pharmacy and Cancer Registry. Following ethics approval and electronic medical record data collection, 21 patients were identified as eligible for comparison to the EV-301 clinical trial. Statistical analyses were conducted using Kaplan-Meier for overall survival.

Results: A total of 21 patients were retrospectively analyzed and compared to the EV-301 trial. Saskatchewan patients' overall survival was shorter (median overall survival, 11.52 vs. 12.88 months)¹. The Saskatchewan patients were older comparatively (median age, 71.95 vs. 68.0) with worse ECOG performance status¹.

Conclusion: Our real-world data highlights the possibility of selection bias in EV-301 when compared to Saskatchewan patients. Additional bladder cancer research in Saskatchewan may give insight into considerations for treatment in the future.



Retrospective Analysis of Metastatic Bladder Cancer Patient Outcomes Receiving Enfortumab Vedotin in the Province of Saskatchewan

Scott Jones PharmD¹, Ambika Chandrasekhar PhD², Prosanta Mondal PhD², Osama Souied MD FRCPC^{1,2}

¹College of Medicine, University of Saskatchewan; ²Saskatchewan Cancer Agency

INTRODUCTORY BACKGROUND

❖ Bladder cancer is common in Canada.

Bladder cancer is the fifth most common cancer in Canada, with most cases occurring in adults aged 50 and older with a higher incidence in men¹.

❖ Medical advancements show little improvement on clinical outcomes.

The median overall survival with chemotherapy and immunotherapy is only 10 to 14 months².

❖ EV-301 brought new hope.

EV-301 clinical trial illustrated increased overall survival with Enfortumab Vedotin (EV) compared to chemotherapy treatment³. EV was a novel treatment approved in Canada for the treatment of unresectable locally advanced or metastatic urothelial cancer in patients who previously received platinum-containing chemotherapy and programmed death receptor-1 (PD-1) or programmed death-ligand 1 inhibitor (PD-L1)³.

❖ EV has been used in Saskatchewan for the past 3 years and the real-world evidence in comparison to EV-301 may differ.

Saskatchewan patients may have sub-optimal outcomes due to EV-301's population being more robust and performance status being better.

OBJECTIVES

We seek to analyze Saskatchewan patients that received EV treatment and compare our results to the EV-301 clinical trial:

1. Overall survival
2. Duration of treatment
3. Objective response rate
4. Progression free survival

We also seek to analyze the following contributing factors:

1. ECOG performance score
2. Underlying comorbidities
3. Number of cycles of treatment



MATERIAL & METHODS

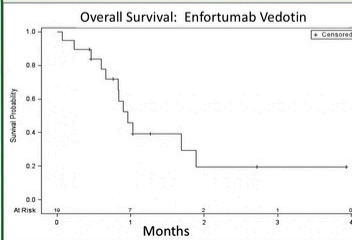
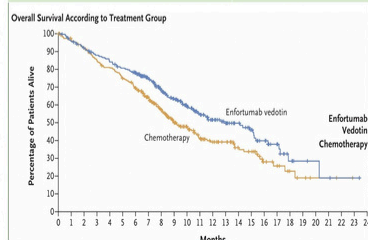
❖ We conducted a retrospective cohort population study on adult patient populations aged ≥ 18 years old in Saskatchewan diagnosed with locally advanced or metastatic urothelial bladder cancer that only received Enfortumab Vedotin (EV) treatment between January 2022 to December 2025.

❖ Project approval was granted from the Saskatchewan Cancer Agency and Biomedical Research Ethics Board of the University of Saskatchewan. In collaboration with the SCA Oncology Pharmacy Department and Cancer Registry, 56 patients were identified for clinical chart review. 21 patients of the original 56 were identified to have received EV in a similar manner as the clinical trial EV-301.

❖ Patient information was extracted such as age, rural or urban residence location, sex, ECOG performance status score, co-morbidities, and if relevant, date of death. We collected the date of metastatic diagnosis, start and end date of cancer treatment, number of treatment cycles, and last date the patient was seen in the oncology clinic. Using the Kaplan-Meier we analyzed our data with the key focus of overall survival.

RESULTS

EV- 301 Clinical Trial Data ² (N= 301)		Saskatchewan Clinical Trial Data (N= 21)	
Median age – yr	68.0 (34.0-85.0)	Median age – yr	71.95 (57.0-86.0)
Male – %	79.1	Male – %	71.4
Female – %	20.9	Female – %	28.6
ECOG Performance Status Score of 0 – %	39.9	ECOG Performance Status Score of 0 – %	23.8
ECOG Performance Status Score of 1 – %	60.1	ECOG Performance Status Score of 1 – %	38.1
Median Overall Survival	12.88 Months	Median Overall Survival	11.52 Months
Duration of EV Treatment (Median)	5.0 (0.5 to 19.4) Months	Duration of EV Treatment (Median)	6.4 (0.7 to 47.0) Months
Geographic Region:		ECOG Performance Status Score – Mean	1.29
Western Europe – %	41.9	Rural	66.7%
United States – %	14.3	Urban	33.3%
Rest of the World – %	43.9		



DISCUSSION

❖ Our data illustrates that Saskatchewan patients had a reduced overall survival rate compared to the EV-301 trial.²

❖ Duration of EV treatment in Saskatchewan patients was longer which could suggest a more aggressive treatment approach.

❖ Saskatchewan patients were older and had worse ECOG performance status scores.

❖ The Saskatchewan patient population results have a greater variability due to decreased sample size, comparatively.

CONCLUSION

❖ Our real-world clinical data provides insight into the possibility that selection bias may have occurred during the enrollment of patients included in the EV-301 clinical trial when compared to Saskatchewan patient population. Based on our Saskatchewan sample size of 21 patients, it is evident that a larger population would be required to reduce the inter-patient variability in our data.

❖ A key learning point from our research highlights the importance of considering selection bias and interpersonal variability when assessing clinical outcomes for patients receiving bladder cancer therapy.

❖ Further bladder cancer research is essential in Saskatchewan, as the province's distinct demographics have real-world implications for meaningful clinical outcomes.

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ACKNOWLEDGEMENTS

This project was supported by the College of Medicine 2026 Dean's Summer Project Program with funding from the Mach-Gaensslen Foundation and conducted in collaboration with the Saskatchewan Cancer Agency.



Janice Mak (Dr. Yuliang Wu)

DDX41 in Nuclear Speckles and Myeloid Malignancies

DEAD-box helicase 41 (DDX41) is an RNA helicase that contributes to coordination of pre-mRNA splicing. Mutations in DDX41 predispose individuals to myeloid malignancies, notably myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). Nuclear speckles (NS) are membraneless organelles within the nucleus that regulate gene expression through pre-mRNA splicing. Our lab hypothesizes that DDX41 localizes to NS as a modulator of pre-mRNA splicing and that common germline DDX41 variants disrupt its localization. Variant-mimicking GFP-DDX41 constructs were generated using site-directed mutagenesis, transfected into HeLa cells, and visualized alongside an NS marker using confocal microscopy. DDX41 localized to NS, with the first intrinsically disordered region (IDR1) being required for nuclear and NS localization. Common N-terminal germline truncation variants resulted in cytoplasmic mislocalization and accumulation of DDX41 in stress granules (SGs). Additionally, DDX41 mutations were associated with a decrease in the integrated stress response (ISR), suggesting that DDX41 dysfunction may perturb the cellular stress response. These findings suggest that disease-associated DDX41 mutations may contribute to myeloid malignancy predisposition through altered subcellular localization and disruption of stress-granule-associated responses. The impact of this study is the identification of a previously uncharacterized connection between DDX41 localization, nuclear speckle biology, and the cellular stress response, providing insight into how DDX41 dysfunction may contribute to disease development.

DDX41 in Nuclear Speckles and Myeloid Malignancies

Janice Mak¹, Harmony Grainger¹, Yuliang Wu¹

¹ Department of Biochemistry, Microbiology, and Immunology



Introduction

DDX41

- A DEAD-box RNA helicase
- Assists in pre-mRNA splicing coordination.¹



Figure 1. DDX41s ATP-dependent helicase ability. Generated with BioRender.

Nuclear Speckles (NS)

- Membraneless organelles within the nucleus
- Comprised of RNA-binding proteins and assorted RNAs.²
- Helps enhance splicing of nearby foci.

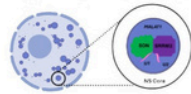


Figure 2. Core NS components: proteins SON and SRRM2, RNAs MALAT1, U1, and U2. Generated with BioRender.

Splicing & Malignancies

- DDX41 and NS are independently associated with splicing.
- Mutations in DDX41 carry susceptibility to myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML).³

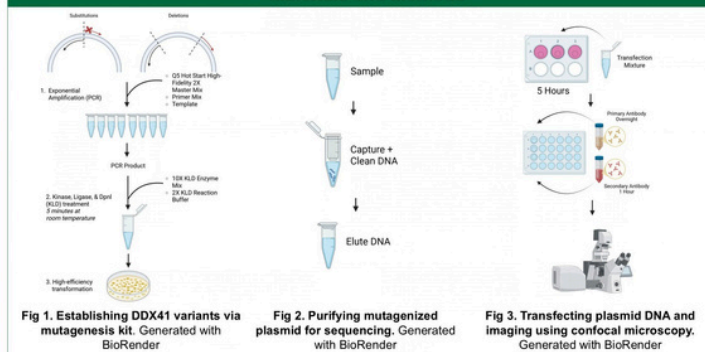
Hypothesis

We hypothesize that DDX41 is enriched in NS, where it functions as a modulator of pre-mRNA splicing. Mutations in DDX41 disrupt its localization and function within NS, predisposing to malignant transformation.

Objectives

- Determine the critical sequence required for DDX41 localization within the NS
- Observe the localization of common germline and somatic variants of DDX41.
- Resolve the effects of mislocalization in context of MDS/AML disease pathogenesis.

Materials and Methods



Results

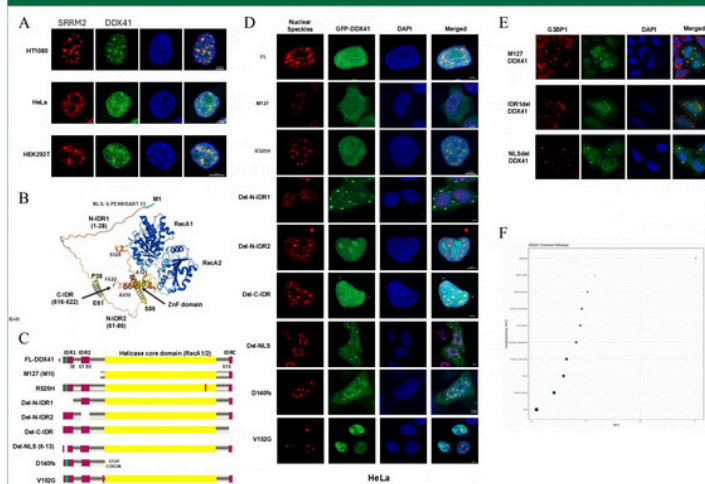


Fig A. Endogenous DDX41 colocalizes with nuclear speckles. Immunofluorescent co-staining of NS core protein (SRRM2, red), DDX41 (green), and DAPI (blue) in indicated cell lines.
Fig B. Alpha-fold protein structure of DDX41 depicting various regions of the protein.
Fig C. Structural schematic of DDX41 constructs. Disordered regions (pink), NLS (green), missense variants (red), and helicase core domain (yellow) are depicted.
Fig D. Representative immunofluorescent images of HeLa cells transfected with GFP tagged FL-DDX41, M127, R525H, Del-N-IDR1, Del-N-IDR2, Del-C-IDR, Del-N-LS, D140fs, V152G.
Fig E. Cytoplasmic DDX41 (M127, IDR1del, NLSdel) are associated with G3BP1 foci, aka stress granules (SG).
Fig F. scRNAseq pathway enrichment analysis of DDX41 germline/somatic variant patient with healthy age-matched controls showed a significant downregulation in integrated stress response (ISR).

Conclusion

- DDX41 localizes to Nuclear Speckles.
- IDR1 containing an embedded NLS is required for DDX41 to localize in the NS subregion and nucleus.
- Some cytoplasmic DDX41 localizes to SG.
- HSCs in a patient with DDX41 mutations led to downregulation in ISR, potentially leading to disease pathogenesis.

Future Directions

- Investigate the differences between sodium arsenite induced SG and DDX41 containing SG in relation to integrated stress response (ISR)
- Create an interactome specific to DDX41 in NS using Mass Spectrometry

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Acknowledgments

I would like to thank Dr. Yuliang Wu and Harmony Grainger for their support and guidance throughout the duration of the project. I would also like to thank Fredrick Vizeacoumar for the RNAseq, lab members Sarah Yang, Isis Moreno Yllescas, Ishrat Maya, and Eulio González for their continued support, as well as fellow cluster members and friends.

This project was funded with help from the Natural Sciences and Engineering Research Council of Canada (NSERC) and the College of Medicine, University of Saskatchewan.



Rhea Martin (Dr. Linda Chelico)

Inhibition of Telomerase by APOBEC3A Decreases Telomere Length

Replication protein A (RPA) is known to protect the genome by binding tightly to ssDNA at replication forks, preventing other proteins from accessing single stranded DNA (ssDNA).^{1,2} Previous research shows that the cytosine deaminase APOBEC3A can displace RPA on ssDNA allowing its mutagenic activity.^{1,2} This raised the question of what other proteins APOBEC3A could displace from ssDNA. iPOND data showed that APOBEC3A can also displace TERT, the protein subunit of telomerase.^{3,unpublished} Since both APOBEC3A and telomere dysfunction are found in most cancers, this connection between APOBEC3A and TERT may reveal an alternative mechanism by which APOBEC3A promotes cancer.^{3,4} To investigate this, 639V and 5637 A3A knockdown cells were tested alongside doxycycline-induced HeLa cells expressing either A3A or A3A E72A (catalytic mutant), in the presence or absence of the telomerase inhibitor BIBR1532. Cells were collected for in-gel TRAP assays and Telomere Length qPCR. Expression of catalytically active APOBEC3A inhibited telomerase activity by ~25%, resulting in decreased telomere length, with synergistic effects observed between APOBEC3A and BIBR1532. Therefore, sustained APOBEC3A expression inhibits telomerase activity, ultimately decreasing telomeric length, possibly demonstrating another way that APOBEC3A can promote genomic instability during cancer. Future assays like ChIP-qPCR will determine the mechanism for APOBEC3A inhibiting telomerase.



APOBEC3A mediated inhibition of telomerase decreases telomere length



Rhea Martin, Ashtalakshmi Ganapathysamy, Sam Allan, Paul Oni, Linda Chelico

Department of Biochemistry Microbiology and Immunology, College of Medicine, University of Saskatchewan

Introduction

- APOBEC3A (A3A) is a cytosine deaminase that cycles on and off ssDNA to deaminate cytosine to uracil.
- A3A has been shown to displace replication protein A (RPA) which is known to bind extremely tightly to ssDNA at replication forks protecting the genome.^{1,2}
- iPOND data showed that A3A can displace other proteins that have bound ssDNA, like TERT, which is the protein subunit of telomerase.^{3,unpublished}
- Since A3A is already known to cause cancer through its mutagenic activity and telomere dysfunction is found in approximately 90% of all cancers, this research may demonstrate an alternative mechanism for A3A to cause cancer.^{3,4}

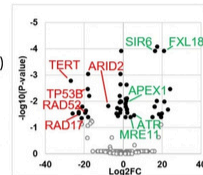


Fig. 1 A3A iPOND data
Displacement of TERT by APOBEC3A, unpublished

Objectives

- Determine whether A3A is deaminating TERC RNA or single stranded telomeric DNA.
- Ascertain if A3A inhibition of telomerase results in decreased telomere length.

Methods

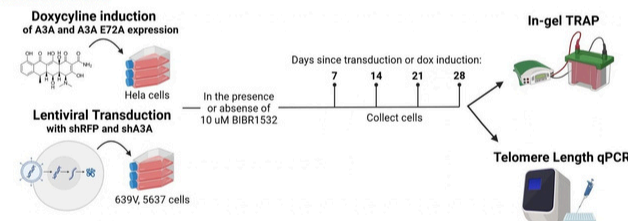


Fig. 2 Assessing Telomerase Inhibition and Telomere Length Methodology
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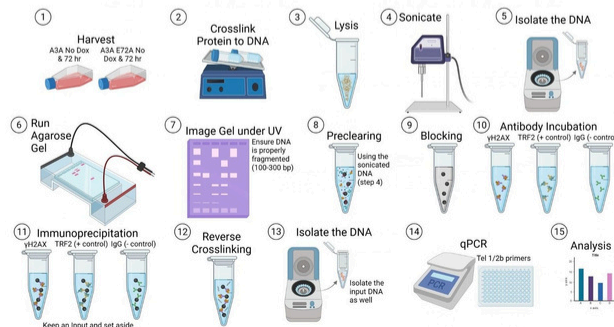


Fig. 3 ChIP Methods Schematic
Created using BioRender.

Results

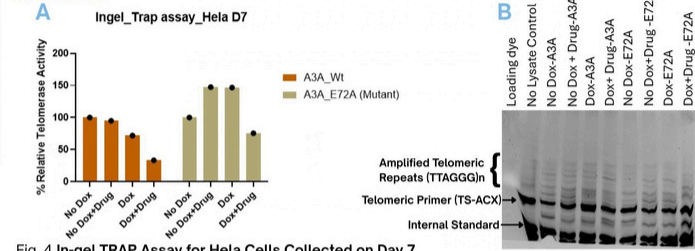


Fig. 4 In-gel TRAP Assay for HeLa Cells Collected on Day 7

HeLa cells were induced with doxycycline for A3A or A3A's catalytic mutant E72A for 7 days in the presence and absence of 10 μ M BIBR1532. Cell lysates were collected and an in-gel TRAP assay was performed (B). Percentage of relative telomerase was normalized to the No Dox condition and graphed in GraphPad Prism, n=1 (A).

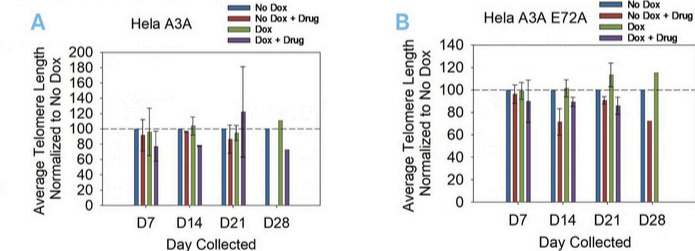


Fig. 5 Telomere Length qPCR for Dox Inducible Cells

A3A and A3A E72A expression was induced in HeLa cells for 7, 14, 21, and 28 days in the presence and absence of 10 μ M BIBR1532. Telomere length qPCR was performed and the average telomere length normalized to the No Dox condition was for A3A (A) and A3A E72A (B) conditions. Bars represent the mean $\pm$ SEM, n=2 for day 7, 14, and 21. Bars represent n=1 for day 28.

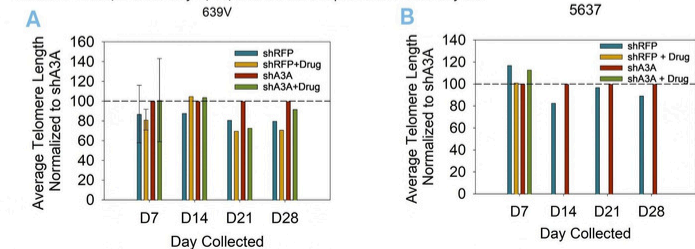


Fig. 6 Telomere Length qPCR for Endogenous A3A cells

Cells were transduced with lentivirus that expressed shRFP (control) or shA3A and harvested 7, 14, 21, and 28 days post-transduction in the presence and absence of 10 μ M BIBR1532. Telomere Length qPCR was performed and the average telomere length normalized to shA3A was determined for 639V (A) and 5637 (B) cells. n=1 for day 7, 14, 21, and 28. Bars represent the mean $\pm$ SEM, n=2 for day 7 of 639V.

Conclusion

- A3A catalytic inhibition of telomerase results in an average decreased telomere length across cell types.
- This inhibition of telomerase by A3A also synergizes with the telomerase inhibitor BIBR1532.

Future Directions

- Continue with the ChIP assay. Optimizing sonication conditions. (Fig. 3)
- Perform more biological replicates for the telomere length and TRAP assays.

Funding

Thank you to the Office of the Vice-Dean of Research for funding my project this summer.

References





Laraib Mehdi (Dr. Anand Krishnan)

Role of CHRM4 in Lung Cancer Progression and Metastasis

Background: Lung cancer remains a leading cause of cancer-related mortality, and brain metastases are associated with poor prognosis and limited treatment options. Muscarinic acetylcholine receptors have been implicated in cancer progression, but the role of the M4 receptor (CHRM4) in lung cancer brain metastasis remains unclear. Previous work from our laboratory suggests that CHRM4 activation may suppress lung cancer cell proliferation, supporting a potential tumour-suppressive role for CHRM4.

Objective: To compare CHRM4 expression across primary lung tumours from patients with and without subsequent brain metastasis and brain metastatic lesions. A secondary objective was to identify morphological differences between non-metastatic primary lung tumours, primary lung tumours from patients who developed brain metastasis, and brain metastatic lesions.

Methods: This retrospective cohort study examined de-identified lung adenocarcinoma tissue samples divided into three groups: primary lung tumours from patients without brain metastasis, primary lung tumours from patients who developed brain metastasis, and brain metastatic lung cancer tissue. Tissue sections were assessed using hematoxylin and eosin staining for histopathologic features, including tumour morphology, necrosis, hemorrhage, and immune-cell infiltration. CHRM4 expression was evaluated qualitatively using immunofluorescence staining.

Results: Qualitatively stronger CHRM4 staining was observed in primary lung tumours from patients without brain metastasis with comparatively weaker staining in both primary tumours from patients who developed brain metastasis and brain metastatic lesions. Qualitative histopathologic assessment suggested greater tumour heterogeneity, necrosis, and hemorrhage. These findings support further investigation of CHRM4 as a candidate biomarker associated with brain metastatic progression.

Conclusion: Qualitatively reduced CHRM4 expression in primary lung tumours from patients who developed brain metastasis and in brain metastatic lesions suggests an association between reduced CHRM4 expression and brain metastatic progression. These findings support further investigation of CHRM4 as a candidate biomarker and potential therapeutic target. Larger studies incorporating quantitative CHRM4 assessment and clinical outcome data are required to establish its prognostic or predictive significance.

Role of CHRM4 in Lung Cancer Progression and Metastasis

Laraib Mehdi B.A., Anand Krishnan PhD

Department of Anatomy, Physiology, and Pharmacology, College of Medicine, University of Saskatchewan

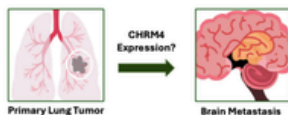
BACKGROUND

Lung Cancer and Brain Metastasis

- Lung cancer is the leading cause of cancer-related deaths worldwide, with ~20-40% of patients developing brain metastases (LCBM) during the course of their disease.¹
- LCBM is associated with poor prognosis, reduced quality of life, and limited treatment options.^{1,2}
- The molecular mechanisms driving brain metastasis remain incompletely understood, highlighting the need for novel predictive markers and therapeutic targets.

CHRM4: Biological Rationale

- CHRM4 (muscarinic acetylcholine receptor M4) is a G protein-coupled receptor involved in neurotransmission, cell signaling, and tumor progression.³
- Emerging evidence suggests CHRM4 may influence cancer cell proliferation, migration, and invasion in other malignancies.^{1,4}
- Its role in lung cancer progression and particularly brain metastasis has not been well defined.
- Recent research in our lab indicated that CHRM4 potentially suppresses brain metastasis of breast cancer.
- Distinguishing morphological and molecular features, including CHRM4 expression, will be informative for the development of AI-based tools for cancer prognosis.



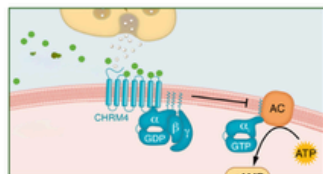
HYPOTHESIS AND OBJECTIVES

Hypothesis

Given the potential tumor suppressor role of CHRM4 in solid cancers, we hypothesize that CHRM4 will suppress lung cancer progression and brain metastasis.

Objectives

- Examine CHRM4 expression in primary and secondary lung tumours and correlate expression with LCBM incidence and progression.
- Identify morphological differences in cancer cells between met, non-met, and brain-metastasized samples.



METHODOLOGY

Tissue Processing	Hematoxylin & Eosin Staining	CHRM4 Immunohistochemistry (Immunostaining)	Pathology Review
- Fresh frozen lung and brain tumour tissues - Sectioned at 10-12 um thickness using a cryostat - Mounted on charged slides	- Stain with hematoxylin (nuclear staining) - Rinse in running water - Counterstain with eosin - Dehydrate, clear and mount with coverslip	- Incubate with primary antibody against CHRM4 - Incubate with secondary antibody (fluorescence-conjugated) - Develop with chromogen - Mount with Dapi containing mounting media	- Reviewed by pathologist to generate trends amongst slides - Assessment of morphology, immune-cell infiltration, necrosis and hemorrhage

Retrospective Cohort Study

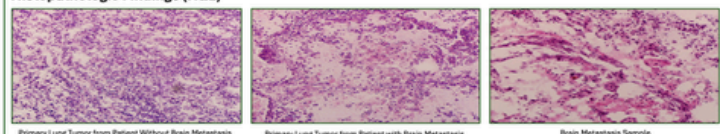
- De-identified tumour samples and clinical data obtained from the Alberta Cancer Research Biobank and Brain Tumor Tissue Bank.
- Total of 90 lung adenocarcinoma samples.
- Patients grouped based on development of brain metastasis.

Group	Sample Type	Patient Context	n
1	Primary Lung Tumour	Patients without brain metastasis	30
2	Primary Lung Tumour	Patients who developed brain metastasis	30
3	Brain Metastasis	Metastatic lung cancer tissue isolated from the brain	30

Clinical variables: age, sex, stage, smoking history, time to brain metastasis, overall survival (where available)

RESULTS

Histopathologic Findings (H&E)



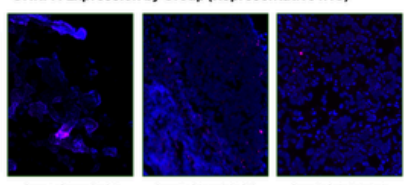
Histopathologic Features (Qualitative Assessment)

Feature	Group 1 (Primary Lung Cancer with no metastases)	Group 2 (Primary Lung Cancer with metastases)	Group 3 (Brain Metastasis)
Tumor Morphology	More organized, better differentiated	More heterogeneous, less differentiated	Metastatic tumor within brain tissue, highly heterogeneous
Necrosis	Minimal to focal	Focal to moderate	Moderate to extensive
Hemorrhage	Rare to focal	Focal	Frequent to prominent
Immune Cells	Mild	Mild to moderate	Variable

Qualitative IHC Assessment (CHRM4 Expression)

Group	Relative CHRM4 Expression (Observed)
1 – Primary (no BM)	Increased
2 – Primary (with BM)	Decreased
3 – Brain Metastasis	Decreased

CHRM4 Expression by Group (Representative IHC)



CONCLUSION

- Qualitative assessment showed that CHRM4 expression was reduced in primary lung tumours from patients who developed brain metastasis and in brain metastatic lesions compared with primary tumours from patients without brain metastasis, supporting our hypothesis.
- Histopathologic analysis demonstrated greater tumour heterogeneity, necrosis, and hemorrhage in metastatic disease, with these features particularly prominent in brain metastatic lesions.
- Validation in larger, multi-institutional cohorts with clinical outcome data is needed to determine the clinical relevance and predictive value of CHRM4.
- Further studies are also needed to define the mechanistic role of CHRM4 signaling in lung cancer progression and metastasis and explore its potential as a therapeutic target.
- Clinical correlation analysis is ongoing.

Overall: These findings support continued investigation of CHRM4 as a potential biomarker of LCBM risk and a candidate molecular target in lung cancer.

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ACKNOWLEDGEMENTS

This project was funded by the University of Saskatchewan College of Medicine, Dean's Summer Projects.



Nanditha Prasad (Dr. Anand Krishnan)

Exploring Perineural Invasion Model for Breast Cancer Recurrence studies

Perineural invasion (PNI) is the invasion of cancer cells into and around the peripheral nerves. PNI is a known risk factor for locoregional recurrence of breast cancer (BC). Our lab recently developed a novel in vitro model to study PNI. In this project we attempted to model the locoregional recurrence in BC using the PNI model. GFP-tagged BC cells (MDA-MB-231) were co-cultured with rat dorsal root ganglion (DRG)-nerve preparations in a 3D system for either 3-days or 7-days, after which the BC cells were washed-off using ice-cold DPBS. Then, the DRG-nerve tissues were reseeded in new culture wells without cancer cells for 7 days. The results suggest that a significantly higher number of BC cells undergo PNI by day-7 compared to day-3. Additionally, BC PNI cells exit events were only observed in day-3 reseeded co-culture suggesting a recurrence like status but this needs further validation. Day-3 and day-7 DRG-nerve sections were stained for Ki-67 to validate the proliferation status of the BC PNI cells. The results suggest that more BC PNI cells lose Ki-67 expression by day-7 compared to day-3 which further suggests that the nerve-invaded BC cells slow down their proliferation the more they are within the nerve niche.

INTRODUCTION

➤ Perineural Invasion (PNI) and Breast Cancer (BC)

- PNI is the invasion of cancer cells into and around peripheral nerves¹.
- PNI is significantly associated with locoregional recurrence in BC².

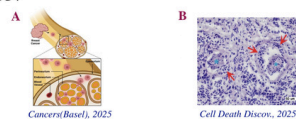


Figure 1: (A) A cartoon showing PNI.³ (B) Hematoxylin and Eosin (H&E) stained human breast tumour section showing PNI (red arrows, the cyan asterisks indicate the nerves).⁴

➤ In vitro PNI model and characterization of PNI cells

- Our lab recently developed a novel *in vitro* model to study PNI and characterized PNI-competent BC cells.⁴
- Our preliminary data suggested a dormant status for PNI cells, as most PNI cells did not express the cell proliferation marker Ki-67.⁴
- However, validation of the proliferation status of PNI cells require quantification of Ki-67⁺ PNI cells.
- Similarly, given that PNI is a risk factor for recurrence, the *in vitro* PNI model may be useful for studying cancer recurrence as well.

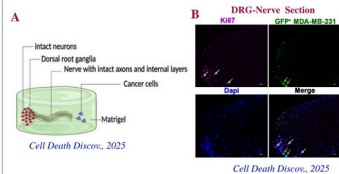


Figure 2: (A) *In vitro* PNI model (involves co-culture of DRG-nerve explant and cancer cells).⁴ (B) Representative images of a section of DRG-nerve from 2-week-old PNI model show no expression of Ki-67 in PNI+ cells.⁴

HYPOTHESIS

Given that PNI is a risk factor for recurrence, we hypothesize that the *in vitro* PNI model can be used for studying locoregional recurrence in BC.

OBJECTIVES

Objective 1: Validate the proliferation status of PNI cells by quantifying Ki-67⁺ PNI cells.

Objective 2: Explore the application of *in vitro* PNI model for studying BC recurrence.

METHODOLOGY

- The cell line used for this project is MDA-MB-231 (Triple negative BC cell line)

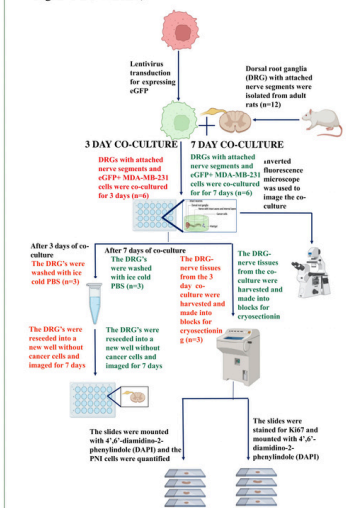


Figure 3: Illustration of the complete experimental workflow

RESULTS

➤ PNI cells (+/-Ki-67) in DRG-nerve sections (Day 3 culture)

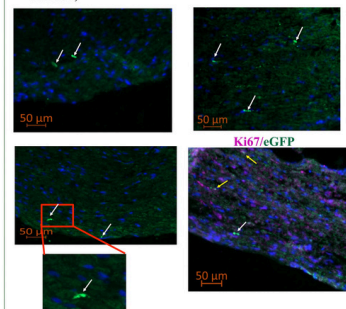


Figure 4: (A) Representative images of DRG-nerve sections at day 3 (images from three technical replicates are shown; PNI cells are shown using white arrows). (B) A representative image of PNI cells with Ki-67 expression is shown using yellow arrows and a PNI cell without Ki-67 expression is shown using a white arrow.

➤ PNI cells (+/-Ki-67) in DRG-nerve sections (Day 7 culture)

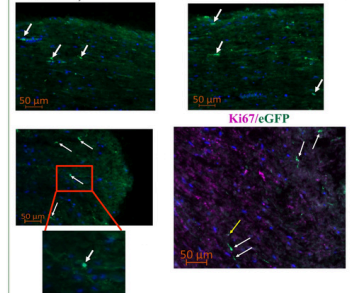


Figure 5: (A) Representative images of DRG-nerve sections at day 7 (images from three technical replicates are shown; PNI cells are shown using white arrows). (B) A representative image of PNI cell with Ki-67 expression is shown using a yellow arrow and PNI cells without Ki-67 expression is shown using white arrows.

➤ PNI cells may enter a non-proliferative state the longer they remain in nerves

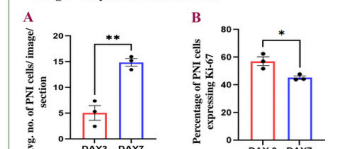


Figure 6: (A) Quantification of PNI cells in Day 3 and Day 7 DRG-nerve sections (n=3; Student's 't' test; **p<0.01). (B) Quantification of PNI cells expressing Ki-67 in Day 3 and Day 7 DRG-nerve sections (n=3; Student's 't' test *p<0.05).

➤ Exploration of PNI model for cancer recurrence studies: 3-day PNI culture reseeding paradigm

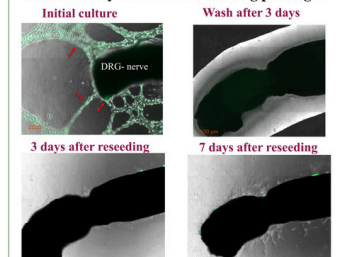


Figure 7: Representative images of PNI culture before and after reseeding the DRG-nerve (DRG-nerve is reseeded after 3 days of initial culture with cancer cells). White arrows show potential exit of PNI cells.

➤ Exploration of PNI model for cancer recurrence studies: 7-day PNI culture reseeding paradigm

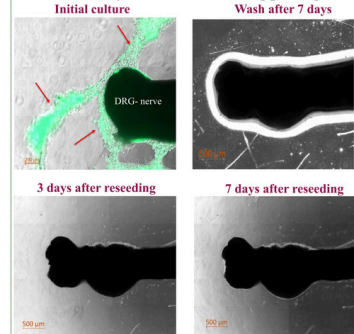


Figure 8: Representative images of PNI culture before and after reseeding the DRG-nerve (DRG-nerve is reseeded after 7 days of initial culture with cancer cells). No exit events are observed.

CONCLUSIONS

- The incidence of PNI is directly proportional to the time of exposure between cancer cells and nerves.
- BC cells participating in PNI lose their ability to proliferate the longer they reside in the nerves.
- In vitro* PNI model shows PNI cell exit events at an early reseeding timepoint, but this observation needs further validation and quantitative analysis.

FUTURE DIRECTIONS

- Repeat the recurrence model experiment with additional timepoints (both reseeding and analysis timepoints)

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ACKNOWLEDGEMENTS

Thanks to Dr. Anand Krishnan, all the Krishnan Lab members, CMSNRC and the funding agencies below for the support of this research.





Jenna Prolius (Dr. Julie Stakiw)

Retrospective Evaluation of Immunoglobulin Replacement Therapy in Relapsed/Refractory Multiple Myeloma Patients Treated with BCMA Bispecific Antibodies

Background: Immunoglobulin replacement therapy (IGRT) is used to mitigate infection risk from secondary hypogammaglobulinemia during bispecific antibody treatment for relapsed/refractory multiple myeloma (RRMM), but optimal timing, dosing, duration, and use of IgG trough levels remain uncertain. We aimed to characterize IGRT use during bispecific therapy for RRMM in Saskatchewan, including IgG trough monitoring, and explore associations with infection outcomes.

Methods: We conducted a retrospective chart review of RRMM patients receiving bispecific antibodies in Saskatchewan from March 2023–April 2026. IGRT use, IgG levels, and infection outcomes were summarized descriptively.

Results: Thirty-nine patients were included; 30 (77%) received IGRT. Before bispecific therapy, 53% had IgG <4 g/L. At IGRT initiation, 79% had IgG <4 g/L and 35% had experienced severe or recurrent infection. IGRT timing and dosing varied: 40% started at the recommended 0.4 g/kg ABW. During IGRT, 59% reached IgG ≥ 7 g/L and 37% reached ≥ 9 g/L. Five patients discontinued IGRT: all subsequently had IgG <4 g/L, 80% restarted IGRT, and 60% developed infection while off IGRT, none grade ≥ 3 .

Conclusion: IGRT use during bispecific therapy varied substantially in timing of initiation and dose. Further study is needed to define the role of IgG trough levels in guiding IGRT duration.

Real-World Patterns of Immunoglobulin Use During Bispecific Antibody Treatment for Multiple Myeloma

Jenna Prollius¹, Dr. Julie Stakiw^{1,2}, Dr. Oksana Prokopchuk-Gauk^{1,3}

¹College of Medicine, University of Saskatchewan ²Saskatchewan Cancer Agency ³Department of Pathology and Laboratory Medicine, Saskatchewan Health Authority

BACKGROUND

- B-cell maturation antigen (BCMA) directed bispecific antibodies, including elranatamab and teclistamab, are highly effective therapies for relapsed or refractory multiple myeloma (RRMM).^{1,2}
- Bispecific therapy causes profound and persistent secondary hypogammaglobulinemia (SHG) in upwards of 70% of patients,³ increasing the risk of infection.
- Infection burden is high during bispecific therapy: pooled real-world data demonstrate severe (grade ≥ 3) infection rates of 34% for elranatamab and 23% for teclistamab.⁴
- Immunoglobulin replacement therapy (IGRT) is used to mitigate infection risk during bispecific therapy.
- Retrospective studies report up to 10-fold reduction in severe infections,⁵ but there is no consensus on appropriate timing, dosing, and duration of IGRT.
- Current guidelines recommend pre-emptive IGRT after evidence of SHG, defined as serum IgG < 4 g/L.^{3,6,7}
- Recent reviews advocate for prophylactic IGRT, regardless of IgG levels, given the apparent inevitability of SHG during bispecific therapy and limitations of IgG measurements in RRMM.^{8,9}
- IGRT use in Canada is rising at a projected 10% per year, requiring careful stewardship to manage supply constraints and health system costs.¹⁰
- There are no Canadian studies on IGRT utilization during bispecific therapy for RRMM, particularly IgG trough level monitoring, to inform stewardship decisions around when IGRT can be safely reduced or discontinued.

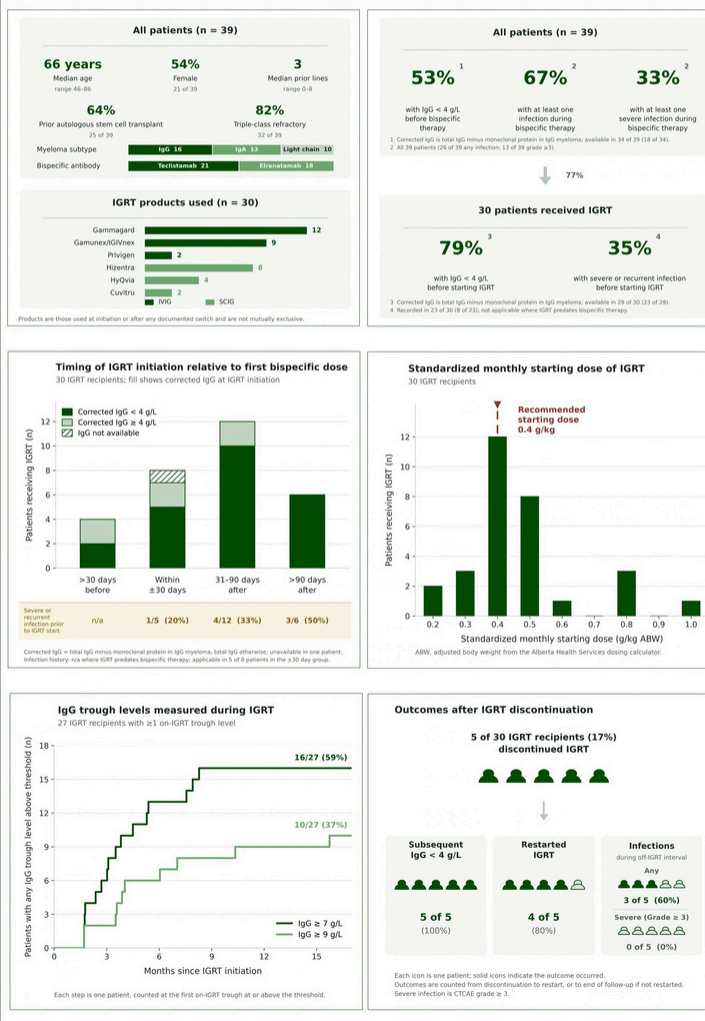
PURPOSE

- The optimal **timing, dosing, and duration** of IGRT during bispecific therapy for RRMM is not yet known.
- The current retrospective study aims to describe patterns of IGRT use during bispecific therapy for RRMM in Saskatchewan and any associations with infection outcomes and serum IgG levels.

METHODS

- Single-center retrospective chart review including RRMM patients who received at least 1 dose of bispecific therapy between March 2023 and April 2026.
- Electronic health records from the Saskatchewan Cancer Agency and Saskatchewan Health Authority were reviewed for demographics, disease characteristics, prior therapies, IgG levels, IGRT use (dose, route, frequency), infection characteristics, and survival outcomes.
- Descriptive statistics were used to summarize patient characteristics, treatment patterns, and infections. Logistic regression will explore predictors of infection, IGRT use, and IgG trough level recovery [in progress].

RESULTS



CONCLUSIONS

- Between March 2023 and April 2026, 39 RRMM patients received bispecific antibodies (teclistamab or elranatamab).
- 53% of patients met criteria for SHG (IgG < 4 g/L) prior to starting bispecific therapy.
- Infection risk is high in this cohort: 33% of patients experienced at least one severe infection.
- Most (30/39) patients received IGRT during bispecific therapy.
- At the time of IGRT start, 79% met criteria for SHG (IgG < 4 g/L) and 35% had a severe or recurrent infection during bispecific therapy.
- Timing of IGRT initiation was variable, with the largest proportion (12/30) starting IGRT 31-90 days after bispecific therapy.
- Dosing of IGRT also varied, with 40% starting at the currently recommended 0.4 g/kg adjusted body weight.
- IgG trough level measurements during IGRT and implications for IGRT stewardship.
- Many patients had at least one IgG trough level within normal range during IGRT, raising the question of whether IGRT could be reduced or discontinued.
- 59% of patients reached IgG ≥ 7 g/L.
- 37% of patients reached IgG ≥ 9 g/L.
- 5/30 patients discontinued IGRT during bispecific therapy:
- 100% had a subsequent IgG < 4 g/L.
- 80% restarted IGRT.
- 60% developed at least 1 infection while off IGRT, but none were severe (grade ≥ 3).
- Further studies are needed to determine whether and how IgG trough levels should guide decisions to continue IGRT during bispecific therapy.

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ACKNOWLEDGEMENTS

This project was funded by the University of Saskatchewan College of Medicine, Dean's Summer Projects.



Hamza Saghir (Drs. Shahid Ahmed & Rabia Shahid)

Impact of Diabetes Mellitus on Pathologic Complete Response and Disease-Free Survival in Following Neoadjuvant Therapy In Stage I–III Breast Cancer

Diabetes mellitus (DM) is a common comorbidity among women with breast cancer and is associated with poorer overall survival. Pathological complete response (pCR) following neoadjuvant chemotherapy is associated with improved survival, particularly in triple-negative and HER2-positive breast cancers. Emerging evidence suggests insulin resistance and diabetes may influence response to preoperative chemotherapy and pCR. The purpose of this study is to evaluate the association of pre-existing DM with pCR and disease-free survival among women with stage I–III breast cancer receiving neoadjuvant systemic therapy. A retrospective cohort study of adult women treated at the Saskatchewan or Allan Blair Cancer Centres from 2019 to 2024 was conducted. Eligible patients received neoadjuvant chemotherapy, with or without immunotherapy or HER2-targeted therapy. The primary endpoint is pCR, defined as ypT0/Tis ypN0. Secondary endpoints include disease-free survival (DFS), treatment modification or delay, treatment completion, and acute care utilization. The results showed that patients with DM had greater comorbidity burden and poorer performance status (both $p < 0.001$). pCR was lower with DM (22.0% vs 30.5%), although not statistically significant ($p = 0.352$). Interestingly, patients with DM received fewer chemotherapy cycles (6.78 vs 7.38, $p = 0.042$) and had lower treatment completion (69.0% vs 86.6%, $p = 0.026$). Crude DFS event (31.4% vs 14.9%, $p = 0.027$) and mortality proportions (28.2% vs 12.2%, $p = 0.014$) were also higher with DM.

Impact of Diabetes Mellitus on Pathologic Complete Response and Disease-Free Survival in Following Neoadjuvant Therapy In Stage I–III Breast Cancer

Hamza Saghir¹, Dr. Shahid Ahmed¹, Dr. Rabia Shahid¹, Dr. Hisham Elshoni¹, Ramy Habib

¹College of Medicine, University of Saskatchewan, Saskatoon, SK, Canada

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer among Canadian women and a leading cause of cancer-related mortality [1,2]. Diabetes mellitus (DM) is a common comorbidity among patients with breast cancer and has been associated with poorer disease-free and overall survival [3,4].

Pathological complete response (pCR) following neoadjuvant systemic therapy is associated with improved survival, particularly in triple-negative (TNBC) and HER2-positive breast cancer [7]. Insulin resistance and DM may influence treatment response and tolerance; however, their impact on pCR remains unclear [5,6].

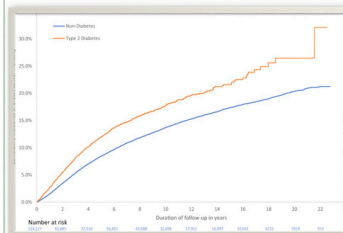


Figure 1. Cumulative incidence curves of breast cancer mortality for type 2 diabetes vs. non-diabetes among patients with non-metastatic breast cancer [6].

OBJECTIVES

Primary Objective

Evaluate the association between pre-existing DM and pCR following neoadjuvant systemic therapy in women with stage I–III breast cancer.

Secondary Objectives

Compare treatment completion and treatment delays/interruptions by DM status.

Evaluate the association between DM and disease-free survival (DFS).

RESULTS

Patients with DM have greater comorbidity burden (multimorbidity: 97.0% vs 49.5%, $p<0.001$) and significantly different performance status ($p<0.001$).

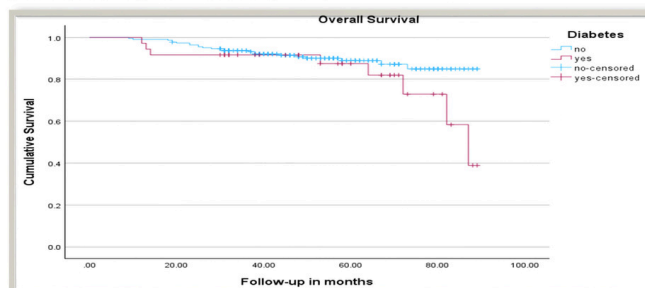


Figure 2. Analysis showed numerically lower overall survival among patients with diabetes, with a median survival of 87.0 months (95% CI 77.4–96.6), while median survival was not reached in patients without diabetes.

Pathological Complete Response

pCR is numerically lower among patients with DM: 22.0% vs 30.5%. However, this difference is not statistically significant ($p=0.352$).

Treatment Delays/Interruptions

Patients with DM received fewer chemotherapy cycles, 6.78 vs 7.38 cycles, $p=0.042$. Completion of planned therapy is lower with DM: 69.0% vs 86.6%, $p=0.026$. Treatment delay/interruption is more frequent with DM (32.3% vs 21.1%), although not statistically significant ($p=0.172$).

Survival Outcomes

Crude invasive-DFS event proportions are higher with DM: 31.4% vs 14.9%, $p=0.027$. Crude mortality is also higher with DM: 28.2% vs 12.2%, $p=0.014$.

Data analysis is still happening and these are preliminary findings.

METHODS

Multicentre retrospective cohort study of adult women with stage I–III breast cancer treated at the Saskatchewan Cancer Centre and Allan Blair Cancer Centre from 2019–2024. Included patients received neoadjuvant chemotherapy, with or without immunotherapy or HER2-targeted therapy.

Primary endpoint: pCR, defined as ypT0/Tis ypN0

Secondary endpoints: DFS, treatment completion, and treatment delay/interruption.

Analysis

Categorical variables are compared using Fisher's exact test and continuous variables using Welch's t-test. Multivariable logistic regression is planned to assess predictors of pCR; Kaplan–Meier and Cox proportional hazards analyses are planned for DFS.

These comparisons are descriptive; adjusted time-to-event analyses are ongoing.

CONCLUSIONS

Pre-existing DM is associated with greater comorbidity burden, fewer chemotherapy cycles, and lower completion of planned therapy.

Although pCR is numerically lower among patients with DM (22.0% vs 30.5%), the difference is not statistically significant.

Patients with DM have higher crude invasive-DFS event and mortality proportions.

These findings suggest that treatment delivery and underlying comorbidity may contribute to poorer outcomes among patients with breast cancer and DM.

Adjusted analyses are needed to determine whether DM is independently associated with pCR and survival.

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ACKNOWLEDGEMENT

I thank Dr. Shahid Ahmed and Dr. Hisham Elshoni for their help, mentorship, and contributions to this project. Findings are based off of preliminary data from approximately 280 of 666 patients, with an updated final analysis to follow as additional data become available.

Pediatrics





Andreea Ababei (Dr. Basmah Ishteiwi)

Clinical Profile of Febrile Infants Aged ≤ 90 Days Admitted to the Pediatric Ward at Regina General Hospital

Fever in infants is a common reason for hospital admission and remains a critical diagnostic challenge, with considerable variation in investigation and treatment. Local patterns of inpatient care in southern Saskatchewan have not previously been described. We conducted a retrospective chart review of infants aged ≤ 90 days admitted to Regina General Hospital with fever or suspected infection between July 2021 and December 2024. We included 44 infants, with a mean age of 18 days (range 2-35). Respiratory infection/bronchiolitis was the most common discharge diagnosis (25.0%). Lumbar puncture was performed in 59.1% (26/44) of infants. Positive results were identified in 23.7% of urine cultures ($n=9$), 9.5% of blood cultures ($n=4$), and 15.4% of CSF cultures ($n=4$). Antibiotics were administered to 68.2%, respiratory support was required in 25.0%, and 18.2% required ICU transfer. Fourteen infants (31.8%) stayed longer than 7 days. Younger infants and those with $\text{CRP} \geq 20$ mg/L were more likely to stay longer than 7 days, while infants receiving antibiotics had longer stays overall. Complications occurred in 22.7%, most commonly respiratory deterioration, while 81.8% were discharged home. These findings characterize inpatient practices and provide evidence for standardized care pathways. Future work should evaluate whether clinical decision tools and procalcitonin can support safe, more focused investigations and treatments.

Clinical Profile of Febrile Infants Aged ≤90 Days Admitted to the Pediatric Ward at Regina General Hospital

Andreea Ababei¹, Montana Mellor¹, Sabiha Sultana², Dr. Basmah Ishteiwi^{1,2}

¹College of Medicine, University of Saskatchewan, ²Saskatchewan Health Authority



WHY THIS MATTERS

- Fever in infants is a common reason for hospital admission and remains a critical diagnostic challenge^{1,2}.
- Despite national guidelines, considerable variation exists in how febrile infants are investigated and treated^{3,4}.
- This variation may contribute to inconsistent care and unnecessary use of hospital resources.
- The Canadian Paediatric Society recommends risk-stratified management to support consistent, evidence-based clinical decisions^{1,2}.
- Local data describing the characteristics and management of febrile infants admitted in southern Saskatchewan are lacking.
- This study provides local data to inform standardized care pathways and future pediatric quality-improvement initiatives.

OBJECTIVE

Describe the clinical profile and hospital course of admitted febrile infants ≤90 days.

METHODS

- Retrospective chart review
- Pediatric ward at RGH
- July 2021 to December 2024
- Exclusion: prematurity, prior hospitalization, chronic illness
- Fisher exact and Wilcoxon tests
- Age- and CRP-adjusted logistic model

COHORT

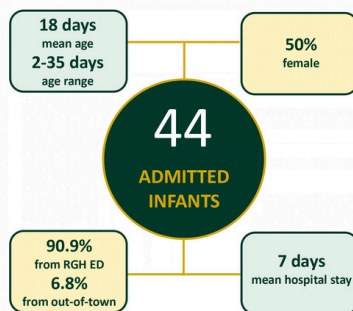
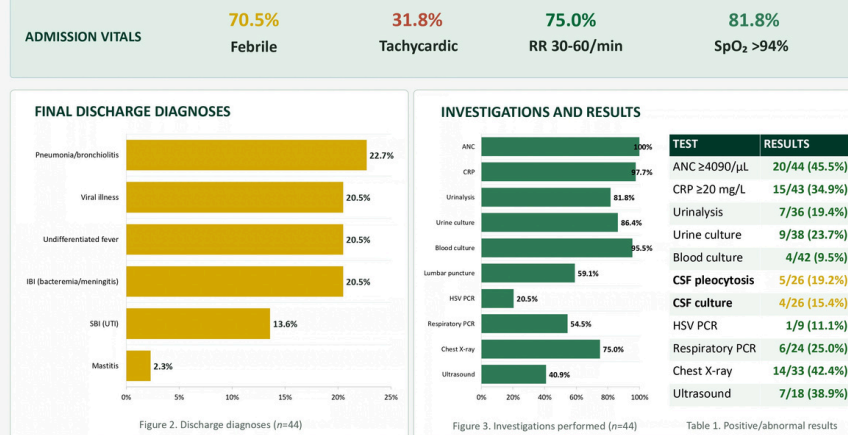


Figure 1. Cohort characteristics

RESULTS



POSITIVE MICROBIOLOGY RESULTS

URINE CULTURE n=9	BLOOD CULTURE n=4	CSF n=4
<i>E. coli</i> 3	<i>E. coli</i> 2	Enterovirus 2
<i>Enterococcus</i> 1	<i>Citrobacter koseri</i> 1	<i>Citrobacter koseri</i> 1
Polymicrobial growth 5	<i>Staphylococcus aureus</i> 1	Gram-positive cocci 1

WHAT HAPPENED?

CARE RECEIVED	68.2% (30/44) Antibiotics	25.0% (11/44) Respiratory support		
HOSPITAL OUTCOMES	18.2% (8/44) ICU transfer	31.8% (14/44) Stay >7 days	22.7% (10/44) Complications	81.8% (36/44) Discharged home

SECONDARY EXPLORATORY FINDINGS

ASSOCIATION	RESULT	P-VALUE
Younger age → prolonged LOS (>7 days)	Median 12.5 vs 20.5 days; aOR/day 0.88 (95% CI 0.78-0.97)	0.009
CRP ≥20 mg/L → prolonged LOS (>7 days)	53.3% vs 17.9%; aOR 5.11 (95% CI 1.20-25.90)	0.027
Antibiotic use → longer LOS (in days)	Univariable association	0.021
Respiratory support → ICU transfer	Fisher exact association	<0.001

Table 2. Exploratory factors associated with clinical outcomes; LOS = length of stay

DISCUSSION

- Respiratory infection/bronchitis were the most common diagnoses (25.0%).
- Investigation and treatment were frequent: 95.5% underwent blood cultures, 59.1% underwent lumbar punctures, and 68.2% received antibiotics. Positive blood cultures were identified in 9.5%, while positive CSF cultures occurred in 15.4%.
- Respiratory support was strongly associated with ICU transfer ($p < 0.001$), suggesting that respiratory support requirements were a marker of acute illness severity.
- 31.8% of infants stayed longer than 7 days, and these infants were younger than those with shorter stays.
- CRP ≥20 mg/L was associated with prolonged LOS (>7 days). After adjusting for age, elevated CRP remained associated with approximately 5x higher odds of prolonged LOS (>7 days).
- Antibiotic use was associated with longer LOS (in days; $p = 0.021$), although this likely reflects treatment indication and underlying illness severity rather than a causal effect.
- Complications occurred in 22.7% of infants, with respiratory deterioration being the most common (70.0%).
- Most infants were discharged home (81.8%), and only 4.5% returned to the ED or were readmitted.
- Findings support re-examining thresholds for LP and empiric antibiotics in carefully selected low-risk infants to reduce testing burden, antibiotic use, hospital stay, and infant and family stress.

LIMITATIONS

- Small sample size ($n = 44$)
- Infants were 2-35 days old, limiting generalizability to infants ages 36-90 days
- Rural and remote referrals may have been incompletely captured
- Retrospective documentation
- Temporal relationships cannot be established

TAKE-HOME MESSAGE

This cohort had diverse diagnoses and generally favourable outcomes but underwent frequent invasive testing and empiric treatment. Overall, our findings support the use of standardized, risk-based evaluation using biomarkers such as procalcitonin.

REFERENCES AND ACKNOWLEDGEMENTS

This project was supported by the College of Medicine 2026 Dean's Project Program. We gratefully acknowledge the support provided by the SHA Research Department.



Ethan Adams (Dr. Tyler Wenzel)

Using Stem Cells to Understand and Treat Early Signs of X-Linked Adrenoleukodystrophy

Introduction: X-linked adrenoleukodystrophy (X-ALD) is a peroxisomal disorder caused by ABCD1 mutations, resulting in impaired VLCFA metabolism and C26:0-LPC accumulation. Cerebral adrenoleukodystrophy (cALD) is its most severe phenotype of X-ALD. Current treatment of cALD relies on allogeneous hematopoietic stem cell transplantation (alloHSCT), which has significant limitations. Microglia transplantation offers a potential alternative capable of brain-wide restoration.

Hypothesis: Transplantation of healthy human induced pluripotent stem cell (hiPSC)-derived microglia can restore VLCFA metabolism in cALD.

Methods: Fibroblasts from a healthy individual and a cALD patient were analyzed by immunoblotting and liquid chromatography-mass spectrometry. Fibroblasts were reprogrammed into hiPSCs and differentiated into healthy microglia and cALD brain organoids for coculture. Postnatal mice were treated with PLX5622 to deplete endogenous microglia, transplanted with hiPSC-derived microglia, and analyzed by fluorescent microscopy.

Results: cALD fibroblasts exhibited impaired VLCFA metabolism, indicated by absent ABCD1 expression and an elevated C26:0/C22:0-LPC ratio. Coculturing healthy microglia with X-ALD brain organoids restored the C26:0/C22:0-LPC ratio to baseline. Transplanted hiPSC-derived microglia survived in postnatal mice following endogenous microglia depletion.

Conclusion: In vitro and preliminary in vivo results support the feasibility of microglia transplantation as a potential treatment for cALD, with potential applications in other neurometabolic diseases.



Using Stem Cells to Understand and Treat Early Signs of X-Linked Adrenoleukodystrophy

Ethan Adams¹, Kasra Khunjush¹, Miku Tibule¹, Olivia Dyck¹, and Tyler Wenzel¹

¹Department of Psychiatry, College of Medicine, University of Saskatchewan, Saskatoon, SK



Introduction

- X-linked adrenoleukodystrophy (X-ALD) is a metabolic disease caused by mutations in the *ABCD1* gene, resulting in the accumulation of very-long-chain fatty acids (VLCFAs) and VLCFA-containing lipids, including C26:0-lysophosphatidylcholine (LPC).¹
- Cerebral adrenoleukodystrophy (cALD) is the most severe phenotype of X-ALD that causes rapid, irreversible neurological damage following symptom onset.²
- Approximately 40% of males with X-ALD develop cALD by 20 years of age; once symptomatic, cALD is rapidly progressive and associated with a median survival of approximately 2–4 years.²

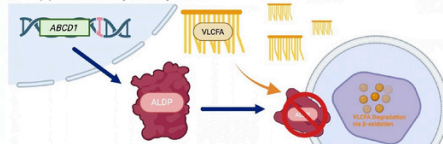


Figure 1. Cellular mechanism of X-ALD. ABCD1 mutation disrupts adrenoleukodystrophy protein (ALDP) function, impairing VLCFA transport into peroxisomes for degradation, thereby promoting their toxic accumulation.

- The only current treatment for cALD is allogeneic hematopoietic stem cell transplantation (alloHSCT), which is associated with 10–25% treatment-related mortality and chemotherapy-induced neurotoxicity.³
- Additionally, alloHSCT requires 12–16 months to achieve disease stabilization which makes patients with progressed neurological symptoms ineligible.⁴
- Microglia are capable of brain-wide restoration as they can move throughout the central nervous system.⁵

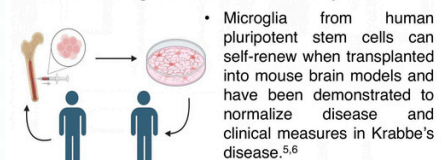


Figure 2. Schematic visualization of alloHSCT.

Hypothesis

- Transplantation of healthy human induced pluripotent stem cell (hiPSC)-derived microglia can restore VLCFA metabolism in cALD and provide a potential alternative to alloHSCT.

Results

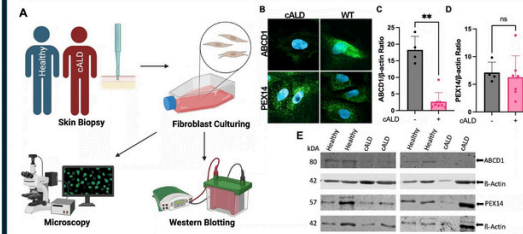


Figure 3. cALD fibroblasts have reduced ABCD1 expression while normal peroxisome formation. (A) Schematic of fibroblast isolation from patient skin biopsies and subsequent analysis by fluorescent microscopy and Western blotting. (B) Preliminary microscopy images showing reduced expression of ABCD1 and normal expression of peroxisomal biogenesis factor 14 (PEX14) in cALD fibroblasts compared to wild-type (WT) fibroblasts. Microscopy results were confirmed with Western Blot analysis (C, D). (E) Representative immunoblots used to quantify ABCD1 (C) and PEX14 (D).

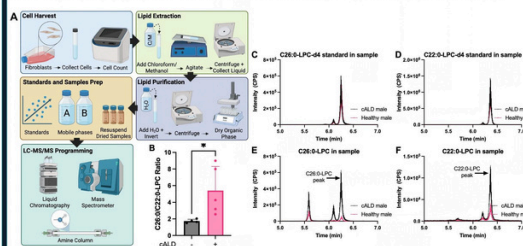


Figure 4. cALD fibroblasts exhibit an increased C26:0/C22:0-LPC ratio. (A) Schematic of modified Folch's lipid extraction method to quantify C26:0-LPC and C22:0-LPC in fibroblasts. (B) C26:0-LPC/C22:0-LPC ratio was elevated in cALD fibroblasts compared with healthy controls. LC-MS chromatograms of (C) deuterated C26:0-LPC and (D) C22:0-LPC analytical standards. Chromatograms of (E) C26:0-LPC and (F) C22:0-LPC in cALD and healthy fibroblast samples used to calculate the C26:0-LPC/C22:0-LPC ratio.

Conclusions

- cALD fibroblasts exhibit impaired VLCFA metabolism, demonstrated by a lack of functional ABCD1 protein expression and an elevated C26:0/C22:0-LPC ratio.
- Co-culturing healthy microglia with cALD brain organoids reduces the ratio of C26:0/C22:0-LPC close to baseline levels.
- PLX5622 effectively depletes endogenous microglia, and hiPSC-derived microglia can be transplanted into mouse pups.

Implications

- Successful treatment of cALD using microglia transplantation could also become a treatment option for other neurometabolic diseases and advance the development of stem cell-based therapies.

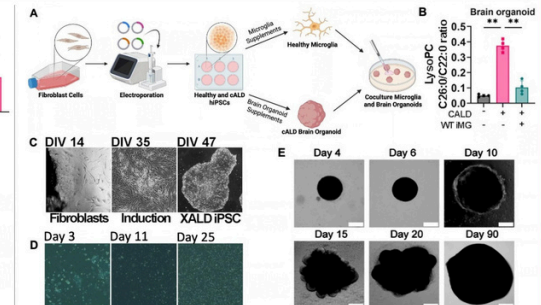


Figure 5. C26:0-LPC/C22:0-LPC was reduced in cALD brain organoids cocultured with microglia. (A) Schematic of experimental design. (B) C26:0-LPC/C22:0-LPC ratio, quantified by LC-MS, was reduced in cALD brain organoids co-cultured with WT microglia. (C) Microscopy images showing the transition of X-ALD fibroblasts to hiPSC after electroporation. (D) Microscopy images showing the development of microglia derived from healthy hiPSCs. (E) Microscopy images of the development of brain organoids derived from cALD hiPSCs.

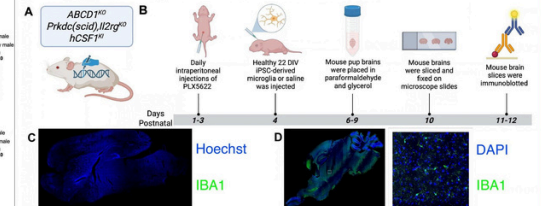


Figure 6. Mice microglia was depleted with PLX5622 and replaced with hiPSC-derived microglia. (A) Mouse model used. (B) Schematic of experimental timeline. (C) Fluorescent microscopy imaging showing the absence of IBA1, indicating the effective depletion of endogenous microglia by PLX5622, and of Hoechst for cell nuclei. (D) Fluorescent microscopy imaging of IBA1 for survival of transplanted hiPSC-derived microglia and of DAPI for cell nuclei.

Future Directions

- Collect mouse brains at 0.5-month intervals from 0.5–4.5 months post-transplantation to assess endogenous microglia depletion, transplanted microglia survival, and X-ALD biomarkers.

Acknowledgements

A special thanks to Deborah Michaels for mass spec. training and assistance.

Funding

RUH FOUNDATION
NSERC CRNSG
UNIVERSITY OF SASKATCHEWAN
SHRF

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Grace Braaten (Dr. Jonathan Gamble)

Eye Taping in Pediatric Anesthesia: A Randomized Pilot Study of Medical Adhesive-Related Skin Injury (MARSI) and Ocular Outcomes

Introduction: General anesthesia increases the risk of corneal injury.^{1,2} Although eye-taping is standard practice to reduce this risk, the optimal method for minimizing medical adhesive-related skin injury (MARSI) in children is unclear[DE1].³ To address the evidence gap, this study compares the safety and efficacy of three eye-taping methods in a pediatric population.

Methods: We conducted a prospective, randomized, three-arm pilot study, examining 119 children aged 2-12 undergoing elective surgery under general anesthesia at JPCH, Saskatoon, SK. Participants received Micropore, Transpore, or Tegaderm eye protection. MARSI and exposure keratopathy were assessed using standardized assessment scale postoperatively.^{2,3}

Results: MARSI incidence differed significantly by tape type ($p=0.004$): Micropore 2.5%, Transpore 17.9%, and Tegaderm 30%. Only mild MARSI reactions were observed. No corneal abrasions or exposure keratopathy were identified.

In an exploratory logistic regression model adjusting for age and eye-taping duration, tape type remained associated with MARSI incidence, whereas age ($p=0.566$) and eye-taping duration ($p=0.597$) were not significant predictors.

Conclusions: Tape selection influenced MARSI incidence in children undergoing general anesthesia. Micropore demonstrated the lowest MARSI incidence, while Tegaderm demonstrated the highest. All tapes appeared to provide effective ocular protection. Larger studies are needed to confirm whether Micropore provides a clinically meaningful skin-safety advantage.

[DE1]In your Poster you state “unknown”. Is it unclear or unknown? Make sure to be consistent. Depending on what you choose, you may need to adjust the sentence that follows: “to address the lack of evidence...” “to clarify this.....”. A few options depending on what you end up with.

Eye Taping in Pediatric Anesthesia: A Randomized Pilot Study of Medical Adhesive-Related Skin Injury (MARSI) and Ocular Outcomes

Grace Braaten BSc, Mary Ellen Walker PhD, Ryan Eidsness MD, Jonathan Gamble MD

INTRODUCTION

- General anesthesia increases the risk of corneal injury^{1,2}
- Eye-taping is standard practice to reduce this risk but may cause medical adhesive-related skin injury (MARSI)
- Pediatric patients may be at elevated risk of MARSI due to sensitive skin^{2,3}
- The optimal eye-taping method in children is unclear

OBJECTIVE AND HYPOTHESIS

Objective: Compare three commonly used eye-taping methods with respect to:

- MARSI
- Exposure keratopathy
- Corneal abrasion

Hypothesis: One eye-taping method would reduce MARSI while maintaining equivalent ocular protection

METHODS

Study Design

- Prospective randomized three-arm (by tape type) pilot study
- 119 children (2-12 years)
- Elective non-ophthalmic surgery

Randomization

- Micropore (n=40)
- Tegaderm (n=40)
- Transpore (n=39)

Post-operative Outcomes

- Primary:
 - MARSI incidence using validated assessment scale
- Secondary:
 - MARSI severity
 - Exposure keratopathy using modified validated assessment scale
 - Corneal abrasion

METHODS

Data Analysis

- Data summarized using counts (%), means (SD), and medians (IQR)
- χ^2 tests for categorical outcomes
- ANOVA/Kruskal-Wallis tests for continuous outcomes
- Exploratory logistic regression adjusting for age and eye-taping duration $p < 0.05$

RESULTS

Study population: average age of 89.9 months, 43.6% female, and 56.3% male

MARSI Outcomes

- MARSI incidence differed significantly by tape type ($p=0.004$): Micropore 2.5%, Transpore 17.9%, and Tegaderm 30%
- Only mild MARSI reactions were observed

Exploratory Adjusted Analysis

- Tape type remained associated with MARSI
- Age was not associated with MARSI ($p=0.566$)
- Eye-taping duration was not associated with MARSI ($p=0.597$)

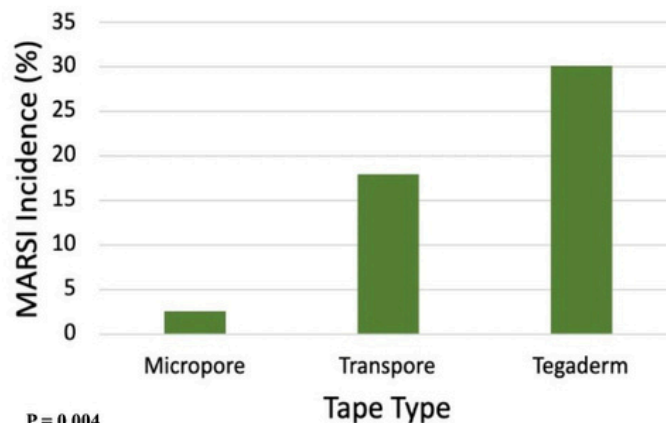


Figure 1. Incidence of MARSI by eye-taping method

Ocular Outcomes

- 1 No exposure keratopathy
- 2 No corneal abrasions
- 3 No differences among groups

CONCLUSIONS

- Tape selection may influence the risk of periorbital MARSI in pediatric patients undergoing general anesthesia
- Results suggest all tapes provided effective ocular protection
- Micropore demonstrated the most favourable skin-safety profile (lowest MARSI incidence)
- Tegaderm demonstrated the least favourable skin-safety profile (highest MARSI incidence)
- Age and eye-taping duration were not independently associated with MARSI incidence
- Larger studies are needed to confirm whether Micropore provides a clinically meaningful skin-safety advantage

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ACKNOWLEDGEMENTS



UNIVERSITY OF SASKATCHEWAN
College of Medicine
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Rowen Greene (Dr. Paul D'Alessandro)

Pediatric cancer presenting with anterior mediastinal mass in Saskatchewan: mixed methods case series

Pediatric anterior mediastinal masses (AMMs) encompass a group of malignancies that often present acutely, requiring emergent transport and workup. In Saskatchewan, pediatric oncology is centralized at Jim Pattison Children's Hospital (JPCH) in Saskatoon, serving a unique patient population over a large geographical area. In this study, we conducted a chart review to report on the timeliness of the diagnostic workup for patients presenting to JPCH with AMM since September 2019. Thirteen pediatric patients (mean age at diagnosis 12.6) and their caregivers were identified to be included in the study. The mean time from admission to diagnosis was 4.0 +/- 3.6 days; however, 23.1% of patients had a recorded misdiagnosis prior to oncology referral and workup. In a second aim, we assessed caregiver thoughts and perspectives around the time of diagnosis via survey. Inductive thematic analysis of caregiver responses identified four themes: caregiver confusion at the time of diagnosis, stress during diagnostics and transport, strong emotions regarding perceived delayed or missed diagnosis, and appreciation for the multidisciplinary team. These findings exemplify timely diagnostic workup at JPCH while outlining a need for procedural standardization and family support in the days leading up to a definitive diagnosis and oncology referral.

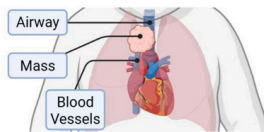
Pediatric cancer presenting with anterior mediastinal mass in Saskatchewan: mixed methods case series

Rowen Greene BSc¹, Paul D'Alessandro MD, MSc, FRCPC¹⁻³

¹Department of Medicine, University of Saskatchewan, Saskatoon, SK S7N 5A2, Canada ²Department of Pediatrics, University of Saskatchewan College of Medicine, Saskatoon SK, Canada ³Jim Pattison Children's Hospital, Saskatoon SK, Canada

Introduction

- Pediatric anterior mediastinal mass (AMM) present with a range of diagnostic challenges due to anesthetic risk, high risk symptoms at presentation, and low incidence rates
- Patients may present with dyspnea, orthopnea, and obstructive symptoms due to mass effects in the mediastinum [1-3]
- In Saskatchewan, there is no standardized protocol for the management of diagnostic workup for AMM
- There is also minimal understanding of the prehospital experience for patients and families during early management



Objectives

- 1) Assess incidence rates of AMM in SK
- 2) Assess timeliness of management and diagnosis of pediatric AMM in SK
- 3) Describe caregiver experiences in the early diagnostic period

Materials and Methods

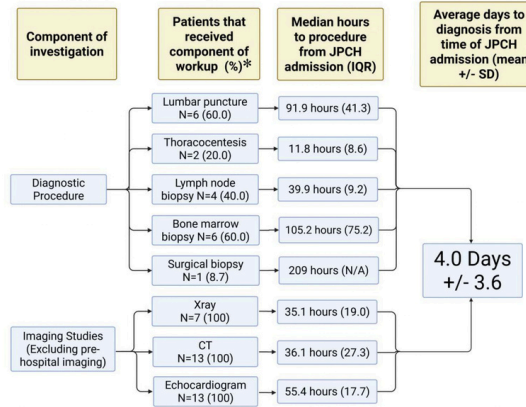
Population: Patients who presented to JPCH under the age of 18 with a diagnosis of AMM

Chart Review: Completed from initial presentation up to the time of diagnosis and summarized using descriptive statistics

Caregiver survey: Surveys were distributed to primary caregivers via REDCap. The survey included check-box responses for demographic data as well as open-text responses for thoughts at the time of diagnosis

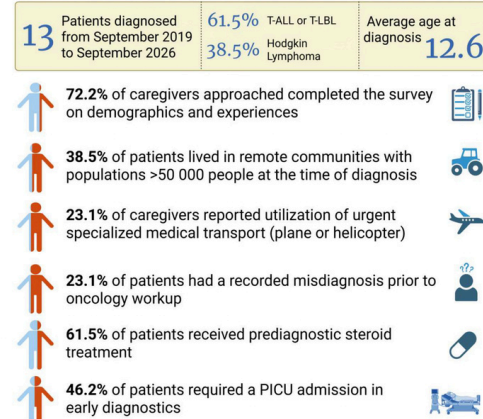
Inductive thematic analysis: performed independently by two authors to code responses, resolve discrepancies, and generate themes

Results: Chart Review of Diagnostics at JPCH



^{*} Two patients were excluded from diagnostic statistics because they were treated in an outpatient setting. One patient was excluded because components of the workup was completed outside of the pediatric oncology program

Results: Demographics and presentation



Results: Thematic Analysis

Theme	Illustrative quotation
Caregiver confusion, uncertainty, and shock regarding an unexpected diagnosis	"It was devastating and felt like our worlds stopped turning" "The feeling was numbing ... [I felt] shocked and blindsided" "[The PCP] excelled at her job by miles ... [she] rushed us to get looked at ... She knew and saved my son's life."
Caregiver stress during early diagnostics and transport	"[My] child had to go alone on the [medical transport] helicopter ... [which was] very scary initially as a parent." "Meeting with so many ... members of the healthcare team was essential, but it was also emotionally exhausting."
Strong emotions regarding perceived delayed or missed diagnosis	"Along with the fear came feelings of guilt as I questioned whether I had acted quickly enough." "My son was sick for another 2 weeks before he collapsed at home—unresponsive for 10 seconds, turning blue."
Appreciation for the multidisciplinary team and reassurance from the pediatric oncologist	"The support ... our family received from [the] health care team was incredible ... their compassion, expertise, and dedication provided comfort and reassurance when we needed it most." "Having such a knowledgeable and compassionate team working alongside us made even the hardest days more bearable."

Conclusions

- Over the course of the study period, 13 cases of AMM were diagnosed at JPCH, equating to almost 2 cases per year
- Diagnostics at JPCH demonstrate a history of efficient management despite the absence of an institutional resource for AMM
- Caregivers experience uncertainty, stress during transport, and strong emotions during the delivery of care before diagnosis

Next steps: Early care resources

Patient partner input will be a key component in building relevant resources in the future

Why is an AMM an emergency?

- The mass in your child's chest could compress their airway and/or blood vessels around the heart
- This may cause a range of symptoms including coughing, shortness of breath, and swelling
- You may notice worsening of these symptoms when lying flat due to further compression

What are the next steps?

- Once it is safe to do so, your child will be transported to Jim Pattison Children's Hospital
- At the hospital, a team of providers will assist in testing that may include blood work, biopsies, and imaging
- The Care team may provide oxygen supports or early medications that will help to shrink the mass and improve breathing
- Once a diagnosis can be made, your care team will propose a treatment plan

Acknowledgements

Thank you to Dr. D'Alessandro and the support from the pediatric research team.
All figures in this poster were generated using BioRender.com



IIne Haan (Drs. Ghita Wiebe & Sarah Tehseen)

Neurodiversity-Affirming Care: a lens through which stories are interpreted and understood

Background: Healthcare workers share a vision of neurodiversity-affirming (NDA) care: individualized, relationship-based, strengths-focused, sensory-aware, and family-led, but realization depends on clinician, practice and system conditions. Methods: Semi-structured interviews with 13 Saskatchewan Health Authority pediatric clinicians across 9 disciplines were analyzed using reflexive thematic analysis (Braun & Clarke, 2019) from a critical realist, contextualist position, with inductive semantic and latent coding. Team members coded in parallel as critical friends with reflexive journaling and field notes. Key Findings: Healthcare workers shared a common vision of NDA care realized across three levels: 1. The clinician: experience becomes curriculum. Healthcare workers rely on self-directed learning and external solutions to overcome outdated health infrastructure constraints. 2. The interaction: care should be responsive to lived experience. Operationalizing NDA care requires flexible, responsive support to reduce the heavy advocacy and administrative burden on families. 3. The system: When capacity shapes care: Organizational and structural constraints like caseloads, resources, and time, often dictate whether NDA care can be implemented and sustained. Conclusion: Realizing neurodiversity-affirming care requires addressing clinician learning needs, supporting family-centered interactions, and expanding organizational capacity.

Neurodiversity-Affirming Care: a lens through which stories are interpreted and understood

IIne Haan^{1,2}, Sara Tehseen^{1,2}, Sarah Ness¹, Ghita Wiebe^{1,2}

¹ College of Medicine, University of Saskatchewan, Saskatoon

² Saskatchewan Health Authority

INTRODUCTION



Healthcare workers in Saskatchewan share a common vision of neurodiversity-affirming (NDA) care in pediatrics, conceptualizing it as individualized, relationship-based, strengths-focused, sensory-aware, and family-led. This collective understanding serves as the core interpretive context for clinicians in healthcare delivery and in partnering with families. However, clinicians consistently identify **clinician, practice, and system-level conditions** that determine whether this vision can be practically realized in clinical environments.

OBJECTIVES

The **Provincial Neurodivergent Advocacy Partnership (PNAP)** is building provincial calls to action from three perspectives: clinicians (this study), parents and caregivers (PNAP), and autistic adolescents to define what neurodiversity-affirming healthcare should look like in Saskatchewan.

This project aimed to use a semi-structured interview to explore what neurodiversity-affirming healthcare means to healthcare workers in SK.

This project was co-developed with lived experience- as part of the SHRF funded PNAP. This project received REB approval (Beh#6231)

POSITIONALITY



Some members of the analytic team identify as neurodivergent and/or parent neurodivergent children, alongside holding clinical and research roles within the system under study.

METHODS: QUALITATIVE



Recruitment via poster with QR code sent to SHA Provincial Autism Programs. Rural area recruitment enhanced with snowballing. Recruitment between April 30- August 14, 2026.



Semi-structured interviews were conducted with 13 Saskatchewan Health Authority clinicians providing direct pediatric care across 9 disciplines (shown below).



Data was analyzed using **reflexive thematic analysis** (Braun & Clarke, 2019) from a critical realist, contextualist position using inductive semantic and latent coding.



Team members coded in parallel as critical friends, supported by **continuous reflexive journaling** and field notes.

Discipline	Family Support Worker	Occupational Therapist	Social Work	Psychologist	Physician	Physical Therapy	Mental Health Therapist	Nurse	Respiratory Therapist
Number	1	1	2	1	2	2	1	2	1

RESULTS: REFLEXIVE THEMATIC ANALYSIS



Experience becomes curriculum

Healthcare workers rely on self-directed learning and external resources to overcome outdated health infrastructure constraints.

Lack of professional training

"neurodiversity education, I think that's what's really lacking"
"a lot of it is on the job learning"
"there's really not a lot of formal training other than experience"

Fragmented connections

"as a new pediatrician, you don't get any orientation on how to navigate these services"
"I would love to have more expert care on my team"
"I've lost so much sleep over it"



Care should be responsive to lived experience

Operationalizing neurodiversity-affirming care requires flexible, responsive support to reduce heavy advocacy and administration burden on families.

Families as the expert

"It's their goals, not mine"
"parent's involvement is the critical piece of their children's care"
"I'm more of a coach"

Families carry too much

"we rely on our families to reach out to us"
"It's hard to navigate. So you just feel for the families knowing that it feels quite hopeless to be honest"
"I see the parents' agony and anxiety all through the years"

Systems should be responsive

"focus on building relationships and taking the time to get to know the community partners as well as the patients and their families"
"go to the people"
"meet the client where they are at"



When capacity shapes care

Organizational and structural constraints like caseloads, resources and time often dictate whether neurodiversity-affirming care can be implemented and sustained.

Scarcity constrains practice

"I'm an autism team of 1"
"We don't actually have a room"
"Not nearly enough staff for the number of clients that we have"

Scarcity creates inequality

"Most kids do not attend school because their school cannot support them, even though they know that they have these diagnoses"
"In rural, there's no therapies that I can refer them to"
"a lot of those services stop because it's just not financially feasible for families"

CONCLUSION AND NEXT STEPS

Clinicians know what good care looks like. They aren't set up to deliver it. **NDA care runs on self-taught staff, persistent families, and workarounds because systems aren't built to hold this.**

All three strands will feed PNAP's provincial calls to action, so recommendations rest on clinician, family, and autistic voices rather than any one vantage point.



TRAIN: NDA content in onboarding and continuing education



LIFT: fund support so families can stop carrying the system



END SCARCITY: caseload, space, and rural access standards

ACKNOWLEDGEMENTS AND REFERENCES

We want to acknowledge and thank the OVDR and SCPOR for their funding and training support for this project. We also want to thank PNAP for the co-creation, support, feedback and continued investment in this project.

Canva and Google AI were used for icon creation.

Braun, V., & Clarke, V. (2019). Reflecting on reflexive thematic analysis. *Qualitative Research in Sport, Exercise and Health*, 11(4), 589–597.



Jenna Schlosser (Dr. Paul D'Alessandro)

Impact of a standardized provincial algorithm on oncofertility practices for pediatric cancer patients in Saskatchewan

Background: Cancer treatments can impair future fertility, yet many pediatric cancer patients do not receive timely and appropriate fertility counselling. The Saskatchewan Oncofertility Algorithm (SOFA) was developed to standardize an oncofertility pathway within the province. We aimed to determine fertility discussion and referral rates for new cancer diagnoses, relapses, and hematopoietic stem cell transplant (HSCT) patients for the 6 months post-SOFA implementation.

Methods: A cross-sectional chart review of pediatric patients (≤ 17 years at diagnosis) being followed by Saskatchewan's Pediatric Oncology Clinic for a confirmed malignancy. Electronic medical records were reviewed for oncofertility discussions and fertility clinic referrals for all new consults/relapses/HSCT patients between February 2 and August 2, 2026. Additionally, pre-appointment questionnaires were reviewed for all patients seen in pediatric oncology/HSCT clinic on treatment, in follow-up, or in survivorship to assess patient interest in oncofertility discussions. Analysis included descriptive statistics and comparisons using Fisher's Exact tests.

Results: Oncofertility discussion rate was 95% (2.7x increase from 35.5% baseline); referral rate was 38% (1.6x increase from 22.6% baseline). Patient demographics were not predictive of discussions/referrals. Patients from each phase of treatment reported interest in oncofertility discussions.

Discussion: SOFA implementation substantially increased pediatric oncofertility counselling and care throughout Saskatchewan.

Impact of the Saskatchewan Oncofertility Algorithm on Fertility Care for Pediatric Cancer Patients

Jenna Schlosser^{1,4}, Merrick Faulkner^{2,4}, Selene Daniel-Whyte⁴, Mita Manna^{1,3,5}, Paul D'Alessandro^{1,2,4}

¹College of Medicine, ²Department of Pediatrics, ³Department of Oncology, ⁴University of Saskatchewan, ⁵Saskatchewan Cancer Agency

INTRODUCTION

- Gonadotoxic effects of cancer treatments can impair fertility and reproductive function.
- Infertility has been identified as a common concern for adolescent and young adult cancer patients.
- Despite the availability of fertility preservation (FP) services, pediatric cancer patients often lack timely and appropriate fertility counselling.
- The Saskatchewan Oncofertility Algorithm (SOFA) was developed to address this gap by creating a standardized oncofertility pathway within the province.

Patient level:

Pre-appointment questionnaires with oncofertility screening prompt.



"Some cancer treatments could negatively impact fertility or reproductive health and the ability to have biological children now and in the future. Would you like to speak to a healthcare professional about this?"

Provider/System level:

New consult physician note template with screening prompt, and integration of standardized patient referral forms.

Template Name
PHY - eMO - New Patient Consult
PHY - eMO - Peds - New Patient Consult

Oncofertility Discussed
☐ Yes, referral for fertility preservation
☐ Yes, no referral for fertility preservation
☐ No, plan to discuss
☐ No
☐ N/A

OBJECTIVES

- Determine fertility discussion and referral rates 6-months post-SOFA implementation and compare with pre-implementation rates.
- Describe the characteristics of patients who expressed interest in oncofertility discussions through the screening prompt.

METHODS

- Study Population:** Pediatric patients (≤ 17 years at diagnosis) followed by the JPCH Pediatric Oncology Clinic and LTFU/Survivorship Clinic.
- Inclusion criteria:** Patients with confirmed malignancy presenting for new consults, relapses/second malignancies, or allogeneic hematopoietic stem cell transplantation (HSCT).
- Exclusion criteria:** Patients with benign or non-oncologic diagnoses.
- Study design:**
 - Pre-implementation** (previously collected): Cross-sectional from May 9-Dec 6, 2024.
 - Post-implementation:** Cross-sectional from Feb 2-Aug 2, 2026; also described participants with a positive response to the pre-appointment questionnaire screening prompt.
- Data Collection:** Electronic health records were reviewed to extract documented clinical variables.
- Analysis:** Included descriptive statistics and comparisons using Fisher's Exact tests.

RESULTS

Objective 1: Post-Implementation Fertility Discussion and Referral Rates

Participant Characteristics (post-implementation):

- N = 23
- Age (mean): 7.09y (range 0-18y)
- Sex: 61% female, 39% male
- Infertility risk: 39% high risk, 62% not high risk
- Appointment type: 61% new consult, 22% relapse/second malignancy, 17% HSCT
- Diagnosis: 30% leukemia/lymphoma, 22% CNS tumour, 30% solid tumour, 17% other

*Patient demographics/clinical variables were not predictive of discussions/referrals ($p < 0.05$).

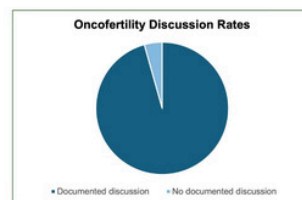


Figure 2: Documented oncofertility discussion rates post-SOFA implementation. 96% had an oncofertility discussion throughout their cancer care. n=23

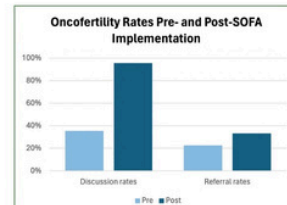


Figure 1: Comparison of oncofertility discussion and referral rates after SOFA implementation. Discussion rates increased by 61% and referral rates increased by 10%.



Figure 3: Documented fertility specialist clinic referral rates post-SOFA implementation. 33% received a referral to a fertility specialist throughout their cancer care. n=21

Objective 2: Uptake of the Patient Facing Screening Prompt

*Out of 895 outpatient visits, 11 patients screened positive to the prompt (1.2%).

No patient checked Yes to the prompt at more than one visit.

Participant Characteristics:

- N = 11
- Age (mean): 15y (range 3-27y)
- Sex: 45% female, 55% male
- Infertility risk: 45% high risk, 55% not high risk
- Diagnosis: 36% leukemia/lymphoma, 18% CNS tumour, 36% solid tumour, 9% other

RESULTS

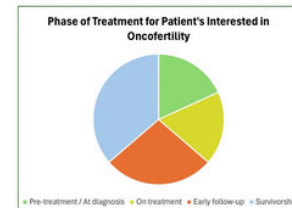


Figure 4: Distribution of patients interested in an oncofertility discussion based on phase of cancer treatment. 18% pre-treatment/at diagnosis, 18% on treatment, 27% early follow-up, 36% survivorship. n=11

CONCLUSIONS

- SOFA implementation substantially increased pediatric oncofertility care in Saskatchewan, with discussion rates increasing by 2.7x.
- Fertility specialist referrals increased modestly by 1.7x, suggesting a likely ceiling effect related to the unavailability of ovarian tissue cryopreservation in Saskatchewan.
- Patient age, gender, and treatment-related infertility risk were not predictive of odds of oncofertility discussion or FP referral.
- Pre-implementation, younger age was associated with lower odds of discussions/FP referrals – SOFA algorithm associated with meaningful practice change that overcame possible healthcare provider bias.
- Patients expressed interest in oncofertility discussions at all phases of care (from diagnosis to survivorship) emphasizing importance of universal screening.

FUTURE DIRECTIONS

- A distance analysis is currently underway to assess if distance from home residence to Saskatchewan's fertility clinic significantly affects the odds of receiving a referral.
- These findings support the expansion of FP services in Saskatchewan, specifically ovarian tissue cryopreservation.

ACKNOWLEDGEMENTS

This project was funded by the College of Medicine 2026 Dean's Project Program and conducted through the Department of Pediatrics.



Sarah Shaban (Dr. Tyler Wenzel)

Understanding Treatment-Seeking Decisions for Patients Needing Stem Cell Transplantation

Hematopoietic stem cell transplantation (HSCT) is a treatment given to restore blood and immune system functioning for many conditions, including cancers, immune disorders, and genetic conditions. X-linked adrenoleukodystrophy (X-ALD) is an inherited disorder. The childhood cerebral form can cause progressive neurological disease for which HSCT can be an important treatment option. However, HSCT is not readily accessible in Saskatchewan, requiring patients and families to travel outside the province. Anecdotal evidence from Canadian metabolic specialists suggests that patients with X-ALD may be more likely to consider seeking HSCT in the United States. However, factors influencing treatment-seeking decisions are not well understood. This study aims to explore patients' and families' experiences and decision-making processes surrounding HSCT, identify barriers and facilitators to accessing care, and examine how the Saskatchewan healthcare system shapes treatment-seeking decisions. Participants are HSCT recipients or parent/guardian care decision-makers from Canada or the United States. Interviews are conducted using grounded theory, exploring diagnosis, information sources, decision-making, barriers and facilitators, and support needs. Early interviews identified themes related to access/availability, perceived expertise, trust/confidence, information, practical considerations, and family support. Recruitment and interviews are ongoing. Continued analysis will refine themes and inform patient-centred educational resources and initiatives supporting HSCT capacity in Saskatchewan.



UNDERSTANDING TREATMENT-SEEKING DECISIONS FOR PATIENTS NEEDING STEM CELL TRANSPLANTATION

Sarah M. Shaban, MSc¹, Spencer Zwarych, MD², Tyler J. Wenzel, PhD¹

¹College of Medicine, University of Saskatchewan, ²Jim Pattison Children's Hospital, Saskatoon, Saskatchewan



Introduction:

- Hematopoietic stem cell transplantation (HSCT) is a treatment in which healthy blood-forming stem cells are given to a patient to restore the blood and immune system¹. HSCT is used for a range of **malignant and non-malignant conditions**, including cancers, blood and immune disorders, and some genetic conditions².
- X-linked adrenoleukodystrophy (X-ALD) is an inherited disorder caused by pathogenic variants in the *ABCD1* gene, and the childhood cerebral form can cause progressive neurological disease³. For individuals with X-ALD, **HSCT can be an important treatment option**.
- HSCT is **not very accessible in Saskatchewan**, meaning patients often travel outside the province to receive treatment, requiring patients and families to remain away from home for HSCT and post-transplant care⁴.
- Anecdotal evidence from Canadian metabolic specialists suggests that patient with X-linked adrenoleukodystrophy (X-ALD) may be more likely to **consider seeking HSCT and post-transplant care in the United States**.
- Understanding how patients and families make decisions about where to seek HSCT may help **identify barriers, facilitators, and concerns** related to accessing care.

Goals:



Better public education resources



Greater confidence in the Canadian healthcare system



Support for capacity-building for HSCT in Saskatchewan

Research Objectives:

- Explore experiences and decision-making processes of patients seeking HSCT, including decisions about where to receive treatment.
- Identify themes describing factors that influence treatment-seeking decisions.
- Use patient experiences to inform the development of educational resources addressing barriers and facilitators to accessing HSCT care in Canada.



Key Questions:

- What influences HSCT-seeking decisions?
- What are the biggest barriers or challenges?
- How does the Saskatchewan healthcare system shape HSCT-seeking decisions?
- What information and support do patients and families need?

Methods:



Participants

- HSCT recipients OR parent/guardian/care-decision maker
- From the U.S. or Canada



Recruitment

- CIHR Centres for Patient-Oriented Research
- ALD Connect
- RareKids-Can



Data Collection

- Interviews using grounded theory
- 1-2 hours each



Interview Guide

- Questions cover key areas such as:
 - diagnosis and understanding
 - information sources
 - decision-making process
 - barriers and facilitators
 - support needs and expectations

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Preliminary Findings:

These are **key themes emerging** from patient and family interviews so far:

1. Access & Availability

- Limited local HSCT options contribute to where families seek care

2. Expertise

- Perceived experience with the patient's condition may influence selection of transplant centre

3. Trust & Confidence

- Perceptions of the healthcare system influence willingness to pursue care

4. Information

- Families may seek information from healthcare providers and independently

5. Practical Considerations

- Finances, travel, accommodation, and time away from home can affect decisions

6. Family

- Family preferences and support may contribute to treatment decisions

Next Steps:



- Continue recruitment and interviews



- Transcribe and analyze interviews



- Explore and establish themes and patterns



- Share findings and develop educational resources

Acknowledgements:



College of Medicine

Thank you to our funding agencies for their support on our project. We extend our utmost gratitude to our Patient Partners who have supported and guided this study so we can better serve our community. We acknowledge this work was conducted on Treaty 6 territory and the Homeland of the Métis. We pay our respects to the First Nations and Métis ancestors of this place and reaffirm our relationship with on another.

Psychiatry





Donovan Buskey (Dr. Senthil Damodharan)

Trends in Psychotic Symptoms Among Adolescents Admitted to the Regina Youth Detoxification Unit: A Retrospective Cohort Study

Objective(s): To examine temporal trends of documented psychotic symptoms amongst youth substance users, explore associations between specific substances and psychotic symptoms, and characterize how demographics effect symptom prevalence.

Methods: We reviewed the electronic health records of Regina Youth Detoxification Unit patients between 2020 and 2024. Demographics, harmful substance use, and documented psychotic symptoms were extracted and deidentified. Descriptive statistics characterized cohort trends over time; associations between substances and psychotic symptoms/diagnoses were assessed using chi-square or Fisher's exact tests, with odds ratios reported where applicable.

Results: 212 patients were identified with a mean age of 15.54 (± 1.32) years. Prevalence of psychotic symptoms increased from 18.75% in 2020 to 40% in 2024, with a significant increase in the odds of adolescents presenting with psychotic symptoms (OR 1.35, $p = 0.04$). Cannabinoid and stimulant/methamphetamine use were most frequently co-documented with psychotic symptoms, particularly hallucinations. No significant demographic differences were found between affected and non-affected groups.

Conclusion: Documented psychotic symptoms were common among youth admitted for detoxification and showed an overall increase over the study period. The frequent co-documentation of cannabis and stimulant/methamphetamine use with psychotic symptoms highlights the need for integrated assessment of substance use and mental health among youth receiving detoxification services.

Trends in Psychotic Symptoms Among Adolescents Admitted to the Regina Youth Detoxification Unit: A Retrospective Cohort Study

Donovan Buskey¹, Shirmin Kader², Senthil Damodharan MD³

¹ College of Medicine University of Saskatchewan, ² Research Department Saskatchewan Health Authority, ³ Saskatchewan Health Authority and College of Medicine University of Saskatchewan

BACKGROUND

- Substance use is a known risk factor for psychotic symptoms, particularly among adolescents with substance use disorders [1,2].
- Approximately 40% of youth who use substances experience psychotic-like experiences [1].
- Early identification may help prevent progression to more severe psychiatric outcomes [1].
- Despite frequent clinical observation of psychotic symptoms at the Regina Youth Detoxification Unit, their prevalence in Saskatchewan youth has not been systematically studied.
- We hypothesized that documented psychotic symptoms have changed over time among youth admitted to the Detox Unit.

OBJECTIVES

The **primary objective** of this study was to examine rates and temporal trends of documented psychotic symptoms amongst adolescents admitted to the Regina Youth Detoxification Unit (YDU).

The **secondary objectives** were:

- To explore associations between specific substances and the incidence of psychotic symptoms, and
- To identify demographic characteristics associated with the experience of psychotic symptoms in this population.

METHODS

Design: Retrospective review of electronic health records for patients aged 12–18 years discharged from the Regina Youth Detoxification Unit (2020–2024).

Data: Demographics, harmful substance use, and documented psychotic symptoms were extracted and deidentified in REDCap.

Analysis: Descriptive statistics assessed trends over time; chi-square or Fisher's exact tests examined associations between substance use and psychotic symptoms, with odds ratios reported where applicable.

RESULTS

212 adolescents were included; mean age was 15.54 ± 1.32 years, with 60.4% female. 169 (79.7%) had documented psychotic symptoms. The proportion with psychotic symptoms increased from ~19% in 2020 to 40% in 2024, with a significant increase in odds over time (OR 1.35, $p = 0.04$). (Figure 1)

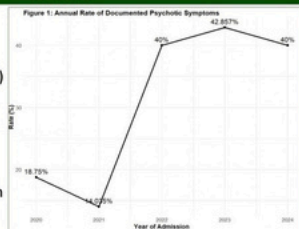


Figure 1. Year over year trend of documented psychotic symptoms prevalence.

RESULTS

All four psychotic symptom categories showed an overall increase from 2020 to 2024.

Hallucinations were the most prevalent, reaching ~40% in 2024 after fluctuations across the study period.

Delusions increased from ~5.5% in 2020 to ~20% in 2024.

Disorganized behaviour increased from ~3% in 2020–2021 to ~20% in 2024.

Paranoia/unspecified psychotic symptoms showed the most consistent rise, from ~4% in 2020 to ~20% in 2024.

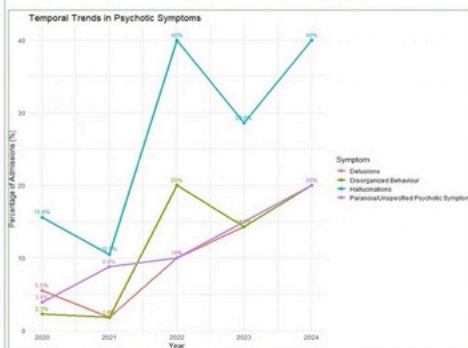


Figure 2. Trends in Documented Psychotic Symptom Categories, 2020–2024

Cannabinoid and stimulant/methamphetamine use were most frequently co-documented with psychotic symptoms, particularly hallucinations. (Figure 3)

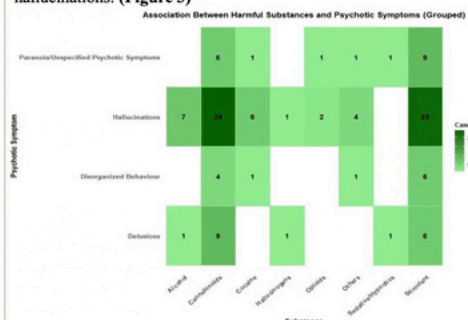


Figure 3. Distribution of harmful substances used across the psychotic symptoms.

RESULTS

No significant demographic differences were found between those with vs without psychotic symptoms, which may be attributed to our modest sample size. (Table 1)

Table 1. Comparison of adolescents with vs without psychotic symptoms.

Variable	Psychotic Symptoms	No Psychotic Symptoms	P-value
Age (mean (± SD))	15.50 (± 1.33)	15.67 (± 1.27)	0.464
Geography			
Urban	145 (81.92)	32 (18.08)	0.162
Suburban	10 (66.67)	5 (33.33)	
Rural	14 (70.00)	6 (30.00)	
Sex			
Male	66 (78.57)	18 (21.43)	0.184
Female	103 (80.47)	25 (19.53)	

CONCLUSIONS

- The prevalence of psychotic symptoms among adolescents with substance use disorders admitted to the YDU has significantly increased in recent years.
- Policy aimed at both managing youth exposure to harmful substances and the detection and treatment of psychotic symptoms in this population are primary measures that could prevent the development of clinical psychotic conditions and long-term adverse outcomes.
- Further research is needed to explore associations and causations between specific substances and psychotic symptoms and potential demographic characteristics that might predict psychotic symptoms in this population.

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ACKNOWLEDGEMENTS

We would like to thank the University of Saskatchewan College of Medicine for funding and the Saskatchewan Health Authority for their research support.



Elizabeth Byambatseren (Dr. Darrell Mousseau)

Investigating Monoamine Oxidase-A Protein Interactions in the Context of Alzheimer's Disease.

Alzheimer's disease (AD) is characterized by amyloid- β (A β) accumulation, mitochondrial dysfunction, and oxidative stress. Monoamine oxidase-A (MAO-A), located on the outer mitochondrial membrane, metabolizes neurotransmitters and produces hydrogen peroxide, potentially contributing to oxidative stress. Presenilin-1 (PS1), a catalytic component of the γ -secretase complex, processes amyloid precursor protein (APP) to generate A β and has been implicated in mitochondrial protein interactions. This study investigates interactions between MAO-A, PS1, and mitochondrial proteins in the context of APP-associated pathology. Multiple cell lines were screened for endogenous MAO-A expression, identifying LNCaP cells as an appropriate model. Subcellular fractionation was optimized using differential centrifugation and mitochondrial and cytosolic markers. Co-immunoprecipitation and western blotting were used to investigate protein associations and localization. APP WT and APP S/I were expressed to assess effects on MAO-A and PS1. PS1 was detected in both mitochondrial-enriched (P2) and cytosolic (S) fractions, with no apparent change in distribution following APP WT or APP S/I expression. MAO-A expression was also validated in J20 mouse brain tissue. These findings provide a basis for further investigating how APP-related changes may influence mitochondrial protein interactions and oxidative stress in AD.

Investigating Monoamine Oxidase-A Protein Interactions in the Context of Alzheimer's Disease

Elizabeth Byambatseren, Justin Lukan, Darrell Mousseau, Cell Signalling Laboratory, Department of Psychiatry

INTRODUCTION & BACKGROUND

Alzheimer's Disease (AD) is a progressive neurodegenerative disorder associated with amyloid- β (A β) accumulation, oxidative stress, and mitochondrial dysfunction.

Monoamine oxidase-A (MAO-A) is an enzyme located on the outer mitochondrial membrane that metabolizes monoamine neurotransmitters and produces hydrogen peroxide (H_2O_2) as a by-product. Increased oxidative stress may contribute to mitochondrial and neuronal damage in AD.

Presenilin-1 (PS1) is a component of the γ -secretase complex that cleaves APP to yield A β . Mitochondrial translocase proteins, including TOMM40 and TIMM23, found on the outer and inner mitochondrial membrane, respectively, regulate transport across the mitochondrial membrane.

Rationale: PS1 is known to interact with MAO-A, but the role of this interaction in AD remains poorly understood. Investigating these interactions may help clarify how APP/A β pathology is linked to mitochondrial dysfunction and oxidative stress.

OBJECTIVES

- 1. Cell Line Selection:** Identify an appropriate cell model with sufficient endogenous MAO-A expression for subsequent studies.
- 2. Subcellular Localization:** Determine the cellular and mitochondrial localization of MAO-A and PS1 using subcellular fractionation and mitochondrial and cytosolic markers.
- 3. Protein Interactions:** Investigate interactions between MAO-A and mitochondrial proteins, including TOMM40, TIMM23 and PS1, using co-immunoprecipitation.
- 4. APP-Associated Effects:** Determine whether APP expression, including APP WT and APP S/I, alters MAO-A localization or interactions with mitochondrial proteins.
- 5. In Vivo Validation:** Validate MAO-A associated findings in J20 Alzheimer's disease mouse brain tissue across different brain regions and ages.

1. Cell Line Selection

- MAO-A expression was assessed across multiple cell lines.
- LNCAp cells demonstrated strong endogenous MAO-A expression and were selected for subsequent experiments (Figure 1).

2. Subcellular Fractionation

- P1, P2, and cytosolic fractions were made using differential centrifugation.
- Mitochondrial and cytosolic markers were used to evaluate fraction enrichment and purity.
- The five stroke homogenization protocol was selected for further optimization (Figure 2).

3. Protein Interaction Studies

- Co-immunoprecipitation experiments were established to investigate MAO-A associations with PS1, TOMM40, and TIMM23.
- Western blot conditions were optimized for detection of MAO-A and mitochondrial marker proteins.

4. APP/MAO-A Studies

- APP WT and APP S/I were expressed to investigate whether altered APP processing influences MAO-A localization and protein interactions.
- The interaction between PS1 and MAO-A in LNCAp cells is shown in Figure 3.

5. In Vivo Validation

- J20 and control mouse brain lysates were analyzed to validate the Alzheimer's disease model and assess regional protein expression.
- Cerebellum samples from J20 and control mice were analyzed by co-immunoprecipitation and Western Blotting (Figure 4).

RESULTS

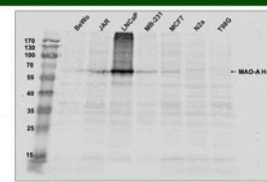


Figure 1. Endogenous MAO-A Cell Line Screening. Western blot analysis of MAO-A expression across multiple cell lines. LNCAp expresses high levels of MAO-A.

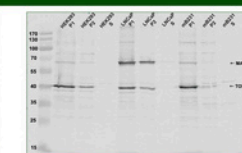


Figure 2. Subcellular Fractionation Optimization & Marker Purity. MAO-A and TOMM40 detection in P1, P2, and S fractions from HEK293, LNCAp, and MDA-MB-231 cells.

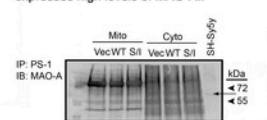


Figure 3: Co-immunoprecipitation of PS1 with MAO-A in LNCAp cells transfected with APP(WT) or APP(S/I). Endogenous PS1 was immunoprecipitated (IP) and probed for MAO-A in the mitochondrial (Mito) and cytosolic (Cyto) fractions of LNCAp cells transfected with either the Vector (Vec), or with APP wildtype (WT) or APP bearing the Swedish and Indiana (S/I) mutations that are related to AD.

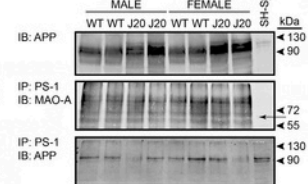


Figure 4: Co-immunoprecipitation of PS1 with MAO-A and APP in mouse tissue. PS1 was immunoprecipitated (IP) and probed for MAO-A (top) and APP (bottom) by immunoblot (IB). MAO-A signal was weak; APP signal differed in the J20 lanes. The top panel shows the slightly higher APP expression in these cerebellar samples.

MATERIALS & METHODS

Cell Culture & Transfection

Multiple cell lines were evaluated for endogenous MAO-A expression. LNCAp cells were transfected using Lipofectamine 3000 kit with pcDNA3.1, APP WT, APP S/I, MAO-A, and PS1 constructs.

Subcellular Fractionation

Cells were homogenized and subjected to differential centrifugation to obtain:

- P1:** nuclear/unbroken cell fraction
- P2:** enriched mitochondrial fraction
- S:** cytosolic fraction

A five versus ten stroke homogenization protocol was evaluated to optimize fractionation quality using HEK293, LNCAp, and MDA-MB-231 cell lines. Mitochondrial and cytosolic marker proteins were used to assess fraction purity.

Western Blotting and Protein Detection

Protein expression and fraction localization were assessed by SDS-PAGE and Western Blotting. MAO-A, TOMM40, TIMM23, TOMM70, cytochrome c, 14-3-3, SHP1/2, and PS1 were detected using specific primary antibodies. Infrared fluorescence detection was performed using the LI-COR Odyssey system, with additional fluorescent detection performed using a Bio-Rad ChemiDoc system.

Co-immunoprecipitation

LNCAp cell samples, along with J20 and control mouse cerebellum tissue samples were used for co-immunoprecipitation. Protein complexes were captured using Sepharose beads and antibodies targeting PS1, 6E10, or TOMM40.

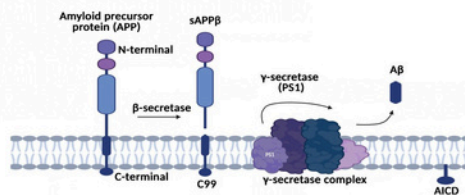


Figure 5. APP/PS1 Processing Mechanism APP is first cleaved by beta-secretase to generate C99. C99 is subsequently cleaved by the gamma-secretase complex, which contains PS1, to generate amyloid- β (A β) and the APP intracellular domain (AICD). Altered APP processing may influence PS1-associated protein interactions and downstream mitochondrial dysfunction.

CONCLUSIONS & FUTURE DIRECTIONS

- Cell Model Selection:** LNCAp cells provide a strong *in vitro* model for studying endogenous MAO-A expression and translocase dynamics.
- Genotypic & Regional In Vivo Confirmation:** Re-probing mice brain lysates (cerebellum) with 22c11 successfully confirmed J20 versus WT genotypes.
- Complex Formation:** Co-IP supports a weak association between MAO-A and PS1 in transfected cells.
- Future Directions:** Analyze J20 mouse samples at 6 to 12 months across regional brain tissues (*hippocampus versus cortex*) to assess age-dependent accumulation of the PS1/MAO-A interaction. Transfected N2a cells will also be evaluated using PS1 loop constructs.

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ACKNOWLEDGMENTS

- Dr. Darrell Mousseau (PI) and Justin Lukan (Research Technician), Department of Psychiatry, are both gratefully acknowledge for their support throughout this project.
- Stipends were provided by the College of Medicine Dean's Summer Research Project Program and NSERC/Undergraduate Student Research Awards (USRA).



Emmanuella Ehidiamhen (Dr. John Howland)

Optimizing a Two-choice odour span task for working memory

The Odour Span Task (OST) assesses working memory in rodents using a delayed non-match-to-sample rule. This project aimed to optimize a Two-Choice OST (2COST) that better separates behavioural events for future neural analysis. Two Long-Evans rat cohorts underwent DNMS training, with correction trials removed in Cohort 2. Cohort 1 remained near chance, while Cohort 2 showed only modest improvement during later training and did not reach consistently reliable performance. Further optimization is therefore needed before the 2COST can be used for future fibre-photometry studies of dopamine and calcium activity during working memory.

What's that Spice Again? Optimizing a Two-Choice Odour Span Task for Working Memory



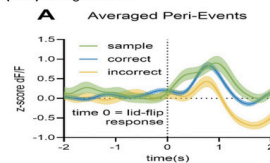
Emmanuella A. Ehidiemhen, Ronin G. Sawitsky, Aiden E. Glass, Caleb L.G. White, John G. Howland
Department of Anatomy, Physiology, and Pharmacology, University of Saskatchewan



1. INTRODUCTION

- Working memory** temporarily maintains and manipulates information needed to complete a task.
- The **Odour Span Task (OST)** is a well-established test of working memory capacity and follows a **Delayed Non-Match-to-Sample (DNMS)** rule, requiring rats to identify a novel odour among increasing familiar odours.
- Previous work from our lab used **fibre photometry** to measure dopamine in the **nucleus accumbens core (NAC)** during the task.

Fig 1: Previous Nac dopamine findings during OST using fibre photometry



- In the traditional OST, rats can sample, reject, and choose odours in rapid succession, making rejection events difficult to isolate in neural recordings.
- We are optimizing a **Two-Choice OST (2COST)** to better separate these events for future analysis of neural activity during working memory.

2. METHODS

- Two cohorts of male and female Long Evans rats (cohort 1 n=4, cohort 2 n=6) underwent DNMS training.
- Following cohort 1, the protocol was modified for cohort 2 by removing correction trials, so an incorrect first choice ended the trial.

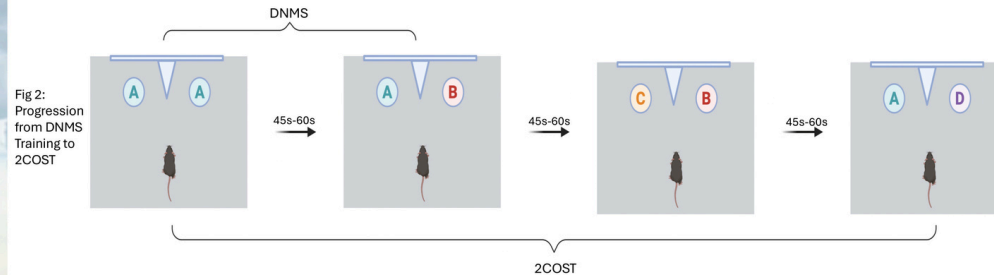


Fig 2: Progression from DNMS Training to 2COST

3. COHORT 1

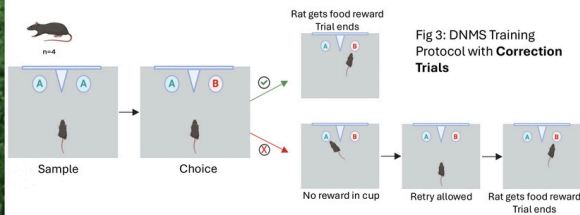


Fig 3: DNMS Training Protocol with Correction Trials

Training Days by Stage

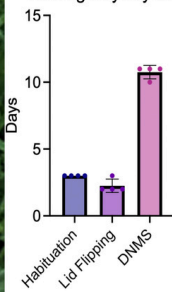
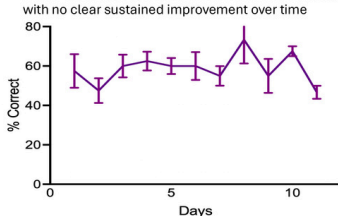
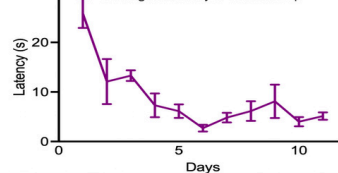


Fig 5: Training progression across stages

DNMS accuracy remained at chance across training with no clear sustained improvement over time



Averaged Latency to First Lid Flip



4. COHORT 2

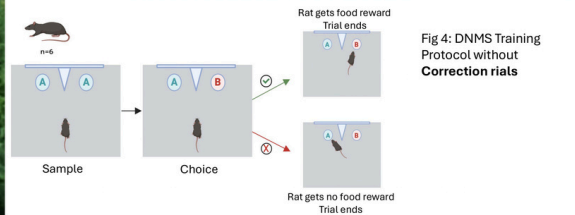


Fig 4: DNMS Training Protocol without Correction trials

Training Days by Stage

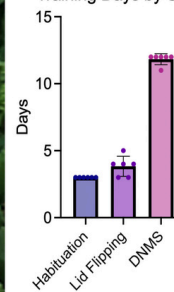
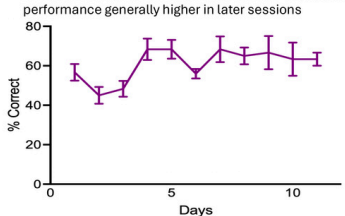
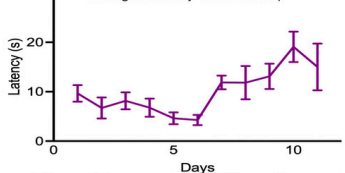


Fig 6: Training progression across stages

DNMS accuracy showed a modest upward trend, with performance generally higher in later sessions



Averaged Latency to First Lid Flip



5. CONCLUSION & FUTURE DIRECTIONS

- The current 2COST protocol did not produce consistently reliable DNMS performance, although Cohort 2 showed a tendency toward improved accuracy during later training.
- Variable DNMS performance may have been influenced by inconsistent motivation for the food reward and the need for a more rigorous, consistent training schedule to establish stable task performance.
- Continue optimization with an additional cohort, retaining the no-correction DNMS approach while refining training criteria and the progression from DNMS to the 2COST.
- Use fibre photometry to measure dopamine and calcium activity in the NAC, and potentially the prefrontal cortex, during distinct stages of 2COST task performance including odour sampling, decision-making, and reward.
- Investigate how neural activity changes with changes in memory load and the recency of previously encountered familiar odours.

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- Research was funded by a Natural Sciences and Engineering Research Council of Canada (NSERC) Undergraduate Award and a University of Saskatchewan Biomedical Summer Research Project award. Project was supervised by Dr. John Howland. Illustration were created in Biorender.



Lacey Gibson (Dr. Eric Noyes)

When Shadows Take Shape: Hallucination Progression and Prognosis in Parkinson's Disease

Background: Hallucinations are among the most burdensome non-motor manifestations of Parkinson's disease (PD) and are thought to progress from minor hallucinations with preserved insight to structural hallucinations without insight; the timing of this progression and its relationship to dementia remain poorly understood.

Methods: We conducted a retrospective chart review of 124 patients with autopsy-verified PD hallucinations. Analyses included Fisher's exact test, multivariable logistic regression, and Mann-Whitney U tests.

Results: Hallucinations with preserved insight predicted subsequent hallucinations with loss of insight (adjusted OR = 7.74, $p < 0.001$). The mean time to this transition was 3.27 years, with 87.5% progressing within five years. Structural hallucinations and dementia showed no consistent directional ordering ($p = 0.37$). Median survival duration was 5.6 years after hallucinations with preserved insight versus 1.6 years for those without insight ($p = 0.02$).

Conclusions: Hallucinations with insight likely represent an early stage in the progression of hallucinations. Structural hallucinations and dementia did not consistently precede one another, arguing against a directional relationship and, together with previous literature, suggesting a possible shared disease process. Differences in survival duration suggest that loss of insight, rather than hallucinations alone, may be more clinically meaningful for PD prognosis.

When Shadows Take Shape: Hallucination Progression and Prognosis in Parkinson's Disease

Lacey Gibson, Ali H. Rajput, Alex Rajput, Eric Noyes College of Medicine, University of Saskatchewan

Introduction

Parkinson's disease (PD) has been traditionally understood, defined, and classified primarily by its motor symptoms.¹ However, there has been increasing recognition of the contribution of non-motor symptoms to both quality of life and prognosis.²

Among the non-motor manifestations of PD, psychosis is subjectively rated as more burdensome and is associated with lower quality of life compared to other non-motor symptoms.³ Furthermore, a recent cohort study found that hallucinations were associated with more than twice the mortality hazard compared to patients who had not yet developed hallucinations.⁴

PD psychosis includes a heterogeneous spectrum of symptoms, including both hallucinations and delusions.⁵ Hallucinations can be classified based on their content, degree of formation (minor vs. structural), and whether insight is preserved or lost.^{6,7} Minor and structural hallucinations are thought to exist on a spectrum with minor hallucinations preceding structural hallucinations.⁸ It remains less clear whether hallucinations with preserved insight also precede hallucinations without insight, and if so, by what interval.

Finally, the relationship between PD psychosis and dementia remains under debate. Dementia is thought to be one of the most important endogenous risk factors for the development of psychosis, but multiple studies report that visual hallucinations precede dementia diagnosis.^{2,9,10}

Research Questions

1. What is the relationship between hallucinations with preserved insight and those with loss of insight?
2. What is the relationship between dementia diagnosis and hallucinations?
3. What is the typical survival duration once hallucinations or dementia begin?

METHODS

1. Prospective longitudinal cohort study through the Saskatchewan Movement Disorders Program
2. 279 autopsy-verified PD patients
3. Previous chart review identified 124 charts with hallucinations or delusions meeting inclusion/exclusion criteria
4. Detailed retrospective chart review collecting motor and non-motor symptoms plus patient context
5. Analyze and report the data collected in step 4

Minor hallucinations

Illusions, presence hallucinations, passage hallucinations, formed hallucinations with preserved insight

Structural hallucinations

Formed hallucinations with loss of insight

Dementia

MMSE consistently < 24, or no MMSE score with severe cognitive problems causing functional impairment

Exclusion criteria

Drug induced - hallucinations or delusions starting shortly after a medication change and resolving after medication discontinuation

Delirium - hallucinations due to physical illness (e.g. UTI) that resolve upon treatment

RESULTS

1. LOSS OF INSIGHT OVER TIME

3.27 yrs
mean time from preserved-insight to loss of insight hallucinations

87.5%
of those who convert do so within 5 years

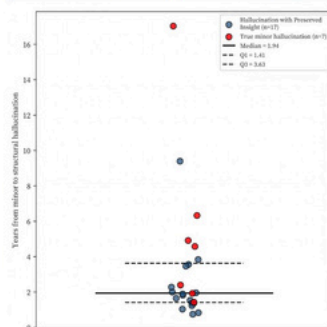


Figure 1. Scatter plot with superimposed density showing time from first hallucination with preserved insight to first structural hallucination (n = 24).

	Structural without insight present	Structural without insight absent	Total
Minor / preserved insight present	24	14	38
Minor / preserved insight absent	8	25	33
Total	32	39	71

Table 1. 2x2 contingency table of hallucinations with preserved and loss of insight (n = 71). Patients with unknown minor or structural hallucination status were excluded (n = 53).

OR 5.36
unadjusted odds of structural hallucination
95% CI [1.91, 15.06], p = .002

OR 7.74
adjusted for age at motor onset and survival duration
95% CI [2.33, 25.68], p < .001

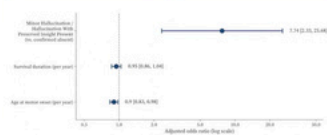


Figure 2. Forest plot of adjusted odds ratios for predictors of structural hallucinations (n = 70). Patients with unknown minor or structural hallucination status were excluded (n = 53). Patients with unknown age at motor onset were excluded (n = 1). Model: logit(p) = β₀ + β₁(minor/preserved insight status) + β₂(survival duration) + β₃(age at motor onset).

CONCLUSIONS

- Hallucinations with preserved insight likely represent an **earlier stage** on the hallucination spectrum, converting to loss of insight in a mean 3.27 years.
- Neither structural hallucinations nor dementia consistently preceded the other, arguing against a directional relationship and, with prior literature, pointing to a **shared disease process**.
- The survival difference between preserved and lost insight **suggests insight**, rather than hallucinations alone, **may be the more clinically meaningful** prognostic feature in PD.

2. HALLUCINATIONS & DEMENTIA

42
patients developed both events

Median = 0.00 yrs
hallucinations and dementia diagnosis cluster temporally

Temporal ordering	n (%)
Hallucination without insight before dementia	17 (40.5)
Dementia before hallucination	18 (42.9)
Same day	7 (16.7)
Timing difference (years)	
Median (IQR)	0.00 (-0.86, 1.66)
Range	-6.04 to 11.44
Mean (SD)	0.38 (3.22)

Table 2. Timing of structural hallucinations without insight relative to dementia diagnosis among patients who developed both. Calculated as (date of dementia diagnosis) - (first recorded date of structural hallucination) + 365.25. Positive values indicate hallucinations preceded dementia.

No directional order

the interval between events did not differ by which occurred first (U = 180.5, p = .37)

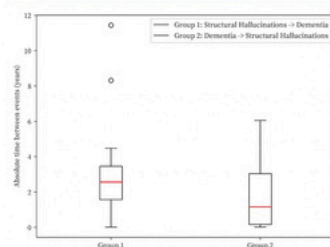


Figure 3. Absolute time between structural hallucination onset and dementia diagnosis, stratified by order of events (n = 35). Patients diagnosed with both on the same date were excluded (n = 7).

3. SURVIVAL AFTER ONSET

1.57 yrs
median survival after structural hallucination onset

5.60 yrs
median survival after minor hallucination onset
U = 559.0, p = .023

Event	n	M	SD	Median	IQR	Range
Minor hallucination only	20	5.05	3.41	5.60	2.16-7.16	0.27-13.36
Structural hallucination only	41	3.29	3.85	1.57	0.56-5.23	0.02-15.16

Table 3. Survival duration once event onset. Survival Duration = (date of death) - (date of event onset), measured in years. Patients with both minor and structural hallucinations were removed to preserve independent groups for statistical analysis (n = 24).

DISCUSSION

Among patients who progressed from hallucinations with preserved insight to hallucinations with loss of insight, the mean conversion time was 3.27 years, with 87.5% progressing within 5 years. This is in keeping with the current literature supporting the idea that minor hallucinations represent an earlier stage on a spectrum of psychosis progression.¹¹

Patients experiencing hallucinations with preserved insight had 5.36-fold higher odds of developing structural hallucinations without insight (p = .002). This association strengthened, rather than attenuated, after adjustment for age at motor onset and survival duration (adjusted OR = 7.74, p < .001), suggesting that the progression from preserved insight to loss of insight is not simply an artifact of longer disease exposure or older age.

Structural hallucinations without insight clustered tightly around the date of dementia diagnosis, with no consistent directional ordering; hallucinations preceded dementia in 40.5% of patients, dementia preceded hallucinations in 42.9%, and the two occurred simultaneously in 16.7% of cases. We did not detect a difference in the absolute interval between events according to which occurred first (U = 180.5, p = .37). Nonetheless, combining our findings of tight clustering with current literature demonstrating overlapping neuropathological features raises the possibility that hallucinations and dementia may reflect a shared disease process rather than a sequential or causal relationship.^{12,13}

Finally, the median survival duration after structural hallucination onset was 1.57 years, compared with 5.60 years after minor hallucination onset (p = .02). This is consistent with prior evidence that hallucinations are associated with increased mortality in PD.⁴ However, our findings extend the current literature by providing evidence that it is the loss of insight, rather than the presence of hallucinations per se, that marks the point at which PD prognosis meaningfully changes.

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ACKNOWLEDGEMENT AND FUNDING

Thank you to the University of Saskatchewan College of Medicine for the opportunity and funding to complete this Dean's Summer Research Project.



Azra Hadzihasanovic (Dr. Justin Botterill)

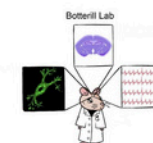
Evaluating the electrophysiological properties of hippocampal engram cells that support fear learning and memory

Engram neurons are cell ensembles that are thought to represent the physical basis of a memory following learning¹. Specifically, engram neurons undergo changes in neuronal excitability and synaptic connection, allowing memory storage in the brain. Despite advances showing the critical role of engram neurons in learning and memory, we have a poor understanding of whether their physiological properties change over time or in response to new experiences. The present study addresses this knowledge gap by studying the electrophysiological properties of engram and non-engram neurons in mice that underwent contextual fear conditioning². Using Targeted Recombination in Active Populations transgenic mice crossed with tdTomato (Ai9) reporter mice (TRAP2^{iCreERT2}xAi9), we permanently labelled engram neurons following learning with a red fluorescent protein via tamoxifen-dependent recombination³. We found differences in the biophysical properties and spontaneous synaptic activity between engram and non-engram cells in the hippocampus 3 days after learning. The strongest effects were observed in the dentate gyrus' granule cells, with increased inhibitory synaptic activity and reduced intrinsic excitability. In CA1 pyramidal cells, fewer differences were observed, possibly due to the early post-conditioning time point. We will continue to investigate the properties of 14-day engram cells to identify how engram neurons persist with time.

Evaluating the Electrophysiological Properties of Hippocampal Engram Cells that Support Fear Learning and Memory

Azra Hadzihanovic, Alina Trofimova, Justin Botterill

Department of Anatomy, Physiology and Pharmacology, Botterill Neuro Lab



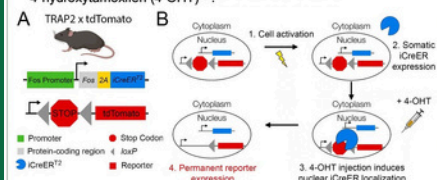
INTRODUCTION

- Engram cells are ensembles of neurons that are thought to represent the physical basis of memory following a learning event¹.
- Engram neurons undergo changes in excitability and synaptic connectivity to support storage of memories in the brain². Previous studies have found that reactivation of engram neurons is required for memory recall³⁻⁵, whereas silencing or ablation of engram neurons impairs memory recall⁶⁻⁸.
- However, there is limited data on whether the physiological properties of engram cells differ across cell types, how long these changes persist, and whether engram properties differ by sex.
- In the present study, engram neurons were permanently labeled following a robust learning and memory test known as contextual fear conditioning⁹. We then used electrophysiological recordings to study the synaptic and firing properties of hippocampal engram and non-engram cells at 3 days or 14 days after learning.

METHODS & MATERIALS

Subjects:

- Targeted Recombination in Active Populations (TRAP2) mice were bred with tdTomato reporter mice. TRAP2 x tdTomato offspring (8-12 weeks old) were used to permanently label cells involved in fear encoding (engram cells) via the tamoxifen metabolite 4-hydroxytamoxifen (4-OHT)^{5,6}.



4-OHT Injections:

- 50mg of 4-OHT (Hello Bio) was dissolved in 2.5mL of 100% ETOH and 2.5mL of Cremaphor (Kolliphor). 4-OHT stock was frozen at -20°C until use.
- 4-OHT stock was dissolved 1:1 in 0.1M PBS on the day of experiments and injected immediately following contextual fear conditioning (50mg/kg, i.p.).

Contextual Fear Conditioning:

- Training/Memory Encoding:** Mice were placed in a fear conditioning chamber (MedAssociates). Baseline freezing was assessed for 2 minutes, followed by 5 foot shocks (0.5mA, 2 seconds), delivered once per minute.

- Analysis:** Freezing behaviour was scored with VideoFreeze software.

Slice Electrophysiology:

- Mice were perfused 3d or 14d after contextual fear training.
- 3 days or 14 days after the 4-OHT injection, mice were deeply anesthetized, and their brain was rapidly extracted and cut in neuroprotective ACSF solution at 300µm in the horizontal plane.
- We patched dentate granule cells (DG GCs) and CA1 pyramidal cells (CA1 PCs) in the hippocampus. We considered engram cells to be tdTomato⁺, whereas non-engram cells were tdTomato⁻.
- Spontaneous inhibitory postsynaptic currents (sIPSCs) were measured by voltage clamping neurons at 0mV. Spontaneous excitatory currents (sEPSCs) were measured by voltage clamping neurons at -60mV. Spontaneous activity was recorded for up to 10 minutes.
- Data was analyzed in Wolfram Mathematica using custom scripts.

RESULTS – 3d

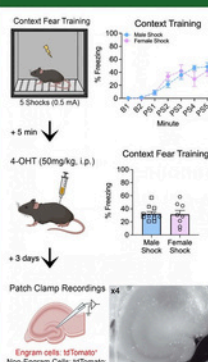


Figure 1. Experimental design for engram and non-engram cell analysis 3 days after fear conditioning (FC). Freezing behavior increased progressively across shocks, with no significant sex differences in freezing behavior observed during FC.

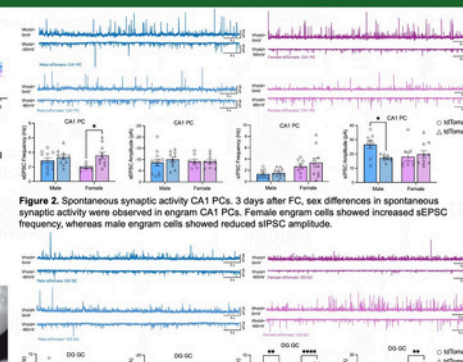


Figure 2. Spontaneous synaptic activity in CA1 PCs 3 days after FC. Sex differences in spontaneous synaptic activity were observed in engram CA1 PCs. Female engram cells showed increased sEPSC frequency, whereas male engram cells showed reduced sIPSC amplitude.

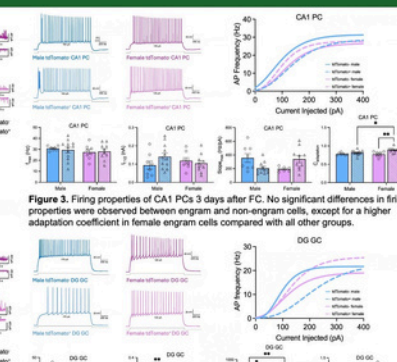


Figure 3. Firing properties of CA1 PCs 3 days after FC. No significant differences in firing properties were observed between engram and non-engram cells, except for a higher adaptation coefficient in female engram cells compared with all other groups.

RESULTS – 14d

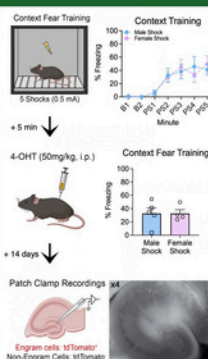


Figure 6. Experimental design for engram and non-engram cell analysis 14 days after fear conditioning (FC).

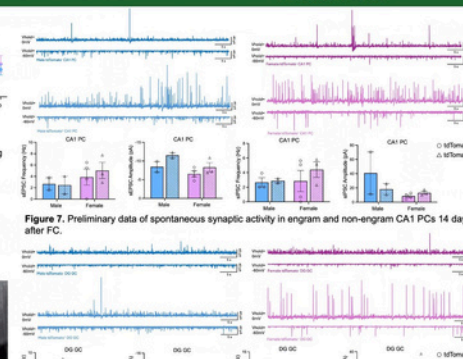


Figure 7. Preliminary data of spontaneous synaptic activity in engram and non-engram CA1 PCs 14 days after FC.

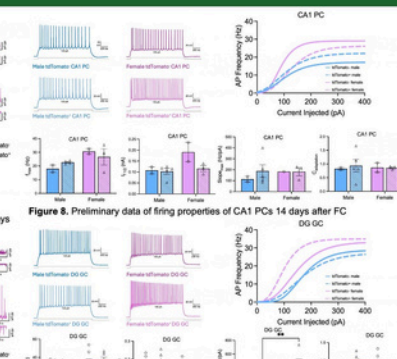


Figure 8. Preliminary data of firing properties of CA1 PCs 14 days after FC. Between sexes, female DG engram GCs showed increased excitability, seen in an increased F-I slope that indicates increased firing gain compared to males.

CONCLUSION

- Mice that underwent contextual fear conditioning showed similar learning, regardless of sex.
- 3 days after contextual fear conditioning, we observed differences in the biophysical properties and spontaneous synaptic activity between engram and non-engram cells in the hippocampus. The strongest effects were observed in DG GCs, with increased inhibitory synaptic activity and reduced intrinsic excitability. In CA1 PCs, fewer differences were observed, possibly due to the early post-conditioning time point.
- Data collection is ongoing for engrams at 14 days after fear learning. The current sample size is insufficient for statistical analysis. We intend to continue the study this Fall for my Honour's project.

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ACKNOWLEDGMENTS

Social Media: @jib930 **Lab Funding:**





Nicolas Henao (Dr. Peter Hedlin)

Postoperative cognition in elderly patients: is there an association with their preoperative baseline

Background: Postoperative cognitive decline is a complication among adults undergoing surgery. This study examined changes in cognitive performance after surgery and whether preoperative frailty was associated with postoperative cognitive change.

Methods: We conducted a retrospective cohort study of 114 adults aged ≥ 60 years at Royal University Hospital (RUH) or Saskatoon City Hospital (SCH). Preoperative cognition was assessed using the Montreal Cognitive Assessment (MoCA) and frailty using the Edmonton Frailty Scale (EFS). Postoperatively, patients completed an alternate MoCA. Pre- and postoperative scores were compared using Wilcoxon signed-rank tests; frailty-cognition associations were assessed using Spearman correlations.

Results: The cohort had a mean age of 71.1 years (66 males, 48 females). In SCH, total MoCA scores did not significantly change, although declines occurred in domains. In RUH, total MoCA scores significantly decreased, with additional declines in delayed recall and the MoCA Memory Index Score (MIS). Greater preoperative frailty was associated with poorer preoperative MoCA performance in SCH, but not RUH. Frailty was not significantly associated with postoperative MoCA change in either cohort.

Conclusion: Older surgical patients demonstrated postoperative declines in cognition and domains, particularly in RUH. Preoperative frailty was associated with baseline cognitive performance in SCH but did not predict postoperative cognitive change.

Postoperative cognition in elderly patients: is there an association with their preoperative baseline?

Nicolas Henao-Romero, Ally Seifert, Mary Walker, Darcie Earle, Peter Hedlin

Introduction

Cognitive deficits following surgery such as perioperative cognitive dysfunction (POCD) and post-operative delirium (POD) are common post-operative complications among older adults. POCD affects 15-60% while POD has an incidence of 40% in patients ≥ 65 years of age. (Feng et al., 2025; Inouye et al., 2014). The etiology of these conditions has been associated with socioeconomic as well as biological factors (Li et al., 2025; Yu et al., 2025). Therefore, this study aimed to examine the risk factors associated with cognitive decline after surgery. We hypothesize:

1. Cognitive function will significantly decline following surgery.
2. The frailty scores will be associated with preoperative cognitive function as well as postoperative cognitive dysfunction.

Methods

The study cohort consisted of 114 elderly patients (≥ 60 years of age) who underwent preoperative consultation at the Pre-Assessment Clinic at the Royal University Hospital (RUH) or Saskatoon City Hospital (SCH). Patients completed the Montreal Cognitive Assessment (MoCA) as well as the Edmonton Frailty Scale (EFS). Following surgery, they were reassessed with an alternate version of the MoCA and the Confusion Assessment Method (3D-CAM and CAM-ICU). Finally, a retrospective chart review was conducted for each patient. Statistical analyses included the Wilcoxon signed-rank test to compare pre- and postoperative scores, and Spearman's rho correlation to assess associations between frailty and cognitive function.

Variable	Male (n=66)	Female (n=48)	Total (n=114)
Age, years (mean)	70.2	72.1	71.1
Assessment-Surgery interval, days	8.9	4.8	8.9
Cardiac Surgery, n	25	6	31
General Surgery, n	10	6	16
Orthopedic Surgery, n	26	30	56
Neurosurgery, n	4	4	8
Obstetrics, n	0	1	1
Urology, n	1	1	2

Table 1. Descriptive Statistics. The study cohort consisted of 114 patients, including 66 males and 48 females, with a mean age of 71.1 years (70.2 years for males and 72.1 years for females).

Results

1. Postoperative Cognitive Decline: Evidence of Significant Changes After Surgery (SCH vs RUH)

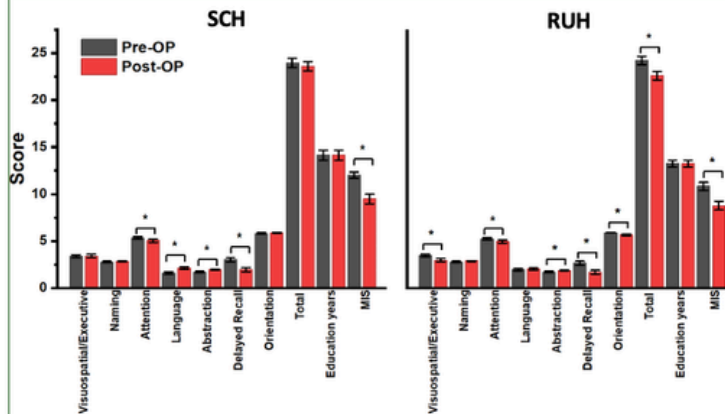


Figure 1. Comparison of preoperative (black) and postoperative (red) performance across individual domains and summary measures of the Montreal Cognitive Assessment (MoCA) in SCH and RUH surgical cohorts. In the SCH cohort, no significant change was observed in total MoCA score following surgery. In contrast, the RUH cohort demonstrated a significant postoperative decline in total MoCA score, with additional significant changes observed across several individual cognitive domains and the MoCA Memory Index Score (MIS) (* $p < 0.05$). These findings suggest greater postoperative cognitive decline among patients undergoing surgery at RUH vs SCH.

2. Association Between Frailty and Cognitive Change Following Surgery

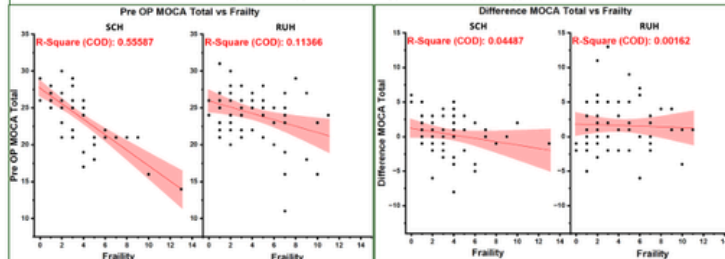


Figure 2. Association between frailty and cognitive performance before and after surgery. Scatter plots demonstrate the relationship between Edmonton Frailty Scale (EFS) scores and preoperative MoCA total scores (left) and change in MoCA total score following surgery (right) in the SCH and RUH cohorts. Each point represents an individual patient. Solid lines represent linear regression fits, with shaded areas indicating the 95% confidence intervals. R^2 values are shown for each regression model. Higher EFS scores indicate greater frailty.

Conclusion

This study demonstrates significant postoperative declines in overall cognitive performance and selected cognitive domains among elderly surgical patients, particularly in the RUH cohort. Declines were observed in delayed recall and the MoCA Memory Index Score (MIS), while changes in naming and abstraction should be interpreted with caution because of limited variability within these domains. Preoperatively, greater frailty was associated with poorer cognitive performance in the SCH cohort, whereas this relationship was not observed in the RUH cohort. Furthermore, no significant association was observed between frailty and postoperative change in MoCA scores in either cohort. These findings suggest that although frailty may be associated with baseline cognitive vulnerability in some surgical populations, it may not independently explain the magnitude of postoperative cognitive change.

Future Directions

1. **Multivariable analysis** to identify independent predictors of postoperative cognitive decline.
2. **Retrospective analysis** of comorbidities, medications, and other perioperative risk factors.
3. **Risk-prediction models** to identify high-risk patients and guide targeted interventions.

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Acknowledgements



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Hani Rukh-E-Qamar (Dr. Scott Adams)

Development and Evaluation of LifeLine: A Mixed-Methods Study of an AI-Powered Mental Health Application

Background: Marginalized populations face higher depression and anxiety rates, pointing to health inequities. Artificial intelligence and mobile applications may address these inequities by creating continuity in care between patients and their providers and offering more immediate psychosocial support.

Objective: This study aimed to explore users' perceptions of trustworthiness, acceptability, empathy, privacy, reasons for disengagement, and appropriate boundaries of use.

Methods: Saskatchewan adults used LifeLine for three weeks, with engagement data, weekly user-experience ratings, an exit survey, and virtual semi-structured focus groups collected. Qualitative data were analyzed using Braun and Clarke's thematic analysis with deductive Health-ITUEM mapping. Quantitative data were descriptively analyzed using medians, IQRs, and engagement counts.

Results: Among eight participants, ease of use remained at the highest-rated usability dimension across the three-week study (Mdn=4.00; IQR narrowed from 3.00-5.00 in Week 1 to 3.75-4.00 in Week 3), whereas perceived helpfulness and emotional support remained lower.[GU1] Qualitative findings identified that participants valued reminders, chatbot support, and personalization but raised concerns about tone, speed, privacy, and trust. Health-ITUEM mapping identified 54 negative and 42 positive occurrences, concentrated on error prevention and information needs, respectively.

Conclusion: Sustained engagement with the application depends on features being useful, responsive, trustworthy, and relevant to needs.

[GU1]To ensure the abstract is balanced we may want to present the highest-rated dimension as well as the lowest-rated dimension.

Development and Evaluation of LifeLine: A Mixed-Methods Study of an AI-Powered Mental Health Application

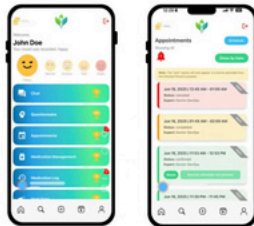
Hani Ruhk-E-Qamar^{1,2}, Gabrielle Givelichian², Joon Ko², Mayra Samaniego², Mahmood Islam², Scott Adams^{1,2}, Ivar Mendez^{1,2}

1. College of Medicine, University of Saskatchewan; 2. Virtual Health Hub, Saskatoon, Saskatchewan

INTRODUCTION

- Marginalized populations face higher depression and anxiety rates, pointing to inequities within the healthcare system^{1,2}.
- Artificial intelligence (AI) and mobile applications have the potential to address these inequities by creating continuity in care between patients and their providers and offering more immediate psychosocial support^{2,3,4}.
- LifeLine is an AI-enabled mental health and wellness platform that integrates self-management tools, provider connectivity, mood and medication tracking, virtual appointments, and an AI-powered companion to support ongoing mental health care.

Figure 1: LifeLine Patient-Facing Mobile Application



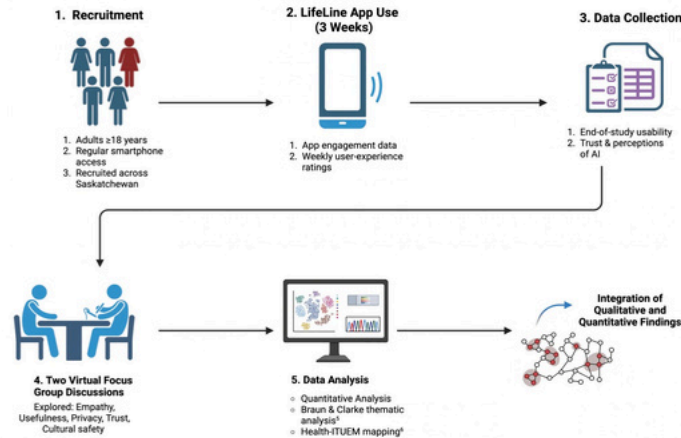
Note. Screenshots illustrate the LifeLine home dashboard and appointments interface.

OBJECTIVES

This study had two primary objectives:

1. To examine how user experience and engagement varied across the 3-week study period.
2. To explore users' perceptions of the AI tool's trustworthiness and acceptability, including perceptions of AI empathy, privacy, reasons for disengagement, and appropriate boundaries of use.

METHODS



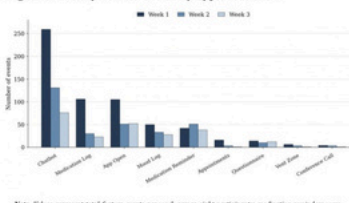
RESULTS

Table 1: Participant Demographics

Characteristics	n (%) Summary	Notes
Age, years	Mean (SD) 39.8 (4.5)	
Sex		
Male	4 (50.0%)	
Female	4 (50.0%)	
Ancestry		
White/European	5 (62.5%)	Collected from questionnaire response
Latin American	2 (25.0%)	Collected from LifeLine
First Nations	1 (12.5%)	

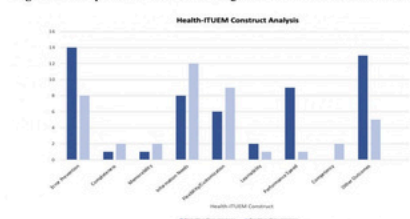
Note. Demographics are presented in aggregate to protect participant privacy. Ethnicity categories were collapsed where appropriate because of the small sample size.

Figure 2: Weekly Feature Events by Type, Weeks 1-3



Note. Values represent total feature events per week across eight participants; medication reminders were custom-generated.

Figure 3: Comparison of Positive and Negative Health-ITUEM Occurrences



Note. Bars represent coded occurrences mapped to Health-ITUEM constructs; 14 negative and 42 positive occurrences were identified.

Figure 4: Braun and Clarke Thematic Analysis



Note. Six themes were identified from focus group data using Braun and Clarke's thematic analysis.

CONCLUSIONS

- This pilot study highlights that mental health applications require a complex approach to succeed.
- Sustained engagement with applications appears to depend on whether features are perceived as useful, responsive, trustworthy, and relevant to users' needs.
- Strengths included a mixed-methods design and repeated usability assessment; limitations were the small sample (n = 8), short 3-week study period, and limited generalizability.
- Future development should prioritize meaningful personalization, intuitive functionality, privacy and trust, and tools that help users translate self-monitoring into actionable insight and ongoing support.

Learn more about our app below:



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Acknowledgements

We thank the study participants, the LifeLine development team, and research staff who supported recruitment, data collection, and analysis. We acknowledge the University of Saskatchewan College of Medicine for its support. The figures in this poster were created through support of BioRender, Microsoft PowerPoint and Canva.



Ethan Schultz (Dr. Evyn Peters)

Patient Experiences During Treatment as Predictors of Response to Ketamine for Treatment-Resistant Depression

This study evaluates the safety and efficacy of intranasal racemic ketamine for treatment-resistant depression (TRD), and examines predictors of treatment response. Forty five inpatients with TRD were treated on up to four consecutive days with 50, 75, or 100 mg doses. Symptoms were measured pre- and post-treatment using the Symptom Checklist-90 (SCL-90) and the Suicidal Ideation Attributes Scale (SIDAS). The SCL-90's Interpersonal Sensitivity subscale was used to measure self-consciousness and feelings of inferiority. Patient experiences during treatment were measured using two subscales of the Mystical Experiences Questionnaire: positive mood and dissociation.

Ultimately, 28 participants (62.2%) were responders (defined as a 50% or greater reduction in depression scale scores). Suicidal ideation and interpersonal sensitivity scores also declined significantly. Positive mood (euphoria) during treatment was a significant positive predictor of treatment success, but dissociation had no predictive value. The treatments were relatively well-tolerated: systolic blood pressure increased only modestly, and no participants needed medication to manage blood pressure during treatment. There were no serious adverse events; the most common adverse effects were sedation, dizziness, and numbness.

Overall, these findings suggest that intranasal ketamine is safe and effective in TRD. However, long-term outcomes were not assessed, and further research is needed.

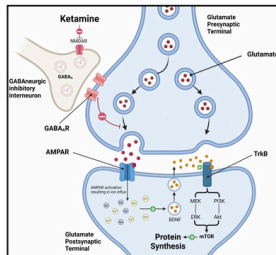
Patient Experiences During Treatment as Predictors of Response to Ketamine for Treatment-Resistant Depression

Ethan Schultz,¹ Dr. Camelia Adams,² Dr. Altaf Masood,² Dr. Dawn Roccamatizi,² Dr. Annabelle Wanson,² Dr. Evyn Peters²

¹College of Medicine, ²Department of Psychiatry, University of Saskatchewan

Introduction

Treatment-resistant depression (TRD) is associated with high morbidity, functional impairment, and increased suicide risk.¹ Traditional antidepressants often require weeks to take effect and have low remission rates for patients with TRD.² Ketamine therapy has emerged as a viable alternative with rapid and powerful antidepressant effects. Biochemically, ketamine functions by blocking NMDA receptors in the brain, which ultimately initiates a repair process called synaptogenesis. However, it is not well understood how patient experiences during ketamine administration modulate efficacy.³



Mechanism of ketamine's antidepressant effects⁴

Objectives

- 1) Evaluate the efficacy and safety of intranasal (IN) ketamine for patients with TRD being treated at Royal University Hospital (Dube Centre & Mental Health Short Stay Unit).
- 2) Explore the effect of ketamine on interpersonal sensitivity (IPS; i.e., self-consciousness, feelings of inferiority, sensitivity to criticism) as a secondary outcome.
- 3) Determine if depression improvement is influenced by subjective experiences (i.e., euphoria, dissociation), hemodynamic changes, or adverse effects experienced during treatment.

Methods

Study Design & Population: Data was collected prospectively from 47 depressed inpatients (unipolar or bipolar) completing a standardized IN ketamine protocol. Two patients did not complete the full treatment course, leaving 45 participants.

Treatment Protocol: Patients received IN ketamine spray (50-100 mg) on four consecutive weekdays. Doses were adjusted based on patient weight and tolerance. Blood pressures were measured at baseline and every 30 minutes for 90 minutes.

Outcome Measures: Symptom Checklist (SCL-90) subscales were used to assess depression as the primary outcome and IPS as a secondary outcome. The Suicidal Ideation Attributes Scale (SIDAS) was added later as an additional secondary outcome. The Mystical Experiences Questionnaire was used to measure ketamine-induced euphoria (Positive Mood subscale) and dissociation (Transcendence of Time and Space subscale). Participants reported adverse effects using structured checklists.

Statistical Analysis: Scores for depression, suicidal ideation, and IPS before and after treatment were analyzed using paired t-tests. Linear regression was used to determine whether MEQ subscales predicted depression change scores.

Sample Characteristics

		Mean
Age		36.5
# of Psychiatric Medications		3.6
	n	%
Female	32	71.1
MDD	34	75.6
GAD	26	57.8
PTSD	16	35.6
SUD	10	22.2
ADHD	10	22.2

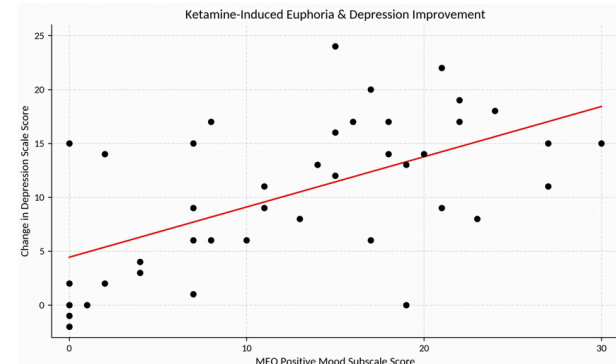
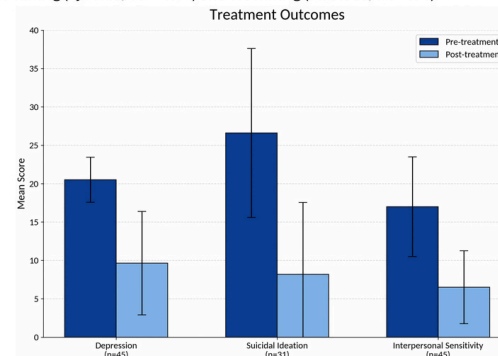
Results

Overall Efficacy: Depression ($t(44) = 10.66$) and suicidal ideation ($t(30) = 8.55$) decreased significantly (both had $p < .001$). Excluding the 12 participants with medication changes did not meaningfully impact these findings or their statistical significance ($t(32) = 8.71$ and $t(21) = 7.14$, respectively; both had $p < .001$). Overall, 62.2% of participants were treatment responders (defined as having a depression score decrease of $>50\%$ from baseline). IPS scores also decreased significantly ($t(44) = 9.37$).

MEQ Subscales: There was a significant effect for the Positive Mood subscale ($b = .45$, $\beta = .56$, $t(41) = 4.47$, $p < .001$), but the Time and Space subscale was not significantly correlated with clinical improvement ($r = .10$, $p = .53$).

Adverse Effects: There were no severe adverse events. The most common adverse effects were sedation (48.9% of participants), dizziness (40.0%), numbness (26.7%), and blurry vision (20.0%). No statistically significant relationship was found between depression score change and number of adverse effects by participant ($r = .02$, $p = .92$).

Hemodynamic Effects: No patients needed medication to control blood pressure. The highest possible dose (100 mg) was associated with mean blood pressure increases of 10.9 mmHg (systolic; SE = 1.05) and 7.0 mmHg (diastolic; SE = .76).



Conclusions

Overall Efficacy: IN ketamine delivers rapid, profound reductions in depressive symptoms, suicidality, and IPS in TRD. It is also relatively well-tolerated.

Role of Positive Mood: Positive mood and euphoria during treatment strongly predicted therapeutic success. Dissociation had no predictive value.

Implications: Further research into the link between ketamine-induced euphoria and clinical improvement could help inform how ketamine therapy is delivered in the future.

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Quality Improvement





Chloe Argue (Dr. Sabira Valiani)

Connect-ICU: Implementing human-centered communication solutions to improve patient and family-centered care in the ICU

Background: Patient and family-centered care in the ICU is often threatened by human and system factors, preventing effective communication. This summer research project is under the Connect-ICU program of research, which aims to leverage communication technology to improve patient and family-centered care (PFCC) in the Intensive Care Unit (ICU). It is hypothesized that the development of a communication strategy using “low tech, high impact” communication tools will improve PFCC outcomes while reducing burnout of healthcare providers.

Objective: We sought to develop surveys to understand 1) PFCC outcomes and 2) ICU healthcare provider burnout and workload.

Methods: We reviewed the literature and found relevant surveys capturing aspects of PFCC and healthcare provider burnout and workload. All surveys questions were copied verbatim into an Excel spreadsheet and reviewed by the project team for repetitiveness and relevance to the project. Repetitive and irrelevant questions were removed. The spreadsheet was reviewed by patient family partners (for PFCC survey) and healthcare providers on the team. We performed pilot testing with the Connect-ICU research team.

Results: We created two survey tools that will measure relevant outcomes for the Connect-ICU communication strategy implementation.

Connect-ICU: Implementing human-centered communication solutions to improve patient and family-centered care in the ICU

Chloe Argue & Dr. Sabira Valiani

Background and Rationale

Patient and family-centered care in the ICU is often threatened by human and system factors, preventing effective communication. This summer research project is under the Connect-ICU program of research, which aims to leverage communication technology to improve patient and family-centered care (PFCC) in the Intensive Care Unit (ICU). It is hypothesized that the development of a communication strategy using “low tech, high impact” communication tools will improve PFCC outcomes while reducing burnout of healthcare providers.

Our research team has used human-centered design to co-create solutions to current challenges with communication in the ICU. These solutions include communication tools which are easily implementable into clinical practice, require minimal resource utilization, and have the potential for a significant impact on the quality of PFCC in the ICU. These co-created solutions can be combined and tailored to each ICU’s unique needs, to develop a low-resource, high-impact communication strategy.

The implementation project will seek to **improve PFCC while reducing healthcare provider workload**. However, there are no widely-accepted survey instruments to assess these outcomes.

Objectives

The objective of this specific project under the Connect-ICU umbrella project was to create surveys on Redcap to assess PFCC outcomes and ICU healthcare provider burnout and workload.

We sought to develop surveys to understand:

- 1) PFCC outcomes
- 2) ICU healthcare provider burnout and workload

Patient-Family Survey Methods

The Patient-Family Surveys were created based on 3 proposed surveys: Patient Perception of Patient-Centeredness Revised (PPPC-R), Quality of Communication (QOC), and Family Satisfaction with Care in the Intensive Care Unit-24 (FS-ICU-24). Survey questions were pasted verbatim into an Excel document and were cross-checked for repetitiveness and assessed for exclusion.

As survey instruments are often analyzed together, we erred on the side of keeping whole survey parts in. Therefore FS-ICU questions on ICU environment, assessment of pain and symptoms were kept in, while we removed the majority of the QOC survey as questions were either repeated or not relevant. In the Excel document, modified questions were created (where needed) for ICU patient family members, and ICU patients. Decisions to include and exclude were reviewed by Patient Family Partners. Using included questions modified for the ICU-Family and ICU-Patient, 2 dedicated surveys were created for ICU patient family and ICU patients. Each survey had 4 parts:

- Part 1. FS-ICU24 – Satisfaction with Care
- Part 2. FS-ICU24 – Satisfaction with Information and Decision Making
- Part 3. Perception of Patient Centeredness – Revised
- Part 4. Overall Communication

Surveys were pilot tested with Patient Family Partners. Patient family partners agreed on inclusion/exclusion of questions in the Excel document.

Edits were then made for clarity when reviewed by the Provincial Research Facilitator of the Anesthesia Department.

ICU Healthcare Provider Survey Methods

All proposed surveys (Barriers to Care, Measure of Moral Distress, Nursing Activities Score, Mini Z Worklife and Burnout) were reviewed.

Survey questions were pasted verbatim into an Excel document and surveys were cross-checked for repetitiveness. Questions that were not relevant to the purpose (i.e. those related to individual healthcare provider-patient communication like eye contact, full attention or those related to dying or getting sicker) were excluded.

As survey instruments are often analyzed together, we erred on the side of keeping whole survey parts in. Decisions to include and exclude were reviewed by healthcare providers.

Survey was pilot tested with healthcare providers and survey edits were suggested by the Provincial Research Facilitator of the Anesthesia Department, reviewed, and edited for clarity.

Results

Two survey tools were created that will measure relevant outcomes for the Connect-ICU communication strategy implementation, for both PFCC outcomes and ICU healthcare provider burnout and workload.

Acknowledgements

I would like to thank members of the Connect-ICU team (Kyle Hertes, Stephanie Bigbsy), patient-partners, Darcie Earle (Anesthesia Provincial Research Coordinator), and RUH ICU staff.



Stefanie Kiriazopoulos (Drs. Tracy Wilson & James Stampien)

Emergency Department Use of Analgesia for Acute Musculoskeletal Pain in Children

Musculoskeletal (MSK) injuries are common reasons for pediatric Emergency Department (ED) visits and are frequently associated with significant pain. However, pediatric pain remains challenging to assess and manage. Previous work identified variation in analgesia practices between Saskatchewan EDs, prompting investigation into factors associated with analgesia administration.

A retrospective chart review was conducted of patients aged 0–16 presenting with acute MSK injuries between 2022 and 2024 across four Saskatchewan EDs: Regina General Hospital (RGH), Pasqua Hospital (PH), Jim Pattison Children's Hospital (JPCH), and St. Paul's Hospital (SPH). Demographic, triage, injury, pain assessment, pre-hospital analgesia, and analgesia administration data were extracted. Associations with ED analgesia use were assessed using chi-square, Mann-Whitney U, and Kruskal-Wallis tests.

Among 3,488 patients, 54.1% received ED analgesia. Analgesia administration varied significantly by site (JPCH 69.8%, SPH 51.3%, PH 44.9%, RGH 36.1%; $p < 0.001$). Significant associations with analgesia use were also identified for pre-ED analgesia use, pre-treatment pain severity, and ED shift. Age, sex, EMS arrival, injury type, and year of presentation were not associated with analgesia administration.

Analgesia administration for pediatric MSK injuries varied across Saskatchewan EDs and was associated with patient and presentation factors. These findings highlight opportunities for targeted interventions to improve equitable pediatric pain management.

Factors Associated with Emergency Department Analgesia Administration for Pediatric Musculoskeletal Injuries

Stefanie Kiriazopoulos, Kyle Guild, Jasmin Ogren, Revathi Nair, Seyara Shwetz, Grazyna Burek, James Stempien, Tracy Wilson

Introduction

- Pain is common in pediatric emergency care. Nearly 60% of childhood emergency department (ED) visits involve pain, with musculoskeletal (MSK) injuries among the most common causes.¹
- Timely and effective pain management is critical. Unmanaged childhood pain can lead to lifelong harms like medical care avoidance and heightened pain sensitivity.²
- Despite growing clinical guidance, children's pain remains under-recognized and under-treated, particularly in the ED setting.^{3,4}
- Our previous analysis of this Saskatchewan cohort demonstrated significant variation in analgesia administration between emergency departments, prompting further investigation into factors associated with analgesia use.

Objective

Identify patient, injury, and presentation factors associated with emergency department analgesia administration for pediatric musculoskeletal injuries.

Methods

- Retrospective chart review of pediatric patients presenting with acute MSK injuries across four Saskatchewan EDs: Regina General Hospital (RGH), Pasqua Hospital (PH), Jim Pattison Children's Hospital (JPCH), St. Paul's Hospital (SPH).
- Included patients aged 0–16 years with acute MSK injuries (e.g., fractures, sprains, strains, and dislocations) presenting between January 2022 and December 2024.
- Data extracted from electronic medical records included demographics, triage characteristics, injury characteristics, pain assessments, pre-ED analgesia use, ED analgesia use, and ED length of stay.
- Primary outcome was use of ED analgesia.
- Descriptive statistics and bivariate analyses were performed using chi-square, Mann–Whitney U, and Kruskal–Wallis tests to identify factors associated with analgesia administration.

Results

Study Population:

- 3,488 pediatric patients with acute MSK injuries were included across four Saskatchewan emergency departments (2022–2024):
 - Jim Pattison Children's Hospital (JPCH): 1,543
 - Pasqua Hospital (PH): 964
 - Regina General Hospital (RGH): 831
 - St. Paul's Hospital (SPH): 150
- Overall median age was 11.3 years (IQR 5).
- Overall sex distribution of 51.4% male (n=1,794) and 48.6% female (n=1,694).
- The most common triage categories were “lower extremity injury” (41.7%, n=1,455) and “upper extremity injury” (35.3%, n=1,231).
- Analgesia was administered to 54.1% of ED pediatric patients overall (n=1,887).

Table 1. Patient, Injury, and Presentation Factors Associated with ED Analgesia Use

Factor	Association with ED analgesia use	P-value
Site	Rate of analgesia use varied significantly between hospital EDs.	<0.001
Pre-ED analgesia use	Patients who received analgesia before presenting to the ED were less likely to receive additional analgesia in the ED (45.3% vs. 57.5%).	<0.001
Pre-treatment pain severity	ED analgesia use increased with documented pain severity (mild 44.0%, moderate 50.9%, severe 63.9%; severity not documented 59.6%).	<0.001
ED shift at time of triage	Greater rate of analgesia use during the evening shift (16:00–23:59; 56.9%) and night shift (00:00–07:59; 57.3%) than during the daytime shift (08:00–15:59; 49.2%).	<0.001

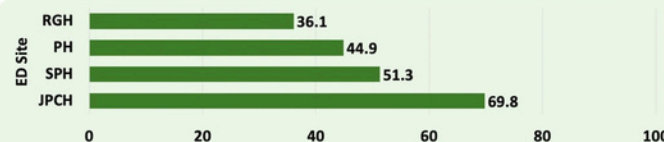


Figure 1: Proportion of pediatric patients receiving analgesia in the ED by site. Regina General Hospital (36.1%, n=300), Pasqua Hospital (44.9%, n=433), St. Paul's Hospital (51.3%, n=77), and Jim Pattison Children's Hospital (69.8%, n=1077) (p < 0.001).

Additional Findings:

- No significant associations were identified with patient age, sex, EMS arrival, injury type, or year of presentation.
- Statistically significant associations were observed with CTAS, injury region, triage category, and mode of injury; however, these variables did not demonstrate clear clinically interpretable patterns.

Conclusion

- Significant variation in ED analgesia administration persisted across Saskatchewan emergency departments, suggesting that local practice patterns and system-level factors may influence pediatric pain management.
- Analgesia use was associated with patient and presentation factors, including pre-ED analgesia use, pain severity, and ED shift.
- Demographic factors, including age and sex, were not associated with analgesia administration, suggesting that differences in treatment were not explained by patient demographics alone.
- Statistically significant associations with CTAS and injury characteristics lacked clear clinical patterns, warranting further investigation.
- These findings identify opportunities for targeted quality improvement initiatives to promote timely and equitable pediatric pain management across emergency departments.

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Acknowledgements

This project was supported by the College of Medicine 2026 Dean's Project Program and conducted through the Department of Emergency Medicine.



Hannah Kolkman (Dr. Angelica Lang)

Ergonomic interventions to reduce shoulder demand in farmers: A pilot study

Shoulder disorders are highly prevalent among farmers due to high levels of exposure to known risk factors, such as extreme or repetitive postures. The purpose of this study was to evaluate two different ergonomic interventions aimed at reducing shoulder demand during farm-related tasks. Thirty adults without shoulder pain completed four sets of farm-related lifting tasks, including different combinations of lifting heights and implements. Each participant received two interventions in randomized order: 1) a video describing posture cues and 2) a shoulder activation exercise protocol. Humeral and scapular angles were extracted for each task and assessed using statistical parametric mapping (SPM) and two-way repeated-measures ANOVAs. Post-intervention lifting postures showed the greatest change after the cues, but only in the low lifting tasks. When examined by intervention order, it was revealed that only those who received the cues first exhibited a lasting effect on lifting postures throughout the testing period. These results suggest that immediate, positive effects from a short-term ergonomic intervention are possible in a healthy population, which can help direct further research on shoulder pain in a farmer-specific demographic.



Ergonomic Interventions to Reduce Shoulder Demand in Farmers: A Pilot Study

Hannah M. Kolkman^{1,2}, Denise Balogh¹, Joel L. Lanovaz², & Angelica E. Lang¹

¹Canadian Centre for Rural and Agricultural Health, College of Medicine, University of Saskatchewan ²College of Kinesiology, University of Saskatchewan



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and Agricultural Health
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Introduction

- Musculoskeletal disorders (MSDs) are highly prevalent among farmers [3].
- One of the most commonly reported MSD of farmers in rural Saskatchewan is shoulder pain [2].
- Ergonomic interventions may help minimize shoulder strain and prevent MSDs during work tasks [1].

Purpose: to assess two ergonomic interventions aimed at reducing shoulder demand during farm-related lifting tasks.

Methods

- 31 healthy adults from a convenience sample who were free from shoulder pain or injury participated in this study (15 males, 16 females, age 26 ± 7).
- All participants were outfitted with optical motion capture markers (Fig. 1) to track motion of the humeri, scapulae, and thorax.



Figure 1: Placement of motion capture markers.

- Participants performed 4 sets of 3 overhead lifts and 3 floor-to-waist lifts each with a milk crate (Fig. 2), seed bag, and pail.



Figure 2: Bag low task.

- Statistical parametric mapping (SPM) and two-way repeated-measures ANOVAs (time x intervention) assessed the effects of each intervention on humeral and scapular angles.

Interventions

Ergonomic Cues

- 3-minute video describing posture cues for safer lifting practices

Exercise Protocol

- 10 exercises, each targeting different muscles to activate the entire shoulder complex

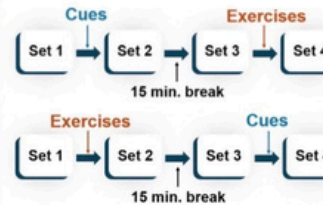


Figure 3: Possible orders of protocol execution.

Results

Overall Change in Humeral Elevation From Ergonomic Interventions

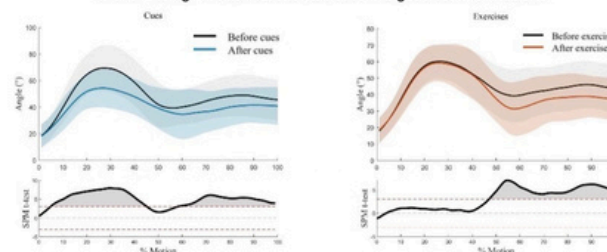


Figure 4: Change in humeral elevation angle between interventions (both intervention orders combined) throughout a floor-to-waist seed bag lift (top). Regions of the t-test curve outside the dotted lines are statistically significant (bottom).

- The cues resulted in **reduced humeral elevation** throughout the whole lift, while the exercises showed a reduction only in the second half of the lift (Fig. 4).

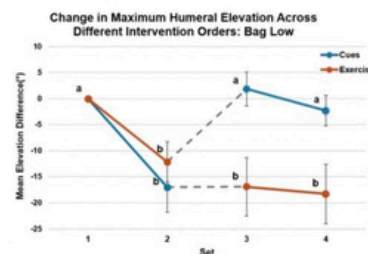


Figure 5: Change in maximum humeral elevation angle ($\pm$ 95% CI) between interventions and intervention orders during floor-to-waist seed bag lift. Sets not sharing the same letter within an intervention order are statistically different ($p < 0.05$).

$n = 17$ received **ergonomic cues** first
 $n = 14$ received **exercise protocol** first

Cues first:

- The initial decrease in humeral elevation **was maintained** after the washout period (Fig. 5).

Exercises first:

- The initial decrease in humeral elevation **returned to baseline** after the washout period (Fig. 5).

Interpretation

- Both interventions resulted in improved humeral kinematics during the low lifts, with **the ergonomic cues being the most effective**.
- Lower humeral elevation signifies lifting the load closer to the body and reducing force demand at the shoulder.
- The positive effects from the cues prevailed past the washout period, suggesting retention of knowledge gained from the intervention.
- Providing individuals with these ergonomic recommendations may encourage them to apply the cues to their own work tasks.
- While previous ergonomics research has shown improved kinematics from longitudinal interventions [4], **these findings suggest that immediate effects from a short-term intervention are possible**.
- Further research is needed to evaluate the effects of these interventions on musculoskeletal pain in a farmer-specific demographic.

References

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Acknowledgments



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Jasmin Ogren (Drs. Tracy Wilson & James Stampien)

I Might as Well Just Suffer at Home”: Understanding Emergency Department Utilization and Decision-Making Among Individuals Living with Chronic Pain

Background: Chronic pain drives substantial healthcare utilization, including disproportionate emergency department (ED) use among a relatively small group of patients. Frequent ED use is increasingly recognized as an indicator of inadequate pain management. This study examined ED utilization and decision-making among individuals living with chronic pain in Saskatchewan.

Methods: An online mixed-methods survey collected demographics, pain characteristics, ED experiences, reasons for attending or avoiding the ED, and open-ended feedback. Preliminary quantitative analyses used descriptive statistics and chi-square or Fisher’s exact tests.

Results: Among 279 respondents, 52.1% reported a pain-related ED visit in the previous year. Common reasons for seeking ED care included pain severity (60.4%), fear of serious illness (44.2%), uncontrollable pain (44.2%), and new or unusual symptoms (40.3%). Despite this, 90.4% reported avoiding the ED during a severe pain episode, most commonly because of long wait times (80.7%), previous negative experiences (64.8%), perceived lack of benefit (61.4%), and fear of stigma (51.1%). ED avoidance was associated with previous negative ED experiences ($p=.002$), not feeling believed by ED staff ($p<.001$), and inadequate pain treatment at the ED ($p<.001$).

Conclusion: Preliminary findings suggest a tension between needing the ED during severe pain and avoidance shaped by previous negative care experiences.

“I Might as Well Just Suffer at Home”: Understanding Emergency Utilization and Decision-Making Among Individuals Living with Chronic Pain

Jasmin Ogren, Stefanie Kiriazopoulos, Mohammad Jamil, Waleed Janjua, James Stempien, Tracy Wilson

Introduction

- Chronic pain is common and contributes to substantial healthcare utilization, including Emergency Department (ED) visits.
- People living with chronic pain account for a disproportionate number of ED visits.¹
- Frequent ED use is recognized as an indicator of inadequate pain management.²
- In Saskatchewan, ED overcrowding and limited access to specialized chronic pain care may further complicate timely, appropriate pain management.
- Existing research has largely focused on patient experiences of chronic pain care within the ED.^{3,4}
- Less is known about who uses the ED, what drives decisions to seek care during pain crises, and why some patients choose to avoid the ED.⁵

Objectives

- Identify factors influencing decisions to seek or avoid ED care during severe pain.
- Describe patterns and predictors of pain-related ED utilization in Saskatchewan.
- Explore experiences and perceptions of ED care among individuals living with chronic pain.

Methods

- Online mixed-methods survey of individuals living with chronic pain in Saskatchewan.
- Recruitment: convenience sampling using posters in Saskatchewan EDs/clinics, social media, and community distribution.
- Survey: demographics, pain characteristics, healthcare utilization, ED experiences, reasons for attending or avoiding the ED, and open-ended responses.
- Preliminary quantitative analyses included descriptive statistics and associations assessed using Pearson χ^2 or Fisher's exact tests.
- Data collection is ongoing.

Results

Sample

n=279 • 76.7% aged 25 – 54 years • 86.7% identified as women

79.2%

chronic pain >5 years

53.5%

constant pain

58/100

mean pain rating

ED Use

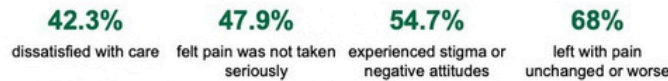
52.1% reported ≥ 1 pain-related ED visit in the past year



Figure 1. Most commonly reported reasons for seeking ED care; multiple responses permitted.

Shorter pain duration, more ED use: Participants with ≤ 5 years of chronic pain were more likely to report ED use than those with >5 years of pain (66.7% vs 48.0%; $\chi^2(1)=4.71$, $p=.030$).

Experiences of ED Care



76.3% reported that negative ED experiences had contributed to avoiding future care.

Avoidance of ED Care

90.4% had avoided the ED during a severe pain episode.



Figure 2. Most commonly reported reasons for avoiding ED care during a severe pain episode. Multiple responses permitted.

Table 1. Associations between prior ED care experiences and subsequent avoidance of ED care.

Factor	Avoided ED Care	p-value
Overall ED experience	97.7% with a negative experience vs 84.1% with a positive/neutral experience	0.002
Feeling believed	96.7% who felt not fully believed by ED staff vs 73.5% who felt often/always believed	<.001
Adequacy of pain treatment	96.6% who felt inadequately treated at the ED vs 74.3% who felt adequately treated	<.001

All associations shown were statistically significant ($p < 0.05$)

ED use was not associated with having a regular pain-care provider or residence.
ED avoidance was not associated with having a regular pain-care provider.

Conclusions

- Preliminary findings suggest a tension between needing the ED during severe pain episodes and actively avoiding it.
- Severe, uncontrolled, or concerning symptoms prompted ED visits, while long wait times, stigma, perceived lack of benefit, and prior negative experiences contributed to avoidance.
- Experiences of care appear particularly important: negative ED experiences, not feeling fully believed by staff, and inadequate pain treatment were associated with subsequent avoidance.
- Ongoing data collection and qualitative analysis will explore how ED experiences and self-management strategies shape future care-seeking decisions.
- These findings may inform emergency and primary care strategies to improve chronic pain care pathways, reduce avoidable ED use, and improve patient experiences of chronic pain care.

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Acknowledgement

This project was supported by the College of Medicine 2026 Dean's Project Program and conducted through the Department of Emergency Medicine.



Abdullah Qureshi (Dr. Anil Sharma)

Diagnostic Delays in Otolaryngology: A Wait time and Cost Analysis of Cone-Beam CT Compared with Multidetector CT

A diagnostic test is only useful if patients can access it in time. Timely, and cost-effective imaging is central to specialty care, yet multidetector CT (MDCT) and cone-beam CT (CBCT) pathways have rarely been compared in real-world practice. This retrospective chart review examined 133 Otolaryngology (MDCT) and 106 Oral and Maxillofacial Surgery (CBCT) patients to compare diagnostic wait times, clinical visit burden, and cost. CBCT patients experienced significantly shorter imaging turnaround (8.5 vs. 61.5 days) and faster result review (10 vs. 80 days; both $p < 0.0001$), along with fewer clinical encounters (1 vs. 4 visits; $p < 0.0001$) and less cumulative travel distance for patients (13 vs. 68 km; $p = 0.020$). CT acquisition costs were modestly lower for CBCT (\$314 vs. \$369; $p < 0.001$); however, total patient-borne costs were contingent on insurance coverage, with uninsured CBCT patients potentially paying more than their MDCT counterparts (\$538.49 vs \$450.68). Because imaging modality was tied to specialty referral rather than randomized, these findings inherently reflect differences in care pathway as much as imaging technology itself. Overall, CBCT-based pathways meaningfully reduce wait time and healthcare utilization, though cost advantages depend on funding structure, supporting further research to try and isolate the effect of imaging modality on access and outcomes.

Diagnostic Access, Patient Burden, and Cost Comparison of Cone-Beam CT versus Multidetector CT for Otolaryngology

Abdullah Qureshi, Tanish Patel, Hamza Arshad, Dr. Kabir Viridi, Dr. Russell Murphy, Dr. Anil Sharma

INTRODUCTION

1) Hospital-based multidetector CT (MDCT) increases delays and visits

- Research demonstrates median of 108 days from ENT specialist to treatment decision for neck masses¹
- MDCT not accessible in the clinic and require additional appointment



A: Clinic-based CBCT². B: Hospital-based MDCT³

2) Saskatchewan continues to face substantial CT access pressure

82 days

10% of patients wait longer than 82 days to receive a CT⁴

8,048 patients

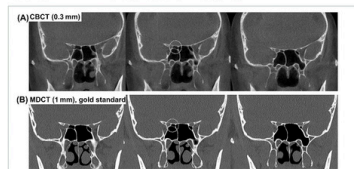
Currently on the provincial CT waitlist⁴

60 days

Target for non-urgent imaging in the province⁴

3) Clinic-based cone-beam CT (CBCT) may streamline care while upholding clinical accuracy in Otolaryngology

- CBCT offers comparable depiction of sinuses compared to MDCT⁵
- American Academy of ENT recognizes CBCT for its utility in ENT diagnostic imaging⁶



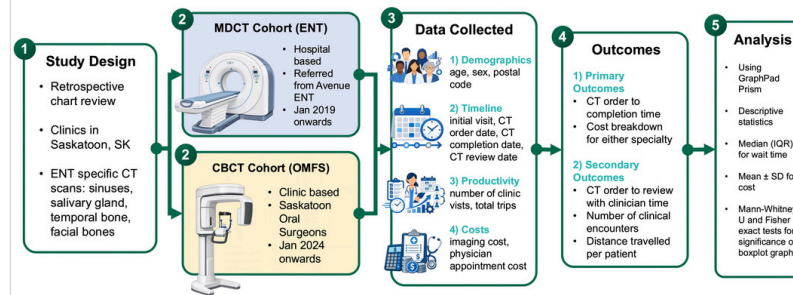
Comparison of CBCT and MDCT for sinonasal imaging⁷

OBJECTIVES & HYPOTHESIS

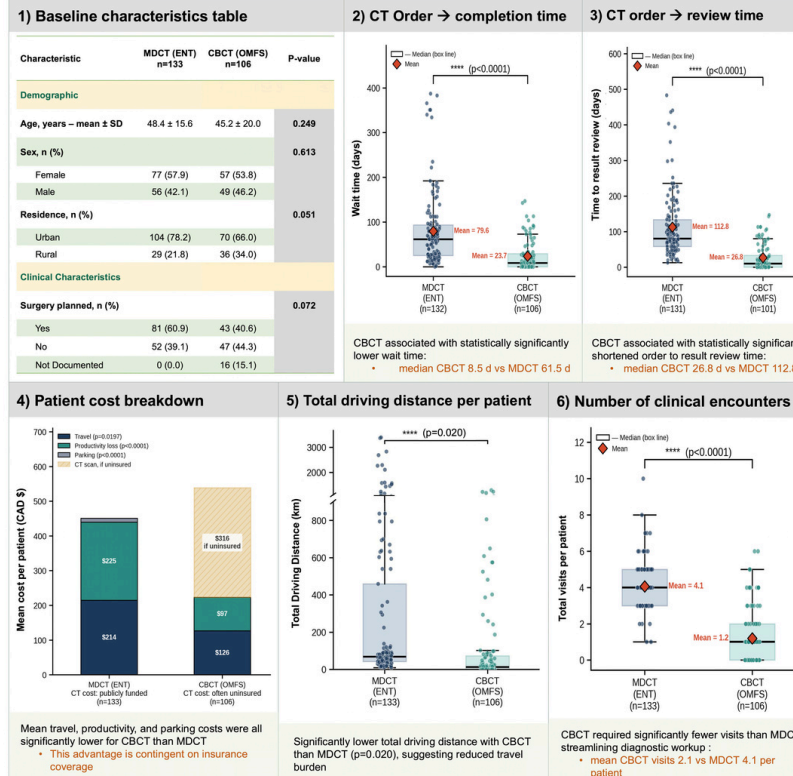
- Compare diagnostic timelines and number of patient visits between CBCT and MDCT.
- Compare public and private costs, including travel, parking, productivity loss, and rural burden between CBCT and MDCT.

Hypothesis: CBCT will be associated with shorter diagnostic timelines, fewer trips, and lower patient costs than MDCT.

METHODS



RESULTS



CONCLUSIONS

- CBCT associated with significantly faster imaging turnaround then MDCT
 - Median time CT order to completion: 8.5 days for CBCT vs 61.5 days for MDCT (p<0.0001) (panel 2)
- CBCT pathway imposes lower health-system utilization and patient travel burden
 - Fewer median clinical encounters and travel distance for CBCT vs MDCT (p<0.0001 and p=0.020) (panel 5&6)
- CBCT cost advantage contingent on insurance coverage
 - CBCT cost significantly exceeded MDCT cost assuming no patients were covered for the cost of imaging (\$538.49 vs \$450.68)
- Data agrees with current literature
 - ~57 day week wait for CT scan in 2024, close to 61.5 days identified in this study⁸
 - Cost-benefit analysis from Singapore demonstrated CBCT cost of 187.50 vs. 475.13 for MDCT. Our results are directionally congruent, but show more conservative reduction⁹

LIMITATIONS

- Unequal Cohort comparisons
 - Temporal mismatch between CBCT data (2024 onwards) and MDCT cohort (2019 onwards) → wait times can change over time
 - CBCT has specialty referral pathway → same day CBCT pathway via OMFS clinic may deflate wait times
- Assumptions in Cost Analysis
 - Travel distance derived from first three letters of postal code
 - Productivity loss estimated using wage/time assumptions rather than direct measurements
 - Exact CBCT payer/insurance status was unavailable
- Generalizability and Interpretation
 - Single health region comparison in Saskatoon, SK
 - Results not applicable to indications where CBCT is inappropriate (head and neck masses, deep neck infections, etc)

FUTURE DIRECTIONS

- Prospective design with randomization to MDCT or CBCT referrals only from ENT → decrease confounders
- Identify # of patients with insurance coverage for CBCT and % coverage → increase accuracy
- Measure outcomes to see if faster pathway leads to appropriate treatment → ensure safety in addition to efficiency
- Measure patient overall satisfaction and access with either imaging modality

ACKNOWLEDGEMENTS & REFERENCES

I would like to acknowledge the support of the Deans Summer Research Project Initiative and the College of Medicine. I would also like to thank Dr. Sharma, Dr. Murphy and Dr. Viridi for providing guidance and mentorship throughout the summer.

1. [Reference text] 2. [Reference text] 3. [Reference text] 4. [Reference text] 5. [Reference text] 6. [Reference text] 7. [Reference text] 8. [Reference text] 9. [Reference text]



Hassan Sabir (Dr. Rabia Shahid)

Understanding Gaps and Needs in Diabetes Care During Hospital Discharge

Background: Hospital discharge is a vulnerable transition for patients with diabetes, particularly when treatment regimens are modified without patients fully understanding the changes. Limited evidence has examined diabetes-specific discharge education from the patient's perspective.

Methods: A cross-sectional survey of patients with diabetes admitted to medical and surgical units at two tertiary care hospitals assessed, prior to discharge, awareness of changes to the diabetes management plan, discharge education received, and comfort managing diabetes at home.

Results: Of 113 participants, 88.5% (n=100) had type 2 diabetes, and 61.1% (n=69) were medical admissions. Only 38.9% (n=44) were fully aware of changes to their management plan; 44.2% (n=50) were unsure or unaware. At discharge, 38.1% (n=43) received no verbal or written diabetes instructions, and 44.2% (n=50) received complete hypoglycemia education. At home, 41.6% (n=47) felt very comfortable and 21.2% (n=24) somewhat comfortable managing diabetes. Lack of discharge instructions was more frequent among surgical patients (47.7%) than among medical patients (31.9%), and complete hypoglycemia education was less frequently provided to surgical patients (36.4%) than to medical patients (49.3%).

Conclusion: Important gaps exist in diabetes discharge education, and these gaps were more pronounced among surgical patients. Standardized, patient-centred discharge education may improve preparedness for safe self-management.

Exploring Gaps and Needs in Diabetes Management at Hospital Discharge

H. Sabir¹, R. Shahid²

1. College of Medicine | 2. Department of Medicine — University of Saskatchewan, Saskatoon, SK, Canada

BACKGROUND

Hospital discharge is a high-risk transition for patients with diabetes. Medication regimens are frequently altered during admission, and patients who do not understand these changes are more susceptible to post-discharge medication errors and adverse events.^{1,2}

Despite guideline recommendations for structured diabetes education and discharge planning, no standardized diabetes-specific discharge protocol is in place at our centres, and limited evidence has examined the quality of this education from the patient's perspective. Also whether these gaps differ between patients admitted to medical and surgical services remains unclear.

OBJECTIVES

Primary: To evaluate diabetes-related discharge education and identify gaps in patients' awareness, understanding, and readiness for self-management after hospitalization.

Secondary: To compare these outcomes between patients admitted to medical and surgical services.

MATERIALS & METHODS

Design: Cross-sectional survey.

Setting: Medical and surgical inpatient units at Royal University Hospital (RUH) and St. Paul's Hospital (SPH), two tertiary care hospitals in Saskatoon, SK.

Participants: Adult inpatients with diabetes, surveyed prior to discharge.

Instrument: An investigator-developed self-report survey (16 closed-ended and 1 open-ended item, ~15 minutes) assessing awareness of changes to the diabetes management plan, diabetes-specific discharge education received, and comfort managing diabetes at home. Responses were collected in REDCap.

Analysis: Descriptive statistics were performed using IBM SPSS Statistics v.31. Pearson's chi-square test was used to compare categorical outcomes between medical and surgical groups.

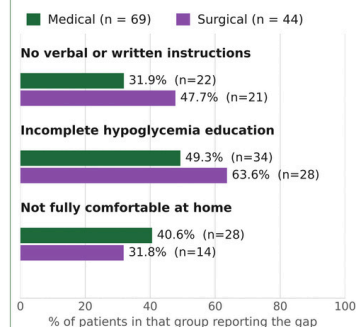
Ethics: USask Behavioural Research Ethics Board (BEH #5224); Saskatchewan Health Authority operational approval.

RESULTS

Table 1. Baseline characteristics (N = 113)

Characteristic	n (%)
Age group (years)	
18–30	4 (3.5)
31–45	17 (15.0)
46–60	23 (20.4)
61–75	46 (40.7)
≥76	23 (20.4)
Sex	
Female	54 (47.8)
Male	59 (52.2)
Type of diabetes	
Type 1	13 (11.5)
Type 2	100 (88.5)
Admitting service	
Medical	69 (61.1)
Surgical	44 (38.9)

Figure 1. Discharge education gaps by service



Proportion of each group reporting the gap; higher is worse. "Incomplete hypoglycemia education" = partial or none; "not fully comfortable" = neutral, somewhat or very uncomfortable.

RESULTS (CONT.)

Table 2. Survey responses, full cohort (N = 113)

Survey item	n (%)
Awareness of changes to the diabetes plan	
Very aware — fully understood	44 (38.9)
Somewhat aware — needs more information	19 (16.8)
Neutral — unsure if changes were made	19 (16.8)
Slightly unaware — did not fully understand	20 (17.7)
Not aware at all	11 (9.7)
Diabetes instructions received at discharge	
No verbal or written instructions	43 (38.1)
Verbal and/or written instructions	70 (61.9)
Education on identifying / managing hypoglycemia	
Complete	50 (44.2)
Partial	29 (25.7)
None	33 (29.2)
Comfort managing diabetes at home	
Very comfortable	47 (41.6)
Somewhat comfortable	24 (21.2)
Neutral	20 (17.7)
Somewhat uncomfortable	16 (14.2)
Very uncomfortable	6 (5.3)

Percentages are of the full cohort (N = 113). One response to the hypoglycemia item was missing (0.9%).

RESULTS (CONT.)

Table 3. Medical vs. surgical patients

Outcome	Medical (n = 69)	Surgical (n = 44)	p-value
Discharge Instructions:			0.091
None received	22 (31.9)	21 (47.7)	
Hypoglycemia Education:			0.366
Complete	34 (49.3)	16 (36.4)	
Partial	16 (23.2)	13 (29.5)	
None	18 (26.1)	15 (34.1)	
Comfort Managing Diabetes At Home:			0.751
Very comfortable	28 (40.6)	19 (43.2)	
Somewhat comfortable	13 (18.8)	11 (25.0)	
Neutral	12 (17.4)	8 (18.2)	
Somewhat uncomfortable	12 (17.4)	4 (9.1)	
Very uncomfortable	4 (5.8)	2 (4.5)	

Values are n (%) within each service. p-values: Pearson chi-square across all categories. One hypoglycemia response missing (medical).

CONCLUSIONS

Substantial gaps exist in diabetes education at hospital discharge: 38.1% of patients received no verbal or written diabetes instructions, fewer than half (44.2%) received complete hypoglycemia education, and only 38.9% fully understood the changes made to their management plan in hospital.

Gaps were more pronounced among surgical patients, who more often reported receiving no discharge instructions and less often received complete hypoglycemia education.

Standardized, patient-centred discharge education, deliberately extended to surgical services, may improve preparedness for safe self-management after discharge.

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ACKNOWLEDGEMENTS & CONTACT

This project was made possible by funding awarded through the Dean's Summer Student Research Program, Office of the Vice-Dean Research, College of Medicine, University of Saskatchewan. We thank the patients who participated and the clinical teams at RUH and SPH.

Contact: has998@usask.ca



Anjali Saxena (Dr. Cody Lewis)

Testing Wisely: Assessing the Appropriateness of Allergen Testing in Saskatchewan

Background: Allergy testing in Saskatchewan primarily involves specific IgE tests and IgE panels. Such testing is costly compared to routine laboratory tests, yet ordering practices are not limited by number or specialty. Ordering trends in Saskatchewan may deviate from national guidelines such as Choosing Wisely, however there is a paucity of allergy testing data to inform quality improvement measures.

Methods: Retrospective analysis of Laboratory Information System allergy testing data was completed across six parameters, including available IgE tests, ordering frequency, test volume per patient, ordering physician specialty, positivity rates, and cost. A proposed model of 5 specific IgE tests per patient was utilized for comparison.

Results: 76,576 tests were ordered from January 2023 to April 2026. 37 tests were available and 23.73% of total tests ordered were non-specific panels. The mean number of tests per patient exceeded the proposed model overall and for 6/17 specialties. 28.89% of all allergy tests ordered had positive results. An estimated 26.15% of testing supply costs was calculated as potential savings when utilizing the ordering threshold and abolishing panel usage.

Conclusion: Excessive testing and panel usage in Saskatchewan deviates from best practices. A 5-test limit may improve allergy testing at a system level.

Testing Wisely: Assessing the Appropriateness of Allergen Testing in Saskatchewan

Anjali Saxena, Ninad Mehta, Ahmed Mostafa, Cody Lewis
College of Medicine, University of Saskatchewan

INTRODUCTION

- Allergen testing in Saskatchewan (SK) involves specific IgE tests and IgE panels.
- Best practices:** Current testing practices deviate from established guidelines through broad allergen panel usage and the absence of restrictions on the number of tests ordered.^{1,2} A 5-test-per-patient model has been suggested (Alberta Precision Labs) to improve test utilization.³
- Cost:** Allergy testing is substantially more expensive than many routine laboratory investigations.⁴ Optimizing utilization will reduce unnecessary expenditure.
- The lack of comprehensive allergy testing data limits the ability to monitor utilization patterns, assess testing appropriateness, and support quality improvement initiatives.

Hypothesis: Allergy testing in SK deviates from best practice guidelines through frequent use of panels and excessive testing, surpassing necessary healthcare costs.

OBJECTIVES

- Quantify the frequency of various IgE blood tests ordered.
- Evaluate the volume of allergen tests and rounds ordered per patient and compare across provider specialties.
- Determine testing positivity rates.
- Calculate cost savings to the healthcare system with appropriate test utilization.

METHODS

- Retrospective analysis of allergy blood tests completed across SK (Jan 2023- Apr 2026)
- Analysis included:
 - Available IgE blood tests
 - Ordering frequency of tests
 - Ordering physician specialty
 - Volume of tests per patient*
 - Test positivity rates
 - Cost analysis of current spending*

* indicates comparison to the proposed 5-test-per-patient model

RESULTS

Objective 1. Frequency of Various IgE Tests Shows High Proportion of Panels Utilized

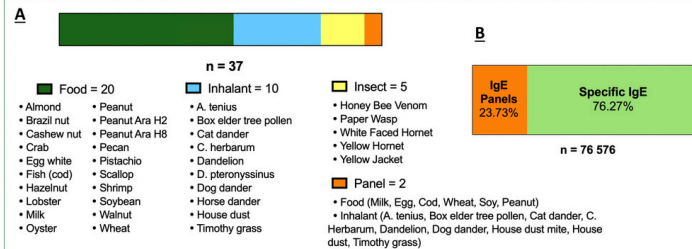


Figure 1. Of the 37 available IgE test, 2 are broad allergen panels (A). 23.73% of tests ordered were panels, leading to additional specific IgE testing (B).

Objective 2. Volume of Testing Crosses Suggested Thresholds

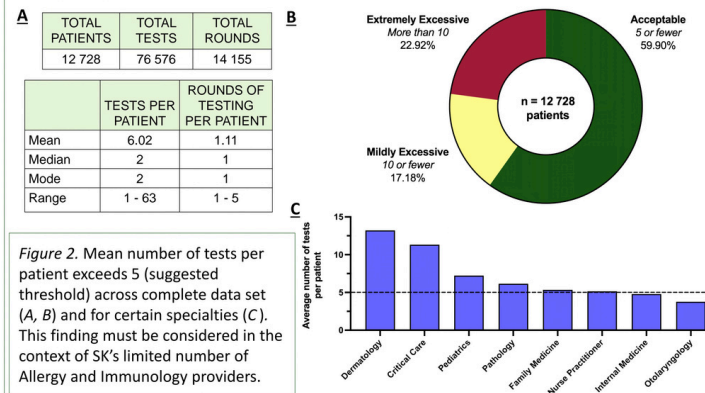


Figure 2. Mean number of tests per patient exceeds 5 (suggested threshold) across complete data set (A, B) and for certain specialties (C). This finding must be considered in the context of SK's limited number of Allergy and Immunology providers.

Objective 3. Test Results Demonstrate High Rates of Negativity

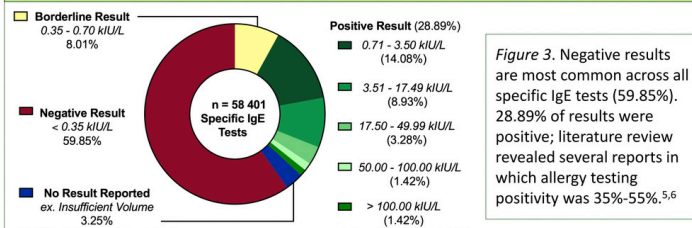


Figure 3. Negative results are most common across all specific IgE tests (59.85%). 28.89% of results were positive; literature review revealed several reports in which allergy testing positivity was 35%-55%,^{5,6}

RESULTS

Objective 4. Expenditure Reduction Possible with Proposed Model

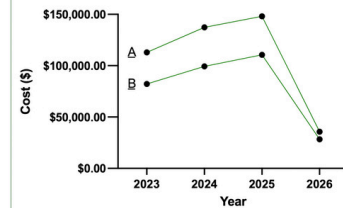


Figure 4. Annual cost of ordered tests (Model A) compared to 5-test-per-patient model with only specific IgE tests (Model B) show potential savings of \$133,477.25 (26.15%).

CONCLUSIONS

- Panels are used significantly compared to specific IgE tests for allergy testing in SK
- Excessive numbers of allergy tests are ordered with high rates of negative results
- Costs of allergy testing can be lowered with use of a 5-tests-per-patient system

ACKNOWLEDGEMENTS

We are grateful for the support of the OVD's Dean's Summer Research Program. Thank you to the SHA, the entire research team and the Department of Pathology and Laboratory Medicine staff.

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Ally Seifert (Dr. Peter Hedlin)

Assessment of Post-Operative Delirium in the Geriatric Surgical Population

Postoperative delirium (POD) is an acute and fluctuating disturbance in attention, awareness, and cognition that is common among older surgical patients. Subclinical and hypoactive delirium may be difficult to recognize, resulting in incomplete documentation and challenges with continuity of care. This study sought to evaluate the utility of the Chart-based Delirium Identification Instrument (CHART-DEL), assess and compare methods for identifying POD, and explore gaps in the clinical documentation of POD. Using an established cohort of patients aged ≥ 65 years who underwent major surgery at Royal University Hospital, we conducted a retrospective chart review using CHART-DEL. Postoperative delirium identified by CHART-DEL was compared with standardized assessments using the confusion assessment method 3D-CAM and/or CAM-ICU, and discharge summaries were reviewed for mention of POD. Among 51 patients, 15.0% had evidence of delirium and 7.8% had probable delirium. CHART-DEL identified probable or uncertain delirium in 15% of patients compared with 7.0% identified by 3D-CAM/CAM-ICU. Delirium was inconsistently documented in discharge summaries, with no mention in 33% of multifactorial delirium cases and 25% of probable delirium cases. These findings demonstrate the utility of CHART-DEL in identifying potential cases of POD and highlight opportunities to improve recognition and documentation of delirium.

INTRODUCTION

- Postoperative delirium (POD) is an acute and fluctuating disturbance in attention, awareness, and cognition following surgery, particularly among older adults.^{1,2}
- Hypoaffective delirium is the most common form of delirium and presents with drowsiness and decreased responsiveness, which can easily be missed, especially in the absence of appropriate screening tools.^{3,4}
- Accurate recognition and documentation are important for continuity of care, as incomplete documentation in the medical record, such as in the discharge summary, may limit clinicians' awareness of a patient's postoperative course.⁵
- Our clinical research team within the Department of Anesthesiology has established a cohort of patients aged 65 years and older who underwent major surgery at Royal University Hospital (RUH). Using this cohort, we conducted a retrospective chart review using the Chart-based Delirium Identification Instrument (CHART-DEL).

OBJECTIVES

- Identify and characterize cases of delirium not detected by the postoperative confusion assessment method (3D-CAM and CAM-ICU) using CHART-DEL.
- Compare CHART-DEL, 3D-CAM and CAM-ICU for the detection of POD.
- Examine documentation of POD in patient discharge summaries across subclinical and overt delirium groups.

METHODS

The study utilized our previously established cohort of patients aged 65 years and older who were assessed at the Pre-Assessment Clinic and underwent major surgery at RUH between June 4 and July 31, 2025, or between May 22 and June 17, 2026. Following surgery, patients were assessed using the 3D-CAM and CAM-ICU. A retrospective chart review was subsequently conducted using CHART-DEL. Clinical documentation, including nursing notes and physician progress reports, was reviewed for key indicators of delirium, including terms such as 'disorientation,' 'altered mental status,' and 'acute confusion,' as well as evidence of CAM criteria.

RESULTS

Table 1. Descriptive Statistics.

	Male (n=35)	Female (n=16)	Total (n=51)
Age*, years (mean)	70.3	72.6	71.3
Cardiac Surgery, n	18	4	22
General Surgery, n	8	8	16
Neurosurgery, n	6	3	9
Orthopedic Surgery, n	3	1	4

Note. *Patient age at time of pre-operative assessment

RESULTS

1. Delirium Status: 15% of Patients had Evidence of Delirium and 7.8% had Probable Delirium

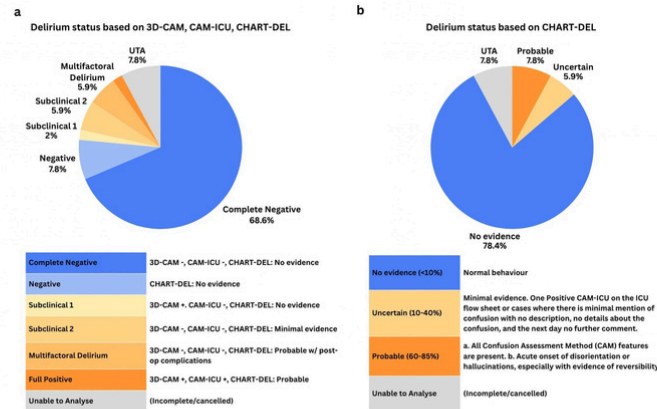


Figure 1. Delirium Status. Delirium status among the study cohort (n=51). a) Patients were categorized based on results from postoperative 3D-CAM/CAM-ICU assessments and retrospective chart review. Negative, patients who did not complete post-operative 3D-CAM/CAM-ICU assessment, and no evidence of delirium was found upon chart review; Unable to Analyse, charts unavailable at the time of analysis (n=3) or surgery cancelled (n=1). b) CHART-DEL groupings, with the corresponding likelihood of POD indicated in brackets.

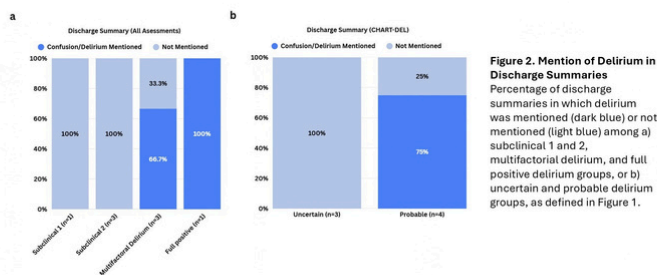
2. Comparison of Assessments: CHART-DEL is More Sensitive Compared to 3D-CAM & CAM-ICU

Table 2. Comparison of Assessments

CHART-DEL (n=47)			Assessment (n=43)*		
Probable	Uncertain	Total	3D-CAM	CAM-ICU	Total
4 (8.5%)	3 (6.4%)	7 (14.9%)	2 (4.7%)	1 (2.3%)	3 (7.0%)

Note. * Four patients were not assessed by 3D-CAM/CAM-ICU.

3. Discharge Summaries Failed to Mention Delirium in all Subclinical and Uncertain delirium, 33% of Multifactorial Delirium, and 25% of Probable Delirium Cases



CONCLUSIONS

- 15% of patients had some evidence of delirium and 7.8% had probable delirium in this study cohort.
- CHART-DEL identified additional cases of potential POD compared with point-in-time 3D-CAM/CAM-ICU assessments, supporting its utility for retrospective identification of delirium.
- POD is likely under-documented in the medical record. One patient with a positive 3D-CAM had no mention of delirium in their chart. Among patients in the subclinical groups, their discharge summaries contained no mention of confusion. Additionally, 33% of multifactorial delirium cases and 25% of probable delirium cases had no mention of delirium or confusion in their discharge summaries.
- This study is limited by its small sample size and ongoing data collection; further investigation in a larger geriatric surgical cohort is warranted.

FUTURE DIRECTIONS

- Expand the Study Cohort: Continue chart review and analysis to increase the sample size and strengthen characterization of POD in the geriatric surgical population.
- Examine Length of Hospital Stay: Investigate the association between delirium and length of hospital stay within the expanded cohort.
- Improve Clinical Documentation: Further characterize gaps in delirium documentation in discharge summaries to identify opportunities to improve communication and continuity of care.

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ACKNOWLEDGMENTS

RUH Pre-Admission Clinic Staff

College of Medicine, Office of the Vice-Dean Research (Dean's Project Funding)

Department of Anesthesiology Staff, Darcie Earle (Provincial Research Facilitator)



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Lauren Smith (Drs. Alison Oates & Valerie Caron)

Moving Minds: A Scoping Review of Walking Interventions in Mild Cognitive Impairment, Early-Stage Dementia and Alzheimer's Disease

Mild cognitive impairment (MCI) and dementia are associated with declines in mobility, gait and independence. Walking interventions may help maintain physical function and independence. Aim: identify and describe walking-based interventions in individuals with MCI, early-stage dementia, or Alzheimer's disease, focusing on intervention dosage and walking-related outcomes. Methods: a scoping review was conducted using the Joanna Briggs Institute framework. Five databases were searched from inception to 2026. Studies were included if they involved individuals with MCI, early-stage dementia, or Alzheimer's disease, evaluated a walking-based intervention lasting longer than 4 weeks, and included a walking outcome measure. Results: Fourteen of 2,554 articles were included, with wrong intervention being the most common reason for exclusion. Walking, gait or aerobic focus was the most common intervention focus (38%). Interventions averaged 3.3 sessions/week and 63 minutes/session, with moderate intensity most commonly prescribed. Walking outcomes varied, with the 6 minute walk test, Timed Up and Go, spatiotemporal parameters, and walking speed amongst most reported. Conclusion: Walking interventions vary in design, dosage and outcomes, emphasizing need for more consistent reporting and outcome selection to establish walking prescriptions for those with MCI and early-stage dementia.

Introduction

- MCI and dementia are associated with declines in mobility, gait and independence.¹
- Walking interventions may support physical and cognitive function.²
- Maintaining walking ability may promote self-initiated physical activity and independence.¹

Objective

- To identify and describe walking-based interventions within a MCI/Dementia/Alzheimer's disease population with a focus on dosage and outcomes for walking.

Methods

- Methodology:** Joanna Briggs Institute (JBI) scoping review methodology.³
- Databases:** Medline (OVID), Embase, CINAHL and PubMed.
- Search period:** database inception-2026.
- Screening:** two independent reviewers, third reviewer for conflicts.

Inclusion Criteria

- Population: MCI, early stage dementia or Alzheimer's disease
- Intervention: Walking-based, ≥4 weeks
- Outcomes: Walking-related function, ability, quality, physical activity, or subjective rating

Exclusion Criteria

- Severe dementia/Alzheimer's disease
- Parkinson's related dementia
- Any other neurological condition
- Animal studies
- Age > 55 years
- Surgery & pharmaceutical interventions
- Interventions with no walking component
- No outcome to assess walking
- Review articles

We gratefully acknowledge **InterD Research** and the organizations below for their support of this project.

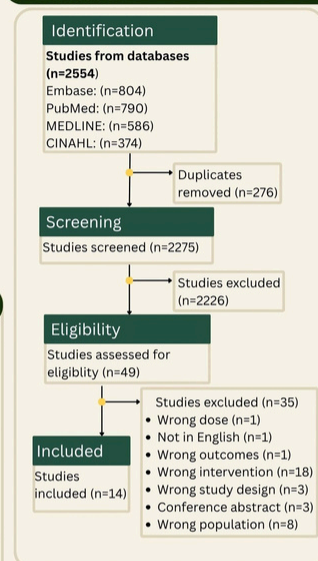


Moving Minds: A Scoping Review of Walking Interventions in Mild Cognitive Impairment, Early-Stage Dementia and Alzheimer's Disease

Lauren Smith, Lauren Roberts, Alison Oates, Valerie Caron



Results:



Included Study Demographics

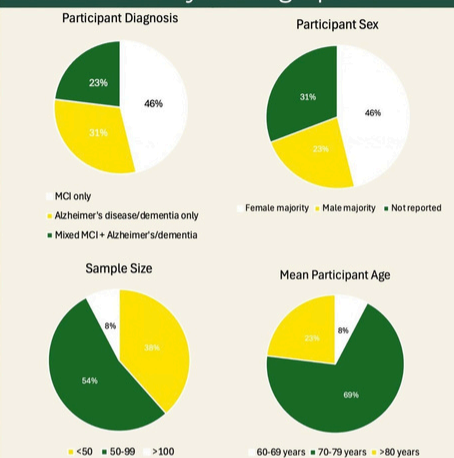


Figure 1. Participant characteristics of included studies. Participants diagnosis, sex, sample size, and mean participant age across included studies

Outcome Measures

Walking-Based Outcome Measure

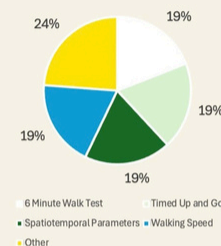


Figure 4. Distribution of walking-based outcome measures reported across included studies.

Primary Outcome Measure

As reported by the study authors, the primary outcome measures were **cognition** (n=4), **gait-related** measures (n=3), **balance** (n=2), and **grip strength, feasibility, MMSE and change in daily step count** (n=1 each).

Intervention

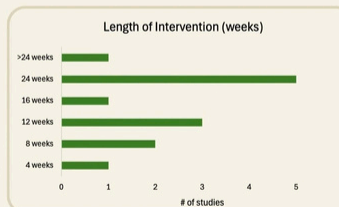


Figure 2. Length of walking intervention reported across included studies.

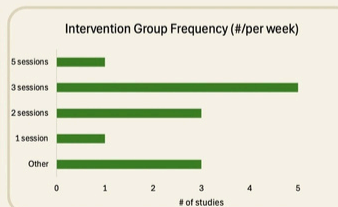


Figure 3. Weekly frequency of walking intervention sessions across included studies

Intensity of Intervention

Exercise intensity was most commonly prescribed as **moderate intensity** (n=7), followed by **step-based** and **individualized** intensity prescriptions (n=2 each), and **resistance-based** intensity (n=1). One study did not report intensity.

- SAGER guidelines recommend clear distinction and appropriate reporting of sex and gender.⁴
- 23% reported gender**, but did not specify how it was collected, potentially reflecting inconsistent use of sex/gender terminology.
 - 0% reported both sex and gender.
- Sex/gender reporting remains inconsistent across interventions.

- According to the **Alzheimer Society of Canada**, individuals should get a minimum of **30 minutes** of physical activity **per day**, at least **5 days per week** for a sum of **150 minutes/week**.⁵
- Interventions averaged 3.3 sessions/week, (~63 minutes/session) **exceeding the 150 minute/week target** but falling **below the recommended frequency**.
- This demonstrates that although there are clear guidelines for physical activity within this population, the majority of interventions have incorrect dosage.

More clinical research interventions are required to clearly identify **appropriate dosage** and **intensity** for walking based physical activity and exercise in people with MCI or early-stage dementia.

¹Zhang et al., 2019 ²Lam et al., 2018 ³Peters et al., 2020
⁴Heidari et al., 2016 ⁵Alzheimer Society of Canada



Dylan Turner (Dr. Peter Dust)

Perioperative Opioid Agonist Therapy Management: A Literature-Based Review and Policy Comparison

Patients receiving opioid agonist therapy (OAT) frequently undergo surgery, creating a challenge between maintaining opioid use disorder treatment, preventing withdrawal, and controlling acute pain. This report reviews the available literature and Canadian guidance on perioperative OAT management. A narrative literature review was conducted using PubMed, OpenEvidence, and publicly available guidelines and health-authority documents, supplemented by a province-by-province policy comparison.

The most consistent recommendation is to continue maintenance buprenorphine and methadone throughout the perioperative period rather than taper or discontinue, as an interruption risks potential withdrawal, destabilization, relapse, and overdose without improving pain control or safety. Acute pain should be treated as a separate problem using multimodal analgesia and short-acting full-agonist opioids if needed. This reveals a shift occurring between 2019 and 2021 away from preoperative discontinuation. Canadian provincial guidance aligns with the literature but is not consistent, often within larger OAT guidelines, and often inaccessible.

The overall evidence is weak as it is mostly from expert consensus, narrative reviews, retrospective studies, and case reports, with no randomized controlled trials and limited data on long-acting injectable buprenorphine. Standardized protocols integrated into surgical and anesthesia guidelines, multicentre trials reporting patient-centred outcomes, are still needed.

Perioperative Opioid Agonist Therapy Management: A Literature-Based Review and Policy Comparison

Dylan Turner, BA, BKin, Dr. Peter Dust, MD, FRCPS

Abstract

Patients receiving opioid agonist therapy (OAT), including buprenorphine and methadone, often require surgical care. Perioperative management can be difficult because clinicians must balance continuation of opioid use disorder treatment, prevention of withdrawal, and management of acute pain. Interruption of OAT may contribute to withdrawal, treatment destabilization, and increased risk of opioid use disorder recurrence or overdose. Current literature supports continuing OAT throughout the perioperative period while treating acute surgical pain separately.

Objectives

- Review the available literature on perioperative management of OAT.
- Compare Canadian guidance and provincial/territorial recommendations.
- Evaluate the strengths and limitations of the current evidence.
- Identify implications for perioperative clinical practice.
- Identify gaps in evidence and areas requiring further research.

Methods

A literature and policy review was conducted using:

- PubMed
- OpenEvidence
- Canadian clinical guidelines
- Health-region and provincial health authority documents
- Search terms included *opioid agonist therapy*, *opioid use disorder*, *buprenorphine*, *methadone*, *perioperative pain*, *acute pain*, and *surgery*. Titles and abstracts were initially reviewed, followed by articles, reviews, guidelines, and policy documents. Canadian provincial and territorial guidance were compared when publicly accessible.
- The evidence was limited by a lack of randomized controlled trials comparing OAT continuation, dose reduction, and discontinuation. Much of the available evidence consists of retrospective and observational studies, case reports, reviews, and expert opinion.



Results

Continuation of OAT

- Most reviewed sources recommend continuing buprenorphine and methadone throughout the perioperative period.
- Discontinuation may contribute to withdrawal, treatment disruption, and challenges in restarting therapy.
- Available evidence does not show a clear analgesic or safety benefit from stopping buprenorphine.
- Acute surgical pain should be managed separately from the maintenance OAT dose using multimodal analgesia, with short-acting full-agonist opioids when necessary.

Pain Management

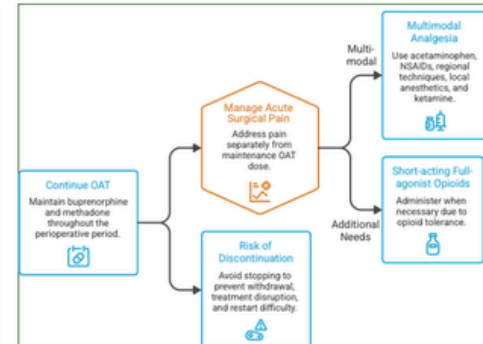
- Patients receiving OAT may require additional opioids because of tolerance.
- Multimodal strategies include acetaminophen, NSAIDs, regional/neuraxial techniques, local anesthetics, and ketamine.
- Maintenance OAT does not provide analgesia for acute surgical pain.

Evidence and Canadian Policy

- Evidence supporting continuation is low quality, with no randomized controlled trials.
- Canadian guidance is consistent with continuation of OAT and separate management of acute pain.
- Saskatchewan, Manitoba, British Columbia, and Alberta guidance support continuation, some policies were not publicly identified for several other provinces/territories.

Evidence Gap

- Relapse, overdose, treatment retention, withdrawal, and patient-directed discharge, are not reported.
- Evidence for long-acting injectable buprenorphine is limited.



Made with Napkin

Conclusions

- Current literature and Canadian guidance generally support continuing OAT throughout the perioperative period rather than tapering or discontinuing treatment. Acute surgical pain should be treated as a separate problem using individualized, multimodal analgesia, with supplemental short-acting full-agonist opioids when required.
- However, the evidence is limited and is mostly based on expert consensus, retrospective studies, narrative reviews, and case reports. Standardized perioperative protocols incorporated into anesthesia and surgical workflows could improve consistency of care.
- Larger multicentre studies are needed to determine optimal management across different OAT medications, surgical procedures, and patient populations

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Surgery





Sameer Ahmad (Dr. Marius Bral)

Doxycycline as an Additive Strategy During Normothermic Ex Vivo Perfusion to Resuscitate DCD Porcine Kidney Grafts

Kidney transplantation is the preferred treatment for end-stage kidney disease, yet donor organ shortages continue to limit access. Donation after circulatory death (DCD) can expand the donor pool, but these kidneys are particularly susceptible to ischemia-reperfusion injury. Normothermic ex vivo perfusion (NMP) provides an opportunity to assess kidney function and deliver therapies during preservation. Doxycycline has anti-inflammatory, anti-apoptotic, and matrix metalloproteinase inhibitory properties that may reduce renal injury. This study aims to determine whether doxycycline administered before procurement, during NMP, or at both stages improves kidney preservation in a DCD porcine model.

Four experimental groups are planned, with six kidneys per group: NMP alone, doxycycline during NMP, doxycycline before procurement followed by NMP without doxycycline, and doxycycline both before procurement and during NMP. Kidney function will be assessed through renal blood flow, urine output, vascular resistance, and perfusion pressures. Biochemical assessment will include perfusate and urine creatinine, blood urea nitrogen, neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and inflammatory cytokines. Histological assessment will evaluate tubular injury, necrosis, apoptosis, inflammation, and fibrosis.

We hypothesize that doxycycline will attenuate ischemia-reperfusion injury, with the greatest protection achieved through combined administration before procurement and during NMP. This study will evaluate doxycycline as an adjunct to NMP and provide preliminary evidence to guide further investigation of its potential to improve the preservation and utilization of DCD kidneys.

Keywords: Kidney transplantation; donation after circulatory death; normothermic ex vivo perfusion; doxycycline; ischemia-reperfusion injury.

Doxycycline as an Additive Strategy During Normothermic Ex Vivo Perfusion to Resuscitate DCD Porcine Kidney Grafts

Sameer Ahmad B.Kin, Dr. Mariusz Bral MD, PhD

INTRODUCTION

The Unmet Need

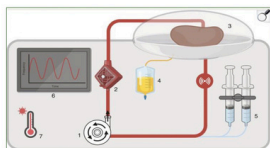
- Kidney transplantation is the optimal treatment for end-stage kidney disease, but organ supply remains limited.²
- Donor after circulatory death (DCD) kidneys can expand the donor pool but are more susceptible to ischemia-reperfusion injury (IRI), leading to delayed graft function and higher discard rates.^{2,3}



1 in 10 patients on the transplant waitlist receive a kidney each year.¹

Normothermic Ex Vivo Perfusion (NMP)

- NMP preserves kidneys at physiological temperature with oxygenated blood or perfusion solution, allowing assessment and potential repair of marginal organs.²
- It provides a platform to deliver targeted therapies to reduce IRI and improve graft function.^{2,3}



NMP may resuscitate kidneys that would otherwise be discarded.

Why Doxycycline?

- Doxycycline is a tetracycline antibiotic with pleiotropic anti-inflammatory, anti-apoptotic and anti-matrix metalloproteinase (MMP) properties.^{4,5}
- Doxycycline has demonstrated protective effects in experimental kidney preservation and DCD models, but its role during normothermic ex vivo kidney perfusion remains incompletely characterized.^{4,6}

↓ MMP Activity • Reduces tissue remodelling and injury

↓ Inflammation • Inhibits cytokine release and leukocyte infiltration

↓ Apoptosis • Preserves tubular and endothelial cells

↑ Microvascular Stability • Maintains perfusion and reduces edema

HYPOTHESIS AND OBJECTIVES

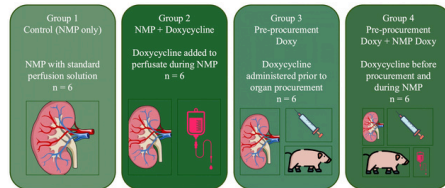
Hypothesis Doxycycline administered before procurement and/or during normothermic ex vivo perfusion will attenuate ischemia-reperfusion injury and improve the function of DCD porcine kidney grafts.

Objectives

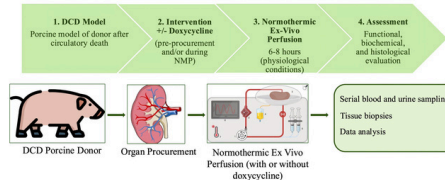
- Compare functional and biochemical parameters between doxycycline-treated and untreated kidneys.
- Assess histological evidence of kidney injury and protection.
- Determine the potential of doxycycline to improve the transplantability of DCD kidneys.
- Evaluate the impact of pre-procurement doxycycline.

STUDY DESIGN

Four Experimental Groups (n = 6 kidneys per group)



METHODOLOGY



Functional Parameters	Biochemical Markers	Histological Analysis
- Renal blood flow (RBF) - Urine output and electrolytes - Vascular resistance - Perfusion pressures - Macroscopic assessment	- Serum and urine creatinine - BUN - NGAL - KIM-1 - Inflammatory cytokines (e.g., TNF-α, IL-6)	- H&E (tubular injury, necrosis) - Immunohistochemistry (apoptosis, inflammation, fibrosis) - Tubular injury scoring (blinded) - Comparison between groups

Expected Outcomes

- Improved renal function (higher urine output, lower creatinine) in doxycycline-treated groups
- Reduced biomarkers of kidney injury and inflammation
- Less tubular necrosis and apoptosis on histology
- Greatest benefit anticipated in combined pre-procurement + NMP doxycycline group

Clinical Significance

- Could increase the number of transplantable kidneys from DCD donors
- May reduce delayed graft function and improve long-term outcomes
- Provides a platform for targeted therapies during ex vivo perfusion
- Aligns with the goal of expanding the organ pool and improving access to transplantations

EXPECTED RESULTS AND FUTURE DIRECTIONS

Expected Results

Improved Renal Function

- Higher renal blood flow and urine output in doxycycline-treated groups.
- Lower serum and urine creatinine levels.
- More stable perfusion parameters (e.g., vascular resistance and perfusion pressures).

Reduced Biochemical Injury

- Lower levels of kidney injury biomarkers (e.g., NGAL and KIM-1).
- Reduced inflammatory cytokines such as TNF- α and IL-6.

Improved Histology

- Less tubular injury, necrosis, apoptosis, and inflammatory infiltration.
- Better preservation of renal microvascular and tubular architecture in doxycycline-treated groups.

Group Comparison

- All doxycycline-treated groups are expected to outperform NMP alone.
- The combined pre-procurement + NMP doxycycline group is expected to show the greatest benefit.

Future Directions

- Optimize doxycycline dose, timing, and duration during kidney preservation.
- Investigate protective mechanisms related to MMP activity, inflammation, apoptosis, and microvascular injury.
- Determine whether benefits seen during NMP translate into improved post-transplant graft function and survival.
- Evaluate longer-term transplant outcomes, including delayed graft function and chronic injury.
- Assess the safety and clinical feasibility of adding doxycycline to NMP protocols.
- Explore whether this strategy can rehabilitate marginal DCD kidneys that might otherwise be declined.

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ACKNOWLEDGEMENTS

This project was funded by the University of Saskatchewan College of Medicine, Dean's Summer Projects.



Ibrahim Al-Azem (Dr. Rick Jaggi)

Assessing Hair Regrowth with Alma-TED™: A Blinded Clinical Study Evaluating TransEpidermal Delivery and Peptide-Based Therapy for Hair Loss Concerns

Introduction: Hair loss affects over half of adults and is linked to reduced self-esteem, anxiety and impaired quality of life. Current treatments carry side effects, invasiveness or commitment. ALMA-TED™ is a needle-free device that uses ultrasound and air pressure to drive a peptide serum across the stratum corneum. Prior evidence is limited to small, unblinded studies, which reported 23 to 34% higher hair density at 3 months.

Methods: This prospective, single-centre, assessor-blinded trial enrolled adults with non-scarring hair loss in Saskatoon. Participants received three ALMA-TED™ treatments about 30 days apart. The primary outcome is percent change in terminal hair density (dermatoscopy, blinded shaft counts). Secondary outcomes are patient-reported visual analogue scale (VAS, 0 to 10) ratings and blinded Norwood-Hamilton and Ludwig scoring, assessed at baseline, 30 and 90 days post-last treatment.

Results: In this interim 1-month VAS analysis, 20 participants with baseline data completed follow-up. Thickness/density improved from a mean of 3.3 to 4.9 (median change +2, $p = 0.008$) and satisfaction from 3.4 to 5.3 (median change +1.5, $p = 0.006$) by Wilcoxon signed-rank test. Self-consciousness did not change clearly (5.9 to 5.3, $p = 0.32$). Objective and 3-month outcomes are pending.

Conclusion: Preliminary patient-reported outcomes suggest improved thickness and satisfaction after ALMA-TED™. Unblinded findings await confirmation from blinded objective outcomes.

Assessing Hair Regrowth with Alma-TED™: A Blinded Clinical Study Evaluating TransEpidermal Delivery and Peptide-Based Therapy for Hair Loss Concerns



Ibrahim Al-Azem¹, Abdullah Qureshi¹, Azmarak Khan¹, Anjali Saxena¹, Abdullah AlAmari², Rick, Jaggi²

¹University of Saskatchewan College of Medicine, Saskatoon Saskatchewan, Canada; ²Division of Otolaryngology, Head and Neck Surgery, Department of Surgery, University of Saskatchewan College of Medicine, Saskatoon, Saskatchewan, Canada;

Introduction

Hair loss affects over 50% of men and women worldwide and is strongly associated with reduced self-esteem, anxiety, depression and impaired quality of life.¹

Non-scarring alopecia preserves the follicle and thus the capacity for regrowth, so it is amenable to hair restoration.²

First-line drugs (minoxidil, 5- α reductase inhibitors) carry adverse effects, indefinite long-term use and regression after stopping.³ Platelet-rich plasma and hair transplants are invasive, costly and variable in outcome.⁴

Many patients would prefer a treatment that is well-tolerated, needle-free and low-commitment.

ALMA-TED™ pairs low-frequency ultrasound with Impact Delivery™ air pressure to drive a peptide-rich serum across the stratum corneum, without injections.

Open-label studies report 23 to 34% increases in hair density at 3 months, mean pain scores of zero and no serious adverse events.⁵⁻⁷ These come from small, unblinded US cohorts.

Purpose

To test whether three ALMA-TED™ sessions improve objective hair metrics and patient-reported outcomes in adults with non-scarring hair loss, using an assessor-blinded design.

Methods

Design: prospective, single-centre, assessor-blind trial at the Face Cosmetic & Reconstructive Surgery clinic, Saskatoon, SK. University of Saskatchewan Biomedical Research Ethics Board approved; written informed consent obtained.

Participants: adults ≥ 18 y with clinical signs of non-scarring hair loss. Excluded: scalp disorders, recent hair-loss therapy changes, prior scalp surgery, concurrent minoxidil, 5-ARI, PRP or JAK inhibitors, pregnancy or lactation, systemic illness affecting hair growth.

Treatment: three sessions about 30 days apart. Scalp priming (30% impact, 2 min), peptide serum, then delivery at 50% impact (2 min).

Timepoints: baseline, 30 and 90 days post-last treatment.

Primary outcome: % change in terminal hair density (hairs/cm²) by dermatoscopic imaging and blinded manual shaft count (3×1 cm² areas).

Secondary: patient VAS (0 to 10) for thickness/density, satisfaction and self-consciousness; Norwood-Hamilton and Ludwig scoring by 3 blinded reviewers; inter-rater reliability (ICC).

Analysis: planned mixed-effects ANOVA or Friedman test. Interim 1-month VAS: paired Wilcoxon signed-rank test (exploratory).

Results

Study timeline



Participant flow



Patient-reported VAS

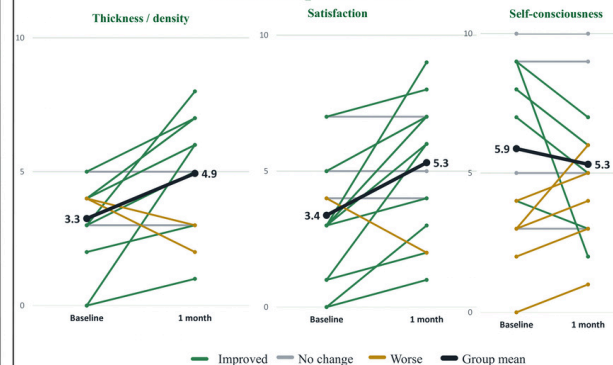


Figure 1. Individual VAS scores (0 to 10) at baseline and 1-month follow-up, n = 16 paired participants.

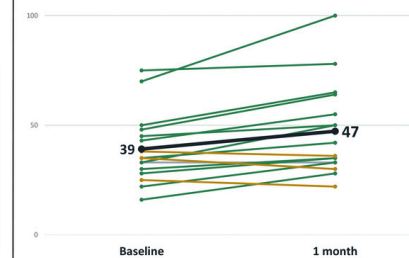
Measure	Base	1 mo	Median change (IQR)	Better / same / worse	P
Thickness / density	3.3	4.9	+2 (0 to 3)	11 / 3 / 2	0.008
Satisfaction	3.4	5.3	+1.5 (0.8 to 3.3)	12 / 3 / 1	0.006
Self-consciousness*	5.9	5.3	0 (-2 to 1)	6 / 5 / 5	0.32

Table 1. VAS (0 to 10), baseline vs 1-month follow-up, n = 16. Wilcoxon signed-rank test, two-sided, normal approximation (tied differences). Exploratory; not adjusted for multiple comparisons. *Lower is better.

Results Con't

Hair density

Hair shaft counts per cm² from one unblinded counter. Blinded student counts and 90-day counts are pending.



3-month (90-day) follow-up

Change from baseline to 3 months, and whether the 1-month improvement is sustained, will be assessed along with the correlation of VAS with objective density.

Discussion

At 1 month, patient-reported thickness/density and satisfaction improved; self-consciousness did not change clearly.

VAS is patient-reported and unblinded. Placebo effect, reduced shedding or hair-quality changes that a shaft count misses could contribute. Agreement with the blinded density counts will strengthen validity.

The assessor-blinded design is the main contribution: earlier ALMA-TED™ studies were open-label. Non-scarring alopecia preserves viable follicles, so needle-free transepidermal peptide delivery is a logical fit.

Conclusion

Preliminary patient-reported outcomes suggest improved perceived hair thickness and satisfaction 1 month after ALMA-TED™ treatment. Conclusions on efficacy await the 3-month follow-up and the blinded objective outcomes, which are pending.

Acknowledgment

This project was completed as part of the Dean's Summer Research Project at the University of Saskatchewan College of Medicine in collaboration with FACE Cosmetic and Reconstructive Surgery, Saskatoon, SK.



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Ashlynn Hill (Dr. Amit Persad)

Extent of Resection of GBM and its Impact on Patient Outcomes: A Scoping Review

Background: Extent of resection (EOR) is a major prognostic factor in glioblastoma (GBM), yet surgical margins and outcome definitions are reported inconsistently across the literature, limiting direct comparison between studies.

Objective: To map how the current literature reports EOR and its association with overall survival (OS), progression-free survival (PFS), and functional status in patients with GBM, and to identify reporting inconsistencies that limit future meta-analysis.

Eligibility criteria: Retrospective cohort and observational studies (published 2016–present) of adults (≥ 18 years) with resected GBM per the 2016 WHO definition (including recurrent, butterfly, multifocal, or diffuse GBM) reporting OS, PFS, the Neurological Assessment in Neuro-Oncology (NANO) scale, or Karnofsky Performance Status (KPS).

Sources of Evidence: MEDLINE, PubMed, and Web of Science were searched for studies published from 2016 onward. Source selection followed the PRISMA-ScR framework using Covidence.

Charting Methods: Data were independently extracted into a custom spreadsheet capturing EOR (continuous and/or discrete), residual tumor volume, imaging modality used to assess resection, GBM subtype, pre- and postoperative KPS, NANO, OS, PFS, and demographic characteristics.

Results: Thirty-five studies met inclusion criteria. EOR was reported as a discrete category in all 35 studies, though definitions of gross total, subtotal, and partial resection varied substantially; only 18 studies reported EOR as a continuous percentage. OS was reported in all 35 studies, and greater EOR was associated with improved OS in the majority. PFS was reported in 21 studies but with considerable definitional heterogeneity. Functional outcomes were captured inconsistently: KPS was reported in 28 studies, often only as a threshold value rather than a continuous score, while NANO was used in only one study. Seven studies incorporated fluid-attenuated inversion recovery (FLAIR)-based resection metrics, four of which showed a significant OS benefit. The recently introduced RANO-resect classification, applied in three studies, consistently showed improved OS with higher resection classes.

Conclusions: Greater EOR is associated with improved survival in GBM across most of the modern literature, but inconsistent definitions of resection categories, PFS, and functional status limit cross-study comparison and future meta-analysis. Standardized, volumetric EOR reporting frameworks such as RANO-resect, alongside consistent PFS and functional-outcome reporting, are needed to strengthen the evidence base.

Extent of Resection of GBM and Patient Outcomes: A scoping review

Ashlynn Hill, Amit Persad (M.D)

INTRODUCTION

Glioblastoma (GBM) is an aggressive, highly invasive brain tumor with a mean survival of only 12–14 months under maximal treatment. Extent of resection (EOR) is a major prognostic factor, but surgical margins and outcome definitions are reported inconsistently across the literature.

"Maximal safe resection" aims to remove as much tumor as possible while limiting neurological deficit. EOR is reported either as a continuous percentage or as discrete categories: gross total (GTR), supramaximal (SupTR), subtotal (STR), or partial (PR) resection, but the thresholds defining each category vary widely between studies.

OBJECTIVES

To map how the current literature reports EOR and its association with overall survival (OS), progression-free survival (PFS), and functional status in GBM — and to identify reporting inconsistencies that limit future meta-analysis.

EXCLUSION CRITERIA

Population Include: • Patients (≥18) with resected glioblastoma (GBM) • Patients with recurrent GBM that was resected OR • Patients with resected butterfly GBM • Patients with diffuse GBM Exclude: • non-GBM malignancies (do not fall under the 2016 WHO definition), e.g. astrocytoma, glioma without WHO definition, gliosarcoma	Intervention / Exposure Include: • Resection Exclude: • chemotherapy • radiation • gene therapy
Comparator / Context Include: • non-resected GBM (e.g. radiation, chemotherapy) • alternative, competing types of resection (e.g. supramaximal vs. subtotal vs. gross total resection vs. biopsy) Exclude: • Missing on comparing single or multiple interventions to other interventions not related to resection	Outcomes Include: • survival (overall survival or progression-free survival) • functional status (neurological deficits, Karnofsky Performance Scale) Exclude: • neurohistology • tumor markers • genetic characteristics
Study Characteristics Include: • retrospective cohort study • observational Exclude: • RCTs • prospective • reviews	

MATERIALS & METHODS

STUDY SELECTION

- Design:** Scoping review following the PRISMA-ScR framework, structured with the Population–Concept–Context (PCC) model.
- Population:** Adults (≥18 y) with resected GBM per the 2016 WHO definition, including recurrent, butterfly, multifocal, or diffuse GBM.
- Sources:** MEDLINE, PubMed, and Web of Science, 2016–present.
- Eligibility:** Retrospective cohort / observational studies reporting OS, PFS, KPS, or the NANO scale.

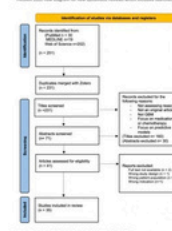
DATA CHARTING

Data were independently extracted into a custom spreadsheet capturing EOR (continuous and/or discrete), residual tumor volume, imaging modality used to assess resection, GBM subtype, pre- and postoperative KPS, NANO, OS, PFS, and demographic characteristics.

Example Search: MEDLINE

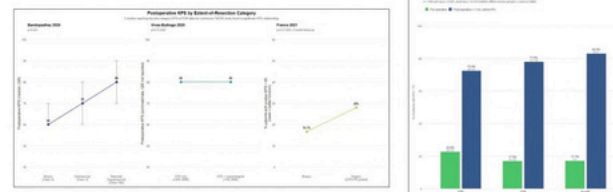
#	Search Terms	Results
1	glioblastoma.mp. or Glioblastoma/	65,516
2	Cytoreduction Surgical Procedures/	5,265
3	resection.mp.	408,204
4	Prognosis/	687,243
5	Survival Rate/	200,670
6	2 or 3	412,403
7	4 or 5	799,510
8	1 and 6 and 7	1,179
9	limit 8 to yr="2016–Current"	635
10	limit 9 to observational study	19

PRISMA 2020 flow diagram for this scoping review (which included searches of Medline and Embase only)

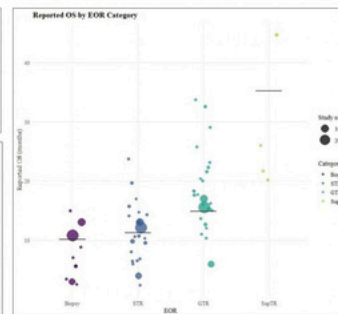
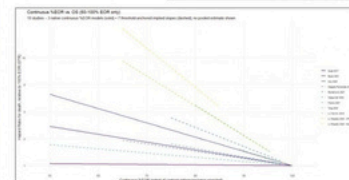


RESULTS

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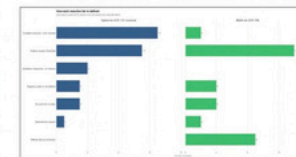


EOR & Survival



LITERATURE REPORTS

DEFINING RESECTION TIERS



CONCLUSION

Greater EOR is associated with improved survival in GBM across most of the modern literature, but inconsistent definitions of resection categories, PFS, and functional status limit cross-study comparison and future meta-analysis. Standardized, volumetric EOR reporting frameworks such as RANO-resect, alongside consistent PFS and functional-outcome reporting, are needed to strengthen the evidence base.

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Full references for [30] available with the manuscript

ACKNOWLEDGEMENTS

Thank you to the College of Medicine for organizing the 2026 Summer Dean's projects and thank you to Dr. Persad for your mentorship and expertise. An extra thank you to the Kelly lab for guidance and organizing weekly meetings and presentations!



Mehrnaz Javadian (Dr. Angelica Lang)

Examining shoulder motion in patients with motion-sparing wrist fusion: does this procedure reduce movement compensations?

Motion-sparing or partial wrist fusions are emerging surgical procedures for managing refractory pain in advanced arthritis. Unlike total wrist fusions, these procedures aim to preserve wrist motion and function. However, post-fusion compensatory changes in movement patterns may predispose this population to secondary musculoskeletal disorders.

This study investigated scapular kinematics in twenty-two participants with partial wrist fusion (PF) compared to previously collected data from participants with total wrist fusion (TF) and sex- and age-matched healthy controls.

Using motion capture, scapular and humeral movement was tracked during seven functional tasks. Scapular kinematics (internal rotation, upward rotation, and anterior tilt) were analyzed at discrete humeral elevation increments.

Kinematic outcomes were assessed using linear mixed models with group as a fixed factor and participant as a random effect, run separately for each task and humeral elevation angle increment.

PF participants demonstrated greater scapular internal rotation and anterior tilt but similar scapular upward rotation to the control group. Overall, the PF group's scapular kinematics more closely resembled those of the control group compared to the TF group.

Therefore, partial wrist fusion may preserve more normal upper-limb mechanics. Understanding these compensatory patterns is important to inform pre-operative decision-making and post-operative rehabilitation to help prevent secondary upper-limb disorders.

Examining shoulder motion in patients with motion-sparing wrist fusion: Does this procedure reduce movement compensations?

¹Mehrnaz Javadian, MKin, ²Laura Sims, MD, & ¹Angelica E Lang, PhD

¹Canadian Centre for Rural and Agricultural Health, College of Medicine, University of Saskatchewan, ²Department of Orthopedic Surgery, University of Saskatchewan

Introduction

- **Motion-sparing** or **partial wrist fusions** are emerging surgical procedures used to manage refractory pain in advanced wrist arthritis.^{1,2,3}
- Unlike total wrist fusions, these procedures aim to **preserve motion and function** including activities of daily living.^{1,4}
- Post-fusion **compensatory changes** in movement patterns of proximal joints and muscles may predispose this population to secondary upper limb disorders.
- We compared the scapular kinematics of participants with partial wrist fusion to previously collected data for total fusion participants and healthy controls to assess for compensatory movement patterns.

Hypothesis:

Scapular kinematics will differ across the three groups, but partial fusion data will more closely resemble the control group than the total fusion group.

Methods

- 22 participants were recruited for the motion sparing group. Data for the total fusion and control groups was collected previously.
- Shoulder motion was tracked using **motion capture** in seven functional tasks (Figure 1): comb hair, wash axilla, tie apron, overhead reach, overhead lift, forward reach, and floor-to-waist lift.

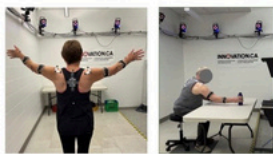


Figure 1. Placement of motion capture markers (left) and forward reach task (right).

- For each task, three dimensions of **scapular motion** were calculated:
 - 1) Internal Rotation,
 - 2) Tilt,
 - 3) Upward Rotation,

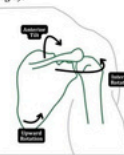


Figure 2. Scapular kinematics.

- Scapular outcomes were extracted from specific humeral elevation levels (i.e., 30°, 60°, 90°) during the tasks.
- Group differences in scapular kinematics were assessed at each humeral elevation angle using **linear mixed models**, run separately for each task.

Participants

	Partial Fusion	Total Fusion	Control
Participants	22	9	22
Sex	19M, 3F	7M, 2F	19M, 3F
Age (yrs)	63.3 (30-87)	58.8 (34-84)	62 (33-82)
Dominance	20R; 2L	8R, 1L	20R; 2L
Fusion Side	4 Bilateral 13 Dominant 5 Non-dominant	2 Bilateral 5 Dominant 2 Non-dominant	-

Table 1. Participant demographic data with values representing [Mean (Range)]

Participant groups were matched for sex and age (±5 years as determined by data availability).

Results

Comparison of all three groups demonstrated:

- The **partial fusion** group's scapular kinematics are closer to the **control group** than the total fusion group.

Compared to the control group, the partial fusion group demonstrated:

- Significantly greater **scapular internal rotation** during the wash axilla task (Figure 3).
- Significantly greater **anterior tilt** during the tie apron and forward reach tasks (Figure 4).
- Similar **scapular upward rotation** in the comb hair tasks (Figure 5).

Scapular Internal Rotation: Wash Axilla

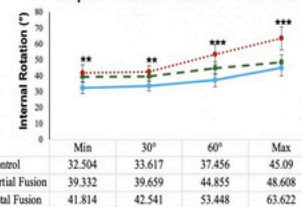


Figure 3. Scapular internal rotation (± 95 CI%) measured at minimum, 30°, 60° and maximum during the wash axilla task (right). * denotes p<0.05. ** denotes p<0.01. *** denotes p<0.001.

Scapular Tilt: Tie Apron

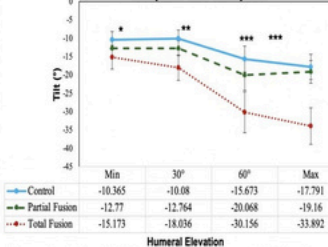


Figure 4. Scapular tilt (± 95 CI%) measured at minimum, 30°, 60° and maximum during the tie apron task. Positive values represent posterior tilt, and negative values represent anterior tilt. * denotes p<0.05. ** denotes p<0.01. *** denotes p<0.001.

Scapular Upward Rotation: Comb Hair

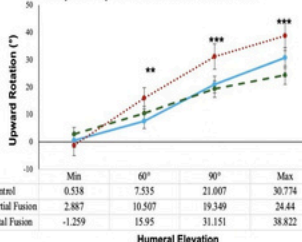


Figure 5. Scapular upward rotation (± 95 CI%) measured at minimum, 60°, 90° and maximum during the comb hair task (left). * denotes p<0.05. ** denotes p<0.01. *** denotes p<0.001.

Conclusion

- The functional tasks revealed **distinct** scapular kinematics profiles for each group.
- The partial fusion group showed significantly fewer and smaller deviations from the control group's scapular biomechanics compared to total fusion.
- **Prior research** from our lab comparing scapular kinematics between total fusion and healthy controls showed similar results with the total fusion group displaying increased scapular motion during functional tasks.

The results suggest the lack of motion available at the wrist may be contributing to the compensations at the scapular level.

- This study proposes that partial wrist fusion may confer a meaningful advantage by reducing the degree of compensatory scapular motion thereby lowering the risk of secondary shoulder injury.

Further research is needed to better understand these compensatory movement patterns to inform pre-op shared decision-making and post-op rehabilitation programming to prevent secondary upper limb injuries.

Acknowledgements



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Azmarak Khan (Dr. Rick Jaggi)

Plant-Based Exosomes for Post Procedural Facial Scar Healing: A Systematic Review

Background: Facial scarring following procedures can significantly impact one's quality of life and self-image. Plant-based exosome like nanovesicles have emerged as a potential scar management therapy, however clinical evidence to date has not been systematically reviewed

Objective: To Synthesize the available clinical evidence on the effectiveness of plant-derived exosomes for post procedural scar healing.

Methods: A search of databases such as MEDLINE, Embase, Web of Science and CENTRAL identified 550 records. After removal of duplicates and screening against an inclusion and exclusion criteria three studies were included: One randomized control trial (n=75) and two case series contributing to a total four facial cases

Results: In the RCT, groups treated with exosomes showed greater improvements than laser alone on the modified Vancouver Scar and observer-rated POSAS (both $p= 0.03$). Plant and human-derived sources both performed comparably. Across the four case-series patients, mVSS improved 71-75% and POSAS improved 55-71%. No serious adverse events were reported in any of the studies.

Conclusion: Early evidence suggests that plant-derived exosomes may improve facial scars when used alongside other forms of care, however the current studies are too small and too few to recommend its use in clinical practice. Larger, well-designed studies with longer follow up are needed to make proper clinical recommendations on its use.

Plant-Based Exosomes for Post Procedural Facial Scar Healing: A Systematic Review



Azmarak Khan¹, Ibrahim Al-Azem¹, Abdullah Qureshi¹, Hamza Arshad¹, Rick, Jaggi²

¹University of Saskatchewan College of Medicine, Saskatoon Saskatchewan, Canada; ²Division of Otolaryngology, Head and Neck Surgery, Department of Surgery, University of Saskatchewan College of Medicine, Saskatoon, Saskatchewan, Canada;

Introduction

- Scar formation is an inevitable process that occurs during wound healing following surgery or injury.
- Scarring, especially on the face, can significantly impact a patient's quality of life, where poor cosmetic outcomes may result in poor psychosocial importance
- Currently, the standard of care for wound management involves the application of topical petroleum jelly with the goal of maintaining a moist wound environment
- Plant-based exosomes have shown potential in promoting wound healing and reducing the appearance of scars
- Exosomes are microscopic vesicles that work by mediating cell-to-cell communication. It achieves this by carrying proteins and other signaling molecules involved in tissue repair (Bai et al., 2024).

Purpose

- Evaluate and synthesize the available clinical evidence on plant-derived exosomes, alone or combined with a procedural adjunct compared with standard scar care for post-procedural facial scar healing

Methods

Inclusion Criteria

- Human adults ≥ 18 with post-procedural or post-traumatic facial scars
- Plant-derived exosomes or PDENs by any delivery route, alone or combined with a procedural adjunct such as fractional CO2 laser or microneedling
- Standard scar care (petroleum jelly, silicone, corticosteroid, laser alone, or no treatment).
- A scar outcome reported, ideally a validated score (VSS, mVSS, or POSAS)
- Human clinical studies, including randomized and non-randomized trials, cohort studies, case series, and case reports
- Full text available in English

Exclusion Criteria

- Adults <18, paediatric populations, non-facial scar populations with no extractable facial subgroup data
- Exclusively mammalian-derived exosome interventions including MSC, PRP, and adipose-derived sources
- Studies with no scar outcome reported at all
- Reviews, editorials, letters, conference abstracts without data, and animal or laboratory (in vitro) studies.
- Studies where the plant-derived exosome component is uncharacterized or a minor, unquantified element of a multi-ingredient preparation

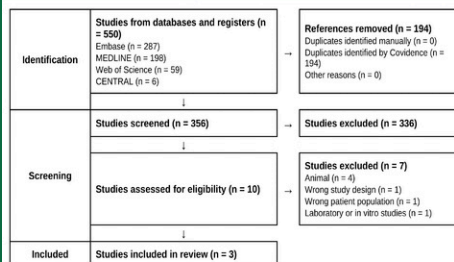


Figure 1: PRISMA Flow Diagram

Results

- Three studies met the inclusion criteria: One randomized controlled trial (n = 75) and two retrospective case series contributing four facial cases, all evaluating plant-derived exosomes for post-procedural or post-traumatic facial scars using validated scar assessment scales.

Study	Design	Patients, n (facial)	Age, y	Scar etiology
1 Park (2026) ¹	Randomized controlled trial, three arms	75 (75)	20 to 75	Postoperative surgical facial scars
2 Majewska (2025) ²	Retrospective case series	4 (1)	24	Traumatic facial injury (post surgical reconstruction)
3 Majewska (2025) ³	Retrospective case series	4 (3)	34 to 52	Dog bite, forehead trauma, iatrogenic laser injury

Table 1 : Study design and characteristics

Study	Product and plant source	Preparation	Delivery route	Procedural adjunct	Regimen	Comparator
1 Park (2026) ¹	Exome, Cosmeceutic; plant source not named	Topical solution	Topical immediately after laser	Laser	5 sessions, every 2 weeks	Laser alone; human exosome arm
2 Majewska (2025) ²	ASCEplus, ExoCoBio; rose (Rosa damascena) reconstituted	Lyophilised powder	Microneedling plus topical	Microneedling, laser, subcision	4 sessions over 4 months	None, single arm
3 Majewska (2025) ³	ASCEplus and ExoBalm, ExoCoBio; rose (Rosa damascena)	Solution, balm or mask	Combined, or topical only in one case	Laser and microneedling, or none	1 to 4 sessions	None, single arm

Table 2 : Product description, procedural adjunct and plant-based sources among the three studies

Study or case (n)	mVSS, pre to post	POSAS observer	POSAS patient	Other outcomes
Park: laser alone (n = 25)	5.1 to 4.4	20.8 to 17.7	13.6 to 11.1	Grayscale intensity 165.8 to 162.9
Park: laser + human exosome (n = 25)	5.3 to 2.8	20.6 to 15.2	14.5 to 11.7	Grayscale intensity 171.6 to 160.3
Park: laser + plant exosome (n = 25)	4.9 to 3.1	21.1 to 15.8	13.1 to 10.4	Grayscale intensity 168.9 to 155.8
Park: between group p value	0.03	0.03	0.26 (NS)	Grayscale intensity p = 0.01
Case 1: traumatic facial (24 M)	8 to 2 (75%)	45 to 16 (64%)	49 to 14 (71%)	Satisfaction 1 of 5 to 5 of 5
Case 2: dog bite (34 F)	7 to 2 (71%)	32 to 14 (56%)	41 to 16 (61%)	No adverse events
Case 3: forehead trauma (M)	7 to 2 (71%)	33 to 15 (55%)	42 to 18 (57%)	No adverse events
Case 4: iatrogenic laser injury (52 F)	8 to 2 (75%)	42 to 13 (69%)	47 to 16 (66%)	Topical exosome only, no device used

Table 3 : mVSS = modified Vancouver Scar Scale; POSAS = Patient and Observer Scar Assessment Scale; NS = not significant. Lower scores indicate a better outcome. Trial values are group means; case values are individual patients with no control group.

Discussion/Conclusion

Key Findings

- All three studies showed improvement in the various scar scores when using the plant-based treatments. However, evidence is still limited due to only three studies being included
- In the RCT, the plant-based exosome group improved more than the laser alone on mVSS and observer POSAS (p = 0.03). Animal and plant-based sources performed comparably
- Case series showed 71-75% improvement across four facial cases for the mVSS and a 55-71% improvement for the POSAS scar outcome.
- One of the cases improved with topical exosomes alone (52F), highlighting an isolated use of plant-based exosomes.
- No serious adverse events were reported between any of the studies using the exosomes.

Limitations

- The RCT was not powered, not registered and only two-week follow up
- Case series were uncontrolled and had multiple treatment adjuncts, so the exosome effects can't be isolated
- The two-case series shared authorship, meaning they are not fully independent observations

Conclusion

- Early evidence suggests plant-derived exosomes may help improve the appearance of facial scars; however, the current studies are too small and too few to recommend the routine use of plant-based exosomes in practice
- Larger, well-designed studies with longer follow up are needed to make proper clinical recommendations on its use

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Acknowledgements

This project was completed as part of the Dean's Summer Research Project at the University of Saskatchewan College of Medicine in collaboration with FACE Cosmetic and Reconstructive Surgery, Saskatoon, SK.





Alanna Liu (Dr. Garson Chan)

Wait Times and Access to Urology Care in Saskatchewan: Rural vs Urban Disparities, Condition-Specific Delays, and the Impact of the COVID-19 Pandemic

Background: Timely access to urology care is critical to optimizing outcomes for patients. COVID-19 significantly impacted healthcare access in Saskatchewan, but its residual impact on patients requiring urologic surgery is not well established. This study aimed to evaluate the impact of the pandemic on urology service delivery and identify wait time disparities between urban and rural patients.

Methods: Retrospective data analysis of patients who received urologic surgery in Saskatchewan from 2018-2025. Data was analyzed across 3 time periods (pre-COVID, during COVID and post- COVID) and by area of residence (urban vs. rural) using Kruskal-Wallis and Mann-Whitney U tests. These were compared with established national waitlist guidelines.

Results: 18,362 urological procedures were performed. Median post-COVID wait times were significantly longer than pre-COVID for most endourologic and uro-oncologic procedures ($p < 0.001$), with increases ranging from 3-22 days. Exceptions were radical nephrectomy, radical cystectomy, and radical orchiectomy. Rural patients experienced significantly longer wait times for partial nephrectomy ($p = 0.01$) and transurethral resection of bladder tumor ($p = 0.001$), but wait times were comparable for all other procedures. Although most oncological wait times increased significantly, procedures were still performed within wait time recommendations.

Conclusion: Study findings suggest COVID-19 significantly impacted surgical wait times for patients residing across Saskatchewan.

Wait Times and Access to Urology Care in Saskatchewan: Urban vs Rural Disparities, Condition-Specific Delays, and the Impact of the COVID-19 Pandemic

Alanna Liu, Leah Medernach, Delores Letourneau, Thuy Le, Dr. Garson Chan

INTRODUCTION

- Timely access to urology care is critical to optimizing outcomes and preventing complications for conditions such as prostate and bladder cancer, kidney stones, and lower urinary tract dysfunction.
- The COVID-19 pandemic had a significant impact on healthcare delivery in Saskatchewan, exacerbating existing resource constraints and contributing to a change in surgical wait times.
- The Canadian Urological Association (CUA) established maximum wait times for a range of malignant and benign urological procedures¹, but it is currently unknown whether our province has satisfied the published recommendations.
- Rurality is also a known barrier to access specialty care. Little is known regarding quantified disparities between rural and urban residing patients waiting for urological surgery in our province.

OBJECTIVES

- Evaluate the impact of COVID-19 on urology service delivery and identify specific conditions most affected by delays.
- Quantify wait time disparities between rural and urban residing patients in Saskatchewan.

METHODS

- Retrospective data analysis of patients who received urologic surgery in Saskatchewan from 2018-2015.
- Data obtained from the Saskatchewan Surgical Registry and Saskatoon Urology Associates Clinic.
- Variables collected:** procedure, year of procedure, wait time in days, patient residence (urban vs. rural).
- 3 time periods derived: Pre- (2018-2019), during (2020-2022), post-COVID (2023-2025).
- Analysis on SPSS involved descriptive statistics, Kruskal-Wallis, and Mann-Whitney U tests. 2-sided p-value <0.05 was considered statistically significant.

RESULTS

Procedures	Pre-COVID, n	COVID, n	Post-COVID, n	Urban, n (%)	Rural, n (%)
TURP/Laser (N = 5515)	1577	1897	2041	62.6	36.4
Ureteroscopy (N = 3135)	518	1235	1319	50.7	49.3
PCNL (N = 216)	78	64	74	49.1	50.9
Partial nephrectomy (N = 314)	52	101	161	51.6	46.2
Radical nephrectomy (N = 1141)	319	417	405	59.4	38.9
TURBT (N = 5614)	1381	2055	2178	62.3	36.9
Radical cystectomy (N = 195)	33	71	91	56.4	43.6
Radical prostatectomy (N = 1598)	330	541	727	57.6	35.4
Radical orchiectomy (N = 634)	176	230	228	67.7	30.1

Table 1. Demographics. TURP = transurethral resection of prostate. PCNL = percutaneous nephrolithotomy. TURBT = transurethral resection of bladder tumor. Patients with area of residency indicated as "Unknown" from the Surgical Registry were considered missing data and removed from analysis. The rate of missing data was 1.52%.

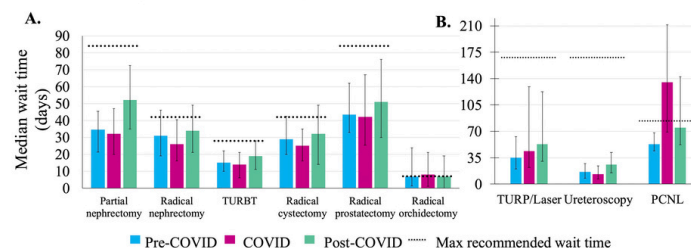


Figure 1: Median wait time comparison by COVID period for malignant condition procedures (A) and endourologic procedures (B). Error bars represent IQR. Significant differences observed for partial nephrectomy ($p < 0.001$), radical nephrectomy ($p < 0.001$), TURBT ($p < 0.001$), radical prostatectomy ($p < 0.05$). Significant differences observed for all endourologic procedures ($p < 0.001$).

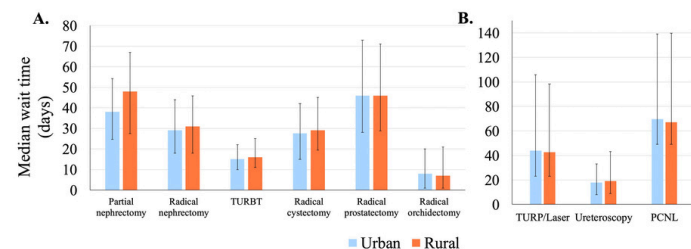


Figure 2: Urban vs. rural patient median wait time comparison for malignant condition procedures (A) and endourologic procedures (B). Error bars represent IQR. Significant differences observed for partial nephrectomy ($p = 0.01$) and TURBT ($p = 0.001$). No significant wait time differences observed between groups for endourologic procedures.

Discussion

- Post-COVID wait times for most oncologic and endourologic procedures were significantly higher than pre-COVID** wait times. Median increase in post-COVID wait times ranged from 3-22 days. The persistence of longer wait times through 2025 suggests that our province has not yet fully recovered from the surgical backlog worsened by the pandemic.
- Urban and rural patients experienced comparable wait times** for most procedures, with significant differences found only in TURBT and partial nephrectomy. This suggests that COVID-related delays in urologic service delivery affected urban and rural patients similarly.
- While overall wait times for all procedures satisfied the recommended wait time guidelines, we lacked enough granular data to stratify patients according to disease severity. Many of the procedures included in this study have shorter benchmarks for more severe disease. Comparing all patients to a single benchmark may have overestimated the number of patients treated within an appropriate timeframe.

Acknowledgments

- Support for this research was provided by the College of Medicine's Dean's Summer Research Project program.
- Thank you to the Saskatchewan Surgical Registry, Clinical Research Support Unit, and the team at Saskatoon Urology Associates for their support on this project.



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Montana Mellor (Dr. Abdalla Butt)

PATHWAYS-SK: Care pathways and outcomes for Peripheral Arterial Disease in Saskatchewan: who gets revascularization?

Background: Peripheral arterial disease (PAD) is a syndrome typically caused by atherosclerosis of the arteries causing obstruction of arteries in the extremities. In Canada there are approximately 800,000 Canadians who suffer from PAD, and it can lead to Major Adverse Cardiac Events (MACE) or limb loss. Some patients may undergo revascularization, in which a procedure (open, endovascular, or hybrid) is done to restore blood flow to prevent limb loss but also to alleviate symptoms of PAD such as pain. In Saskatchewan, there is little understood about how geography and other social determinants of health affect the access to revascularization, and how this will affect patient quality of life and outcomes. Methodology and Analysis: This study would be a retrospective cohort population-based study using South Saskatchewan health databases between 2019-2025. We would be looking at patients who are adults who have new arterial insufficiency, which is criteria defined by ICD-10. We would want to exclude resident not residing in Saskatchewan, suffering trauma, vasculitis, and missing other linkage variables we will be exploring. Our exposure is revascularization, either open, endovascular, or hybrid. The outcomes would be divided into a primary outcome (MALE), and the secondary outcome would be major adverse cardiac events (MACE), strokes, all-cause mortality, amputation free survival, and the rate of readmission at 30- and 90-days post intervention. With the data collected we would analyze the following: Estimate 1-year cumulative incidence of revascularization following PAD diagnosis; Compare outcomes between patients with intervention using a time-to-event analyses; Adjust the confounding and immortal time bias. Results: We looked at 140 patients who were diagnosed with PAD, 67 underwent revascularization and 73 did not. The most significant predictor of a patient receiving a revascularization surgery is the presence of critical limb threatening ischemia (CLTI), aOR of 215, 95% CI 48.2-1558, $p < 0.001$. Initially we thought that diabetes was associated however after adjustment it is not associated with revascularization. According to the 9 deaths that occurred, revascularization made no significant difference (log-rank $p = 0.445$). Age was the only variable that was associated with mortality (HR 1.25/year, 95% CI 1.09-1.44, $p = 0.002$). Major amputations above the ankle were seen more frequently among the revascularized patients (11.3% vs 0%) however after adjustment there was no independent association (OR 3.13, 95% CI 0.16-630, $p = 0.536$). Conclusion: Overall, in our cohort we noted that CLTI was the strongest predictor of a patient receiving a revascularization procedure. Although they did have elevated one-year major amputation rates this was not independent from the patient's clinical picture. This supports that disease severity will increase rates of major amputation, not revascularization alone. There was no significant association between increased mortality and revascularization procedures. The main limitation was our sample size and to better evaluate PAD we would need a larger sample size moving forward.

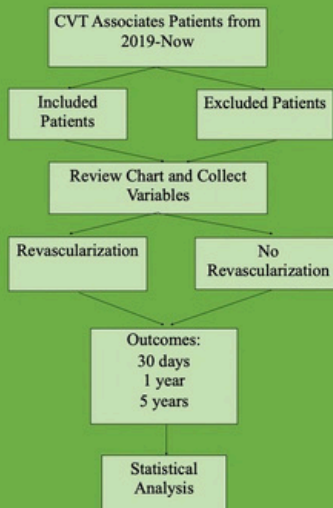
PATHWAYS-SK: Care pathways and outcomes for Peripheral Arterial Disease in Saskatchewan: who gets revascularization?

PRESENTER

Montana Mellor

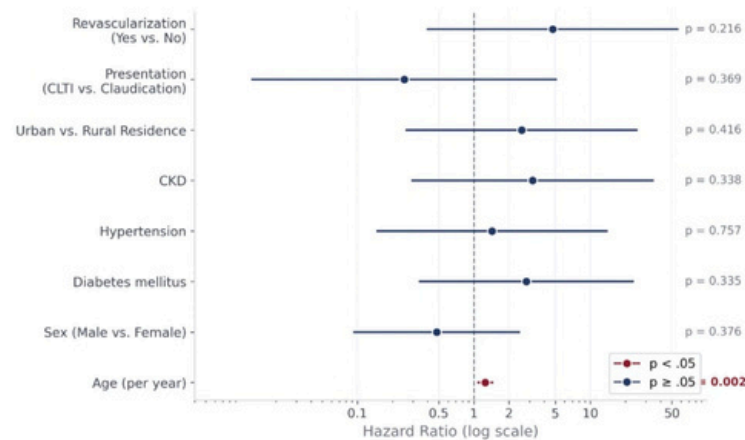
BACKGROUND: Peripheral arterial disease (PAD) is a syndrome typically causes obstruction of arteries in the extremities. In Canada there are approximately **800,000 Canadians** who suffer from PAD, and it can lead to Major Adverse Cardiac Events (MACE) or limb loss. Some patients may undergo revascularization, in which a procedure is done to restore blood flow to prevent limb loss but also to alleviate symptoms of PAD such as pain. In Saskatchewan, there is little understood about how geography and other social determinants of health affect the access to revascularization, and how this will affect patient quality of life and outcomes.

METHODS:



Cox Regression: Predictors of All-Cause Mortality

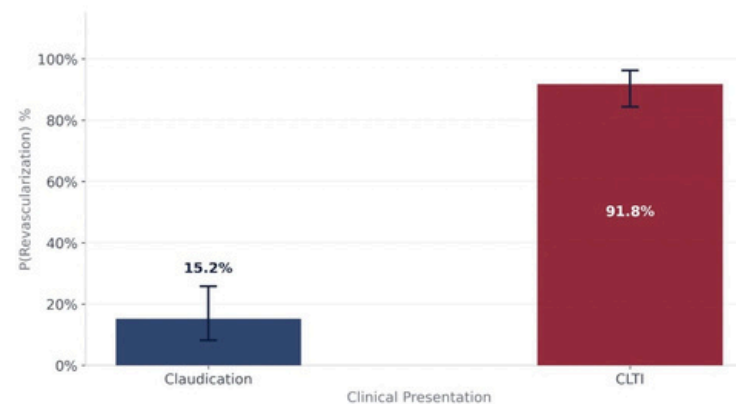
Hazard ratios with 95% confidence intervals — n = 140, 9 events



Only age reached statistical significance (HR 1.25, 95% CI 1.09-1.44, p = .002).
CKD = chronic kidney disease; CLTI = chronic limb-threatening ischaemia.

Probability of Revascularization by Presentation

Observed proportions with 95% confidence intervals



OR = 65.51 (95% CI 20.75-258.52); Fisher's exact test p < .001
CLTI = chronic limb-threatening ischaemia.



RESULTS:

Statistics:

- Univariate and multivariate logistical regression
- Identified various predictors of patient who will be offered revascularization
- We used Odds Ratio (OR) with 95% Confidence Interval (CI)
- Using OR quantified the relationship between the variable and the predictor (revascularization)
- Our 95% CI was used to determine the precision of estimate

What did we find?

N=140
(48% non-revascularization, 52% revascularized)

Urban and Rural did **not** change Revascularization Rates

CLTI Strongest Predictor of Revascularization

Higher Age = Higher Mortality

Diabetes ≠ Revascularization

AUTHORS

Montana Mellor BSc, Andreea Ababei BSc, Dr. Abdalla Butt M.D FRCP, Kirat Shukla PhD.



Jake Neufeld (Dr. Jonathan Norton)

Clinical and Economic Value of Intraoperative Electromyography for Routine Lumbar Pedicle Screw Placement: A Canadian literature review and health-system perspective

Title: Clinical and Economic Value of Intraoperative Electromyography for Routine Lumbar Pedicle Screw Placement: A Canadian literature review and health-system perspective.

Purpose: To evaluate the clinical and economic value of triggered electromyography (t-EMG) in routine lumbar pedicle screw placement by assessing rates of surgical revisions and neurological complications.

Background: Pedicle screw fixation has become the standard for deformity and degenerative work, and with it, pedicle screw (PS) stimulation has become a mainstay of spinal surgery. With the advancement in navigation and robotic surgical techniques, some question whether PS stimulation is still necessary for routine lumbar surgeries.

Methods: A literature search identified peer-reviewed articles through June 2026 that reported pedicle screw malposition, post-operative revision, or neurological complications. The studies were subsequently grouped based on the modality of PS insertion (freehand, fluoroscopic, navigated, or robot-assisted). A cost-analysis was then performed based on Saskatchewan data and the existing literature to estimate the burden of EMG monitoring and revision surgeries in Canada.

Results: Of the 49 studies included, the revision rates were highest in the freehand group at 100/3442 patients (2.91%), followed by FS at 24/969 patients (2.48%), robot-assisted at 5/608 patients (0.82%), and navigation-assisted at 18/2988 patients (0.60%). For neurological complications, fluoroscopy-assisted placement had the highest reported complication rate at 17/312 patients (5.45%), followed by freehand at 35/857 (4.08%), then navigation-assisted at 77/2,303 (3.34%), and lastly robot-assisted placement at 1/261 (0.38%). In our cost analysis, IONM was estimated at CA\$740 per case.

Conclusions: The available literature demonstrates low revision rates with modern navigation and robot-assisted techniques, suggesting that T-EMG may not be necessary for pedicle screw placement in low-risk lumbar cases when these technologies are available.

CLINICAL AND ECONOMIC VALUE OF INTRAOPERATIVE ELECTROMYOGRAPHY

for routine lumbar pedicle screw placement: a Canadian literature review and health-system perspective

Jake Neufeld, Jonathan Norton

Department of Neurosurgery, College of Medicine, University of Saskatchewan



CLINICAL BACKGROUND

PEDICLE SCREW FIXATION

- Pedicle screws fixation is used to stabilize the vertebrae during lumbar spine in deformity and degenerative work.
- Breaches / malposition occur when the screw crosses the pedicle wall.
- Breaches can threaten a lumbar nerve root, causing radicular pain, weakness, and sensory impairment.
- Some breaches require revision, but many remain asymptomatic.

TRIGGERED EMG (t-EMG)

- T-EMG is a type of intraoperative neuromonitoring used to guide pedicle screw placement.
- Pedicle screws are stimulated while muscle responses are recorded.
- A low threshold suggests reduced electrical resistance and possible proximity to neural tissue, prompting inspection or repositioning.

WHY REASSESS ROUTINE USE?

- T-EMG is often discredited for its lack of sensitivity and reliability.
- Once voltage changes are noted, there may already be damage to the nerve root.
- Modern 3D navigation directly visualizes screw trajectory in real-time with high screw placement accuracy.

OBJECTIVE

To evaluate the clinical and economic value of t-EMG in routine lumbar pedicle screw placement by assessing rates of surgical revisions and neurological complications.

METHODS

- MEDLINE search through June 24, 2026
- Adult lumbar/lumbosacral studies reporting malposition, revision, or neurological complications.
- Groups: freehand, fluoroscopy, navigation, and robotic guidance.
- Saskatchewan health system cost estimate.

188

full texts
screened

49

included
studies

39

studies reported
neurological complications

HOW OFTEN WAS MONITORING REPORTED?

28.6%

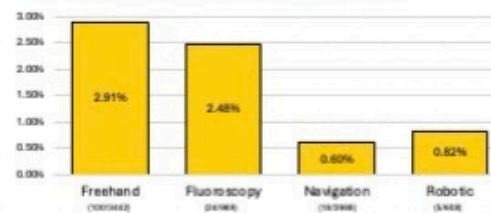
studies reporting any IONM
(14/49)

20.4%

studies reporting t-EMG
(10/49)

POSTOPERATIVE REVISION BURDEN

Participant-level revision rate by placement technique

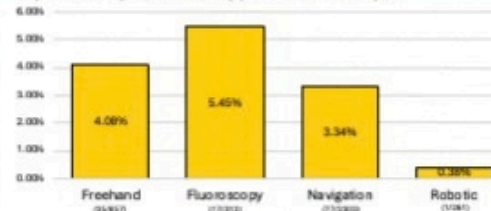


Across 47 studies with extractable revision data

Navigation-assisted placement had the lowest pooled participant-level revision rate: 18/2,988 (0.60%).

NEUROLOGICAL COMPLICATIONS

Reported complication rate by placement technique



Total: 130/3,733 patients across 39 studies (3.48%)

0.51%

unresolved neurological complications (19/3,733)

EVIDENCE LIMITATIONS

- No study in our search directly compared navigation alone with navigation plus t-EMG.
- Breach definitions, imaging protocols, and outcome reporting varied.
- Findings may be confounded by case complexity, surgeon experience, and technological learning curves.

Interpret pooled rates as descriptive—not causal comparisons between technologies.

CANADIAN COST PERSPECTIVE

Estimated Saskatchewan IONM cost per case

CA\$740

Surgeon fee	\$300
Monitoring system	\$240
Technologist	\$150
Disposable supplies	\$50

*Estimate excludes the opportunity cost of constrained personnel and operating room resources.

CLINICAL INTERPRETATION

PROPOSED FRAMEWORK FOR ABSTAINING FROM T-EMG USE

- Routine degenerative lumbar fusion
- Low-risk anatomy
- Reliable 3D navigation available

CONTINUED INTEGRATION OF T-EMG

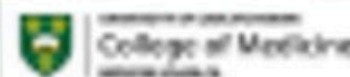
- Revision surgery or deformity
- Complex or high-risk anatomy
- Osteotomy or pediatric cases
- Modern navigation unavailable

CONCLUSION

Low revision rates reported with modern navigation raise uncertainty about the incremental value of routinely adding t-EMG in low-risk lumbar cases

The absence of direct navigation ± t-EMG comparisons prevents a definitive effectiveness or cost-effectiveness conclusion.

Future: prospectively compare navigation alone versus navigation + t-EMG using screw-related revision, neurological deficit, operative time, and Canadian system cost outcomes.





Eric Yu (Dr. Emilie LeRoux)

Impact of Surgical Technique on Outcomes Following Perceval Sutureless Aortic Valve Replacement

Background: This study evaluates Perceval aortic valve replacement outcomes at Royal University Hospital and describes a standardized technique that leads rapid and successful implants across five surgeons and facilitating learning.

Methods: This retrospective study reviewed isolated and combined cases during 2019–2026. Two cases involving extracorporeal membrane oxygenation or salvage surgery were excluded, leaving 63 patients. The technique emphasizes sizing, controlled positioning and deployment, and one prolonged balloon inflation in all cases rather than two shorter inflations. Clinical and operative outcomes were summarized. Early postoperative transthoracic echocardiography assessed valve function. Means are presented $\pm$ 95% confidence interval half-width.

Results: Mean age was 75.3 ± 1.2 years. Mean cross-clamp and cardiopulmonary bypass times were 109.6 ± 10.9 and 135.9 ± 12.1 minutes, respectively. Only eight patients received isolated aortic valve implants. Fifty-two patients received L or XL valves (27 L, 25 XL); 11 received smaller valves. Four underwent pacemaker implantation; one had high-risk preoperative conduction abnormalities, and another implantation was considered premature on clinical review. One trace paravalvular leak occurred, with no mortality, early prosthesis dysfunction, or redo surgery.

Conclusions: Findings demonstrated zero mortality, low pacemaker implantation, and preserved early valve function. Snare-assisted positioning and stabilization support technique standardization. Ongoing follow-up will assess mid-/long-term outcomes and providers' learning curve.



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