UNE COM Research and Scholarship Fall Forum

Friday, November 1, 2024

Innovation Hall, UNE Portland Campus

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11 a.m.-12 p.m. **PRESENTERS SET UP THEIR POSTERS**

12 p.m. **LUNCH**

1 p.m. **WELCOME REMARKS**
Jane E. Carreiro, D.O. '88, *Vice President for Health Affairs; Dean, College of Osteopathic Medicine*

1:15 p.m. **POSTER PRESENTATIONS / JUDGING SESSION #1,** *Odd-numbered posters will present*

2:05 p.m. **BREAK**

2:15 p.m. **Keynote Address**

SUNFLOWER SYNDROME: A POORLY UNDERSTOOD EPILEPSY

Elizabeth Thiele, M.D., Ph.D.
Director, Pediatric Epilepsy Program
Director, Carol and James Herscot Center for Tuberous Sclerosis Complex (TSC)
Professor of Neurology, Harvard Medical School

Thiele is a neurologist and epileptologist at Massachusetts General Hospital. Her research and clinical interests include the role of diet in epilepsy treatment, genotype-phenotype correlation in TSC, the role of epilepsy surgery in management of intractable epilepsy, outcomes following infantile spasms, and neuropsychological profiles in relationship to tuber number and location in TSC.

3:15 p.m. **POSTER PRESENTATIONS / JUDGING SESSION #2,** *Even-numbered posters will present*

4 p.m. **BREAK,** *Tea and coffee will be available*

4:15 p.m. **ORAL PRESENTATIONS**

Student Doctors, Vishva Patel OMS-II and Carleigh Rosenberg OMS-II
Basic Science: Exploring Metabolic Vulnerabilities in Tuberous Sclerosis Complex: The Role of Tryptophan and the Kynurenine Pathway in Macropinocytosis

Student Doctor, Henry Ortiz OMS-II
Clinical Science: Assessing Parasympathetic Function and Hypoalgesia Induced by Noxious Electrical Stimulation

Student Doctors, Jyotika Vallurupalli OMS-II and Sarah Trent OMS-II
Case Study: Resource Constraints and Disease Management: A Case Study of Disease Progression in La Sabana, Panama

5 p.m. **AWARDS PRESENTATION**

Please park in Bishop Street lot.
Shuttle will bring you to campus.

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The following abstracts scored the highest in the Fall Forum Abstract review process. These students will present their work as oral presentations at this years event.

A special congratulations goes to these students for their exemplary work!

Basic Science – Student Doctors Vishva Patel OMS-II and Carleigh Rosenberg OMS-II -Exploring Metabolic Vulnerabilities in Tuberous Sclerosis Complex: The Role of Tryptophan and the Kynurenine Pathway in Macropinocytosis

Clinical Science – Student Doctor Henry Ortiz OMS-II - Assessing Parasympathetic Function and Hypoalgesia Induced by Noxious Electrical Stimulation

Case Study – Student Doctors Jyotika Vallurupalli OMS-II and Sarah Trent OMS-II - Resource Constraints and Disease Management: A Case Study of Disease Progression in La Sabana, Panama

All accepted abstracts are listed hereafter, in alphabetical order by presenting author's last name, except in cases were presenting authors had more than one poster. These were given an odd and an even poster number so they may present both abstracts at the event.

Poster #	Student Name(s)	Graduating Class	Mentor(s)	Project Title
1	Aaronson, Benjamin	2027	Dr. Clifford Rosen	Diet-Induced Weight Loss in Preclinical Models Negatively Affects Bone Remodeling Activities and Reduces Bone Mass
2	Antoniou, Pantelis	2027	Dr. Ling Cao	Optimizing Pediatric Oncology Care: Comprehensive Interventions for Chemotherapy-Induced Peripheral Neuropathy in Pediatric Cancer Patients
3	Baracewicz, Julia	2027	Dr. Kathleen Becker	Investigating the Role of the Saphenous Nerve in Tibial Fracture Healing
4	Berkowitz, Jennifer; Okpoebo, Amanda;	2027	Dr. Marilyn Gugliucci	Aggregate Journal Analyses: Significance of Participating in the 48 Hour Hospice Home Immersion Project
5	Bertaux, Brittany	2026	Dr. Abhishek Chatterjee	Geographical Presence of Plastic Surgeons in Relation to Breast Surgeons in the United States for Breast Reconstruction: A Five-Year Update
6	Bhatia, Karan	2028	Dr. Uma Mahadevan	Evaluating the Efficacy of Upadacitinib, a JAK Inhibitor, in the Management of Ulcerative Colitis and Crohn's Disease: A Real-World Analysis from a Specialized IBD Care Facility.
7	Bigelow, Alexa	2027	Dr. Thomas Gearan	Access to Birthing Care in Rural Maine Counties: Evaluating the Impact of Birthing Unit Closures and Solutions
8	Canonico, Dalton	2027	Dr. Ling Cao	Lumbar spinal cord expression of Tollip and pIRAK1 in iTat mice, a model of HIV-associated peripheral neuropathy
9	Canty, Marissa; Hom, Christina	2027	Dr. Marilyn Gugliucci	End-of-Life Care in a Cardiac Sarcoidosis Patient with a Left Ventricular Assist Device: A Case Report
10	Castro, Ines	2028	Dr. Lauren Fiechtner	Multidisciplinary Perceptions of Implementation and Sustainability of the Healthy Weight Clinic
11	Chen, Sabrina	2027	Dr. Katie Stephenson	Gender Difference in Orthostatic Hypotension Test Outcomes: Implications of a Male-Derived Scale
12	Chong, Jonathan	2027	Dr. Tamara King	Utilizing Machine Learning for the Recognition of Behavior Patterns of Chronic Pain in Mouse Models
13	Cott, Riley	2028	Dr. Diana Goode	Chemotherapy Regimens Impact CD4+ T cells and Nerve Loss in Peripheral Tissue in Chemotherapy-Induced Peripheral
14	DeTroia, Christopher	2026	Dr. Derek Molliver	Cell Signaling in Sensory Neurons
15	Donnelly, PJ	2027	Dr. Ling Cao	Tollip and Cytokine Expression Profile in Doxycycline-Induced Transgenic Tat Mice: A Model of HIV-Associated Peripheral Neuropathy (HIV-PN)
16	Farag, Marina	2028	Dr. Sangita Phadtare	Assessing Composition of Gut Microbiota in Patients with Chronic Pancreatitis and Exocrine Pancreatic Insufficiency
17	Faulkner, Gavin	2027	Dr. Anna Quay Yaffee	Butterflies in the Field: Introducing POCUS to Paramedics in a Rural Emergency Medical Services and Wilderness Environment
18	Gangopadhyay, Anwesha; McCann, Chris	2025	Dr. Gloria A Bachmann	Artificial Intelligence: A Tool for Augmenting Labor and Delivery Management
19	Govindaraj, Anjanadevi	2028	Dr. Kristin Burkholder	Effect of Antimicrobial Peptides on the Antibiotic-Mediated Killing of Bacterial Biofilms
20	Gray, Lindsey	2027	Dr. Cliff Rosen, Samantha Costa	Non-Obese, High-Fat Diet Fed Mice Have Improved Metabolic and Bone Phenotypes Compared to Obese, High-Fat Diet Fed Mice
21	Griffin, Hannah	2027	Dr. Marilyn R. Gugliucci	Geriatrics Education Mentor (GEM) Program: Outcomes from Pairing Students and Older Adults During Medical School
22	Griffin, Ethan ; Joseph, Melisa	2026	Dr. Colleen Yavarow	APC I1307K Homozygosity And Colorectal Cancer Risk: A Review Of The Literature
23	Gurrala, SreeLakshmi	2027	Dr. Tamara King	Differences in Synovial Growth Factor and Immune Cells Between Sexes Contributing to Pain
24	Hansen, Jason	2027	Dr. Clark Dumontier	Frailty and Adverse Events in Veterans with Newly Diagnosed Multiple Myeloma Initiating Treatment
25	Ichikawa, Tsunagu	2026	Dr. Eben Estell	Irisin Deficiency Impairs Weight Maintenance with Voluntary Wheel Running in Mice
26	Ichikawa, Tsunagu	2026	Dr. Douglas Spicer	Navigating the Integration of Generative Artificial Intelligence in Undergraduate Medical Education: Insights from a Survey at University of New England College of Osteopathic Medicine
27	Joseph, Melisa., Tomasch, Megan	2026	Dr. Derek Molliver	Unraveling the Molecular Dynamics of Pain by Investigating Effects of Mitochondrial Uncoupling Drugs on Mouse Dorsal Root Ganglion Sensory Neurons
28	Kaithamattam, Jenson	2027	Dr. Desiree R Azizoddin	Using network analysis to understand pain and psychological symptoms in cancer patients presenting to the emergency department: The impact of recent surgery

29	Kapadia, Jhanavi	2027	Dr. Rachel Wightman	Evaluating the Feasibility and Acceptability of a Novel Biological Drug-Checking Model in Emergency Departments: A Pilot Study
30	Kim, Albert	2028	Dr. Carmela Abraham	De Novo Synthesis of High Purity CD3 Epsilon Peptides Utilizing SUMO Expression System in Bacteria
31	Kobald, Samantha	2026	Dr. Alice Ho	Final Clinical and Biomarker Outcomes of a Phase Ib/II Study of Pre-operative Induction Pembrolizumab with Radiation Therapy in Early-Stage Triple Negative and High-Risk Hormone Receptor Positive Breast Cancer (PEARL)
32	Loiselle, Maggie	2027	Dr. Leal Yonker	Bacterial Metabolic Signaling Drives Neutrophil Responses in Infected Airways
33	Lucey, Evan	2026	Dr. Stephanie Carreiro	Patient Perceptions on Opioid Therapy for Acute Pain: A Qualitative Study
34	Madigan, Emma; McLaughlin, Kathleen	2026	Dr. Marilyn Gugliucci	Identity and Inclusive Sex Education Information: Ascertaining What Parents of LGBTQ+ Youth Want to Know (Pilot Study); Maine
35	McAuliffe, Meagan; McAndrews, Casey; Joseph, Melisa	2026	Dr. Luis Queme	A Want and a Need: Firearm Harm Reduction Education Should Be Included in Medical School Curriculum
36	McGeorge, Gabrielle	2027	Dr. Bernadette Chen	Pde3a Deficiency Plays a Novel Role in Lipolysis
37	Mensah Otabil, Edith	2028	Dr. Bahjat Ghazzal	Recurrence or Persistence of Atrial Fibrillation is Associated with Frailty Phenotype, as well as Adverse Clinical Outcomes: Data from the SAGE-AF Cohort Study
38	Mohammad, Nomon	2027	Dr. Mitchell Goldfarb	Telmisartan is a Cardiac Sodium Channel Gating Modifier: Potential Mechanism of Action
39	Muench, Alicia	2027	Dr. Luis Queme Cobar	Substance Use Disorder Education in New England Medical Schools
40	Najem, Mortada	2027	Dr. Michael Lawrence	Deep Lumbar Muscle Activation During Core Stabilization Exercises in Healthy Subjects
41	Nguyen, Vincent	2027	Dr. Johanna Lantz; Dr. Marilyn Gugliucci	Analysis of Maladaptive Behaviors in Relation to Pain and Illness in Minimally Verbal Individuals with Disabilities
42	Nuki, Gabrielle	2027	Dr. Jessica Bloom-Foster	Exploring Success in Early Breastfeeding at EMMC: A Retrospective Cohort Study on Factors Affecting Exclusive Breastfeeding at Hospital Discharge up to 2 Months of Life
43	Ortiz, Henry	2027	Dr. Scott Stackhouse	Assessing Parasympathetic Function and Hypoalgesia Induced by Noxious Electrical Stimulation
44	Ou, Penhleakhena	2027	Dr. Ling Cao	Impact of demographics and social determinants of health on chronic pain in Maine
45	Patel, Vishva; Rosenberg, Carleigh	2027	Dr. Harry Filippakis	Exploring Metabolic Vulnerabilities in Tuberous Sclerosis Complex: The Role of Tryptophan and the Kynurenine Pathway in Macropinocytosis
46	Patsiogiannis, Vasiliki	2027	Dr. Alexandra Filippakis	Military Exposure to Trichloroethylene and Risk for Parkinson's Disease in New Hampshire: Camp Lejeune and Beyond
47	Peacock, Isaac	2025	Dr. Frank Bailey	Can Medical Students Learn to Code?

48	Pelletier, Connor	2026	Dr. Sammon, Jesse	Modern Trends in Receipt of Adjuvant Chemotherapy From a Single Institution
49	Pham, Luu	2027	Dr. John J. Kowalczyk	Decreased Dose-Response to Fibrinogen Concentrate in Patients Experiencing Postpartum Hemorrhage: A Retrospective Dose-Response Study
50	Pitaro, Ariana; Beecher, Caeli	2027	Dr. Katherine Rudolph	Assessing the Effect of Baseline Parasympathetic Nervous System Activity on Pain Inhibition by Sex
51	Platteter, E OMS I; Robinson, C OMS IV	2028	Dr. Jesse Sammon	Continuing Quality Improvement and the Implementation of MRI targeted Prostate Biopsy at a Regional Medical Center
52	Poulin, Hailee; Biegel, Catherine; Silvia, Sophia	2027	Dr. Geoffrey McCullen	A Systematic Review of Risk Factors and Diagnostic Measures of Postpartum Depression among Military Personnel
53	Poserio, Jefferson	2027	Dr. Clifford Rosen	Deletion of 11β-HSD1 Prevents Craniofacial Bone Loss Caused by Caloric Restriction
54	Powers, Madeleine	2026	Dr. Matthew Grosso	Investigating Postoperative Urinary Retention (POUR): Risk Factors and Post-Surgical Outcomes in Total Joint Arthroplasty
55	Reveche, Hope	2028	Dr. Henry Chase	Functional Connectivity Analysis of the Default Mode Network Using Self-Report of Spontaneous Cognition
56	Sedrak, John	2028	Dr. Punit Patel	Intracranial Hemorrhage after Excessive Licorice Candy Consumption: A Case Report
57	Shah, Bhamini; Swan-Prung, Brandon; Donepudi, Sai; Shrestha, Aishwarya; Chibber, Muskaan	2027	Dr. Douglas Spicer	Using Hands-on Culinary Medicine Education to Increase the Confidence and Ability of Medical Students to Address Lifestyle and Nutrition-related Disease.
58	Shah, Parita	2028	Dr. Daniel Capelluto	Molecular Basis for the Interaction of Phafin2 with the Actin Network During Macropinocytosis
59	Shakespeare, Christopher	2027	Dr. Nicholas Asselin	The Impact of Telecommunicator CPR Program on Out-of-Hospital Cardiac Arrest Outcomes in Rhode Island: A Pilot Study
60	Shin, John (SungJin)	2028	Dr. Jie Zheng	Regulation of Wnt Signaling Genes in Dexamethasone-treated Human Trabecular Meshwork Cells
61	Silvia, Sophia	2027	Dr. Carolyn Chlebek	Bone Marrow Adipose Tissue is Distributed Similarly in the Anterior to Posterior Plane in the Murine Tibia
62	Tanikella, Sruthi	2028	Dr. Jennifer Tjia	Community-Engaged Co-Design of Strategies for Family Caregiver Engagement during Inpatient Stays
63	Tauber, Benjamin	2025	Dr. Gary King	A Case of Aicardi Syndrome
64	Turcotte, Dawson	2028	Dr. Geoffrey Ganter	The Effects of Arrow mRNA Knockdown On The Dendritic Arbor of Primary Nociceptors of Drosophila melanogaster
65	Vallurupalli, Jyotika	2027	Dr. Ina St Onge	Impact of CFTR Modulators on Pancreatic Function in Pediatric Cystic Fibrosis Patients: A Retrospective Analysis of FE-1 Levels
66	Vallurupalli,Jyotika; Trent, Sarah; Herald, Devin	2027	Dr. Marilyn Gugliucci	Resource Constraints and Disease Management: A Case Study of Disease Progression in La Sabana, Panama
67	Vellayappan, Sandhya	2027	Dr. Kyle Scully	Food Insecurity in University of New England Medical Students
68	Walter, Ashley	2027	Dr. Kathleen Becker	Investigating Regional Sensory Distribution of the Saphenous Nerve in Tibial Periosteum
69	Yong, Connor	2028	Dr. Geoffrey McCullen	Probability of Concurrent Incidence of Medial Meniscus Injuries with Anterior Cruciate Ligament Tears: A Literature Review.

Diet-Induced Weight Loss in Preclinical Models Negatively Affects Bone Remodeling Activities and Reduces Bone Mass

Aaronson[1], B, OMS II, Chlebek[2], C, Ph.D., McAndrews[1], C, OMS III, Costa[2], SN, Rosen[2], CJ, M.D.
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[2]MaineHealth Institute for Research, Center for Molecular Medicine, Scarborough, Maine

Introduction: Despite the negative effects of caloric restriction on the skeleton, obese patients are advised to lose weight via calorie restriction before surgical procedures. Although weight loss is known to be beneficial for some aspects of surgery, weight loss due to anorexia significantly reduces bone quality. Similarly, weight loss in obese preclinical models may negatively affect bone remodeling capacity and could increase the likelihood of poor outcomes in procedures requiring osseointegration, such as total knee arthroplasty. We hypothesized that caloric restriction disrupts bone homeostasis and quality in obese mice.

Methods: To induce obesity, male and female C57BL6 mice (8 wks old) received a 60% high fat diet for 12 wks. After obesity induction, mice either continued to receive a HFD (HFD) or acclimated to a control 10% low fat diet for 2 wks before receiving 30% caloric restriction for 8 wks (HFD-CR). A final group received a low fat diet for the experiment duration (LFD). Body composition and weight were recorded at baseline and at the end of each diet. At euthanasia (30 wks), cortical and trabecular bone morphology were assessed (Micro-computed tomography). Hematopoietic progenitor cells were cultured in osteoclast differentiation media. Osteoclast size and number were quantified (ImageJ). Serum P1NP and CTx were measured to evaluate systemic bone formation and resorption, respectively.

Results: Compared to LFD, HFD and HFD-CR mice gained body weight and fat mass during high fat feeding. After the caloric restriction phase, body weight and fat mass were reduced in HFD-CR compared to HFD and LFD mice. Calorie restriction following a high fat diet reduced cortical area and thickness compared to HFD and LFD mice. Compared to HFD, HFD-CR mice had reduced trabecular thickness. In male mice, following caloric restriction, hematopoietic cells generated fewer, but similarly sized osteoclasts compared to HFD. Caloric restriction reduced serum CTx levels in females but not males. Serum P1NP was lower in HFD-CR mice compared to controls in both sexes.

Conclusion: Caloric restriction in obese preclinical models reduced bone mass and remodeling. Bone remodeling was negatively affected by caloric restriction, reflected by decreased osteoclastogenesis and reduced bone formation. Future studies should investigate the impact of weight loss-mediated reductions in bone remodeling and osseointegration success in total joint arthroplasty.

Acknowledgements: This research was supported by the Carmen Pettapiece Student Research Fellowship, University of New England College of Osteopathic Medicine Student Government Association and the Office of the Associate Dean of Research and Scholarship (BA) and the Stryker/ORS Women's Research Fellowship (CC). Animal work was approved by the MHIR IACUC committee (Protocol #2209).

Abstract Category: Original Research

Optimizing Pediatric Oncology Care: Comprehensive Interventions for Chemotherapy-Induced Peripheral Neuropathy in Pediatric Cancer Patients

Antoniou[1], P, M.P.H., OMS II, Weiss[2], A, D.O., Bean[1], EN, Ph.D., Cao[1,3], L, M.D., Ph.D., M.P.H.

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[2] Maine Medical Center/ Maine Children's Cancer Program (MCCP), Scarborough, Maine
[3] Department of Biomedical Sciences, University of New England College of Osteopathic Medicine, Biddeford, Maine

Introduction
Chemotherapy-induced peripheral neuropathy (CIPN) is a common toxic side effect of chemotherapy in pediatric cancer patients. CIPN can be debilitating, impacting quality of life and treatment adherence. Various pharmacologic interventions are used to treat CIPN, but studies, especially in pediatrics, are limited.

Methods
Data were retrospectively analyzed from 648 newly diagnosed pediatric cancer patients (1997–2012) at Maine Children's Cancer Program (MCCP). Of these, 340 patients ages 2 - 21 underwent chemotherapy, among which over 90% developed CIPN. To evaluate the effectiveness of pharmacologic and non-pharmacologic interventions, we first assessed distributions of age, sex, and bodyweight across intervention groups, as these factors influence CIPN severity and duration. Since the data lacked information on the timing and length of interventions, the total duration of sensory and motor neuropathy served as the dependent variables. Preliminary analyses examining the relationships between intervention groups and respective neuropathy durations were performed. Multivariate and regression analyses are on-going. IBM SPSS (v27) was used.

Results
The treatment groups were found to be comparable for sex, but not body weight (before and after treatment) or age distribution. Among pharmacologic interventions used to treat CIPN, a trend appears to show that gabapentin alone (used in 8/340 patients) reduced the duration of sensorimotor neuropathy more than opioid (27/340) or combined opioid-gabapentin therapy (41/340). Nonpharmacologic interventions included physical therapy (PT)/occupational therapy (OT) (130/340), or PT/OT plus osteopathic manipulative treatment (OMT) (6/340). Patients who received nonpharmacologic interventions through PT/OT had a shorter duration of sensory, but not motor, neuropathy compared to those who did not receive PT/OT. No effect of OMT on CIPN duration was seen. The small sample size for some interventions was a limitation for adequate comparison between groups.

Conclusion
This study underscores gaps in the understanding of optimal treatment strategies for CIPN in pediatric patients. Our findings suggest that whilst pharmacologic approaches may reduce the duration of neuropathy, nonpharmacologic interventions also hold promise. Further refinement of CIPN intervention protocols including utilizing nonpharmacologic therapies is critical for improving the quality of life for pediatric oncology patients suffering from CIPN.

Acknowledgements
PA was supported by the University of New England College of Osteopathic Medicine Peter Morgane Research Fellowship. The project used de-identified chart review data previously collected as part of the closed MaineHealth IRB protocol # 4552X and was determined not to constitute human subject research by the MH IRB. We would like to thank Catherine Bixby, DO, Woon Yuen Koh, PhD, and Edward Li, PharmD for participating in data collection for the previous protocol #4552X.

Investigating the Role of the Saphenous Nerve in Tibial Fracture Healing

Baracewicz[1], J, OMS II, Walter[1], A, OMS-II, Erb[1,3], A, Lizotte[1], T, Caradonna[2], P, Long[2], P, Felix[2], A, King[1,2], T, Ph.D., Becker[1], K, Ph.D.

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[2]University of New England, The Center for Pain Research, Biddeford, Maine

[3]University of Rhode Island, College of Engineering, Kingston, Rhode Island

Introduction: Tibial plateau fractures are associated with an increased risk of mortality even after 10 years post-fracture. The peripheral nervous system has been identified as a novel factor influencing both bone remodeling and fracture healing. While sensory innervation has been shown to be important for fracture healing, the specific nerves involved in fracture healing have yet to be identified. The Becker lab has identified that the saphenous nerve provides 45% of the innervation to the proximal tibia. We hypothesize that following tibial fracture, transection of the saphenous nerve will reduce innervation in the fracture site and impair fracture healing.

Methods: The saphenous nerve was transected (SNT) in 8–9-week-old C57Bl6/J female (n=8) and male (n=10) mice. All SNT and sham control mice then underwent a 0.4 μm bi-cortical defect fracture in the proximal tibia. SNT mice were compared to sham mice in all experiments. The fracture was screened by X-Ray at 3, 7, and 14 post-fracture. De-identified images were scored by 2 independent reviewers using a modified radiographic union scale (mRUST) on the anterior posterior (AP) and lateral tibial surfaces. Hindlimb weight bearing was analyzed using Blackbox One video analysis to monitor pain behavior in male mice (n=7/group).

Results: mRUST analysis demonstrated increased healing score over time ($P<0.01$) on the AP and lateral surfaces in both sexes by 2-way ANOVA. No difference in healing was detected with SNT on the AP or lateral surfaces in female mice ($P=0.22$, $P=0.15$) or lateral surface in male mice ($P=0.057$). However, increased healing was detected with SNT on the AP surface ($P=0.04$) with trends of increased healing found with SNT at day 3 on the remaining surfaces. No limb asymmetry or pain phenotype was detected in male mice suggesting healing was not influenced by unloading of the surgical limb. Studies in females are ongoing.

Conclusion: Cortical defect fractures demonstrated almost complete healing over the 14 days of the study. These pilot data suggest that SNT does not impair tibial fracture healing as measured by mRUST X-ray analysis. Interestingly, SNT may increase fracture healing, but further quantification of fracture healing by micro-CT analysis will be needed to explore this relationship. Innervation at the fracture site in the proximal tibial periosteum will be quantified 3 days post-surgery to determine if SNT impacts post-fracture nerve sprouting.

Acknowledgements: The University of New England College of Osteopathic Medicine. A special thanks to the Becker lab for all their support and the opportunity to advance research into bone healing and the nervous system. Thank you to the UNE Histology and Imaging Core for training and use of these novel protocols to produce this work and the UNE Behavioral Core for the surgery behavioral data and analysis. This work has been supported by the Khan Family Foundation Research Fellowship, R16GM150784, and P30GM145497. Animal work was approved by the UNE IACUC committee (protocol 032521-007 and 040324-004).

Aggregate Journal Analyses: Significance of Participating in the 48 Hour Hospice Home Immersion Project

Berkowitz, J, OMS II, Okpoebo, A, OMS II, Gugliucci, M, M.A., PhD., University of New England College of Osteopathic Medicine, Biddeford, ME

Introduction: Traditional palliative and end-of-life care education in US medical schools often fails to fully prepare students for the realities of this field. To address this gap, the University of New England College of Osteopathic Medicine has designed the Learning by Living 48-Hour Hospice Home Immersion (HHI) Project. This innovative program offers medical students a unique experiential learning opportunity by immersing them in an 18-bed acute care hospice home for 48 hours. During this time, students work both independently and as part of an interprofessional team, providing care for individuals who are dying, supporting their families, and conducting post mortem care. This hands-on experience aims to enhance their understanding and skills in palliative and end-of-life patient and family care.

Methods: Utilizing qualitative ethnographic/autobiographical research designs, the HHI program aimed to answer: (1) What lessons will students learn from the 48-hour home hospice immersion? and (2) What skills do they plan to apply in their future practice? Students documented their experiences in journals, which were organized in three stages: pre-fieldwork, fieldwork, and post-fieldwork. Twelve medical student journals from the 2019-20 cohort were selected for analysis. The selected journals were read by each investigator individually to identify individual themes for first level analysis and to make notations of key ideas and quotations. Recurrent themes and sub-themes were categorized, defined and used to create a code book - all of which were agreed upon by both investigators. Journals were then uploaded into NVivo Qualitative Software to conduct paired analyses of data.

Results: Approximately 300 pages of data were analyzed from the twelve journals. Several themes were identified within this project however three key themes emerged for question one: (1) Holistic comfort care/medicine, (2) Subjectivity of suffering, and (3) Religion/spirituality; and three key themes were identified for question two: (1) Increased confidence in caring for dying patients and their families, (2) Improved ability to discuss death, and (3) Enhanced understanding of the physician's role in curing versus caring.

Conclusion: Each student's experience at Gosnell Hospice Home was unique, yet all gained invaluable emotional, physical, interpersonal and spiritual insight that will shape their development into compassionate and skilled physicians in palliative and end-of-life care.

Acknowledgements: University of New England College of Osteopathic Medicine. This work has been supported by the Carmen Pettapiece Student Research Fellowship (to EB). This study was granted IRB exemption by the University of New England Office of Research Integrity (IRB #0424-18).

Geographical Presence of Plastic Surgeons in Relation to Breast Surgeons in the United States for Breast Reconstruction: A Five-Year Update

Bertaux[1], B, OMSIII, Wareham[2], C, M.D., Chahine[2], E, M.D., Homsey[3], C, M.D., Perry[3], D, M.D., Persing[3,4], S, M.D., Nardello[4], S, D.O., Chatterjee[3,4], A, M.D.

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[2]Department of Surgery, Tufts Medical Center, Boston, MA
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Introduction: Despite advances in post-mastectomy reconstruction, there remains a barrier to breast reconstruction, particularly in rural and suburban areas. Although there are almost double the number of plastic surgeons to breast surgeons, access remains a significant issue for breast cancer patients living in rural and suburban areas. We aimed to provide a five-year update to assess new trends in breast reconstruction surgery within urban, suburban, and rural populations.

Methods: A database investigation of the 2024 membership of the American Society of Breast Surgeons and American Society of Plastic Surgeons was performed. The number of breast and plastic surgeons were first totaled by state. Each breast surgeon's zip code was then searched for the presence or absence of a plastic surgeon within 10 or 20 miles. Zip codes were further categorized into urban, suburban, or rural by population density to determine the percentage of surgeons within each category.

Results: Based on the 2024 membership of the above professional societies, there are 1.8 times the number of plastic surgeons compared to breast surgeons. Despite this number, 14% of breast surgeons had no plastic surgeons within 10 miles; 7% had none within 20 miles. When greater than 20 miles away, the average distance of a plastic surgeon was 50 miles. This is compared to 25% and 10% respectively in 2018. 43% breast surgeons practice in urban areas, 32% in suburban, and 25% in rural areas. 43% of plastic surgeons practice in urban areas, 38% in suburban, and 19% in rural areas.

Conclusions: While access to breast reconstruction continues to improve, there are still disparities seen with patients treated in rural areas. Efforts directed towards improving access to breast reconstruction in more rural areas should be pursued.

Acknowledgements: Tufts Medical Center, Division of Plastic and Reconstructive Surgery

Evaluating the Efficacy of Upadacitinib, a JAK Inhibitor, in the Management of Ulcerative Colitis and Crohn's Disease: A Real-World Analysis from a Specialized IBD Care Facility.

Bhatia[1], KK, M.A.S, OMS I, Mahadevan[2], U, MD
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]University of California San Francisco, San Francisco, California

Introduction: Inflammatory Bowel Disease (IBD) encompasses Crohn's Disease (CD) and Ulcerative Colitis (UC). Both are chronic, relapsing, and remitting diseases characterized by chronic inflammation. Targeted biological therapies represent the primary therapeutic option for the management of advanced IBD. However, the costs associated with the delivery and monitoring of these drugs are burdensome for both the healthcare system and patients, lacking options for oral administration, and a high frequency of inadequate response or loss of response over time. Therefore, alternative novel treatments are still needed to aid in addressing these shortcomings in advanced IBD treatment. It is well established that JAK inhibitors are efficacious in inducing and maintaining remission in patients with moderate-to-severe CD and UC. However, among the JAK inhibitors, it is not clear yet if there is a difference in response between patients with CD versus UC. Upadacitinib is a selective Janus kinase inhibitor approved for the management of Crohn's Disease (CD) and Ulcerative Colitis (UC). This study aims to compare response to upadacitinib between patients with UC and CD in a real world tertiary care center.

Methods: Retrospective cohort study of patients with CD vs UC seen at UCSF Colitis and Crohn's Disease Center from 2019-2023. The primary outcome was endoscopic remission as noted in post-induction staging scope. Endoscopic remission was assessed using SES-CD and Mayo scores for CD and UC, respectively. Outcomes were assessed at 3 or 6 months after starting upadacitinib for UC and CD, respectively.

Results: A total of 60 patients were reviewed, 26 with Crohn's Disease and 34 with Ulcerative Colitis, who had taken Upadacitinib and had post-induction follow up data in EHR review. 10 patients with CD achieved remission (38.5%) compared to 17 patients with UC (50%). This difference was found to be nonsignificant (P=0.38).

Conclusion: In this real-world cohort of IBD patients seen at a tertiary care center, there was no significant difference in response between patients with CD or UC.

Access to Birthing Care in Rural Maine Counties: Evaluating the Impact of Birthing Unit Closures and Solutions

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Introduction: Birthing unit closures are becoming an increasingly common occurrence across both the United States and the State of Maine. Closures are disproportionately occurring in rural counties, leaving gaps in access to birthing care. It is well documented that increasing distances to birthing care increases the risk of adverse maternal health outcomes, which is why it is imperative to address declining access to care. Since 2008, Maine has closed 9 hospital birthing units, 5 being in rural counties. This leaves 21 hospitals in Maine with birthing units, 16 of which reside in rural counties. The common reason for closure has been cited as declining birth rates and limited obstetric providers. It is imperative that solutions are addressed to prevent worsening rural maternal healthcare access.

Methods: HRSA data provided information about the ratio of Ob/Gyn to Family Medicine providers by population. Pre-existing public ArcGIS data provided geographic data that displayed the raw distance to a birthing hospital from a given location. These data points were plotted from vital statistics birthing records. For better analysis, distances were subsequently averaged by county and grouped by urban or rural according to RUCC and county characteristics.

Results: Birthing individuals in rural Maine counties travel 12.27±4.03 miles on average to reach a birthing unit and birthing individuals in urban Maine counties travel 6.47±1.32 miles on average to reach a birthing unit. Washington County had the farthest distance at 19.60±10.62 miles. Androscoggin County traveled the shortest distance at 5.00±4.43 miles. The rate of Ob/Gyn to Family Medicine physicians per 100,000 people in a given county is significantly lower statewide, but displays wider gaps in rural versus urban counties.

Conclusions and Recommendations: The need for accessible perinatal care in Maine is increasing as both birthing units close and the population increases. Maine has limited programs in place to support the training of new obstetric providers, with no notable changes being made to the GME system or rural practice incentive system to expand training and education of new providers to help fill the gap. In similar states, data in the years following rural unit closures suggests that there are increased instances of poor maternal health outcomes. To combat this, Maine must enact policies that will prevent further closures and create more robust practice incentives in rural counties.

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Lumbar spinal cord expression of Tollip and pIRAK1 in iTat mice, a model of HIV-associated peripheral neuropathy

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Introduction: HIV-associated peripheral neuropathy (HIV-PN) is a common complication of HIV infection. The HIV trans-activator of transcription (Tat) is a critical regulator for viral replication. Previously, we have shown Tat-induced HIV-PN-like behaviors using doxycycline inducible HIV-1 Tat transgenic (iTat) mice. RNA profiling analysis of iTat lumbar spinal cords (LSC) suggested potential involvement of Toll-like receptor (TLR) pathway in Tat-induced HIV-PN. One of the identified associated genes was Toll-interacting protein (Tollip). Tollip negatively regulates the MyD88-dependent TLR pathway by inhibiting interleukin-1 receptor associated kinase (IRAK1). In this study, we examined the expression of Tollip and the activated IRAK1, phosphorylated-IRAK1 (pIRAK1), at the protein level via immunohistochemistry (IHC). We hypothesized that Tat induction promotes an increase in LSC Tollip expression, which subsequently negatively regulates LSC pIRAK1 expression.

Methods: Adult iTat mice (8 weeks old) were intraperitoneally (i.p.) injected daily with doxycycline hyclate (Dox) from days 0-13. LSCs were collected on day 0 (naïve), 3, 7, 14, 21, 28, and 35 post-Dox injection for IHC analysis (3 mice/sex/time). LSC sections (14 μm) were sequentially stained with two sets of primary and secondary antibodies as follows: rabbit-anti-Tollip (1:1000) and donkey anti-rabbit-AlexaFluor488 (1:1000) followed by rabbit anti-pIRAK1 (1:500) and donkey anti-rabbit-AlexaFluor647 (1:1000). All sections were imaged with the Keyence BZ-X710 inverted widefield digital microscope and images were analyzed via ImageJ software. Image analysis is ongoing. The numbers of Tollip+ and pIRAK1+ cells were obtained and preliminary analysis was performed.

Results: Initial ANOVAs on Tollip+, pIRAK1+, and Tollip+/pIRAK1+ cell counts were conducted respectively via IBM SPSS with time and sex as major factors. No sex differences were detected so far. A significant time effect was observed for Tollip+ cell counts ($p=0.026$, power=0.809) which peaked at day 14. While both pIRAK1+, and Tollip+/pIRAK1+ cell counts also peaked at day 14, no statistical significances were observed.

Conclusion: The changes in LSC Tollip+ cell counts seem to be consistent with previously observed changes in Tollip RNA expression. Potential downstream regulation on IRAK1 by Tollip at cellular level needs further examination. This will help further investigate the role of Tollip-mediated pathways in Tat-induced HIV-PN.

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End-of-Life Care in a Cardiac Sarcoidosis Patient with a Left Ventricular Assist Device: A Case Report

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Introduction: Cardiac sarcoidosis (CS) is an infiltrative cardiomyopathy resulting from granulomatous inflammation of cardiac myocytes. CS will progress to end-stage advanced heart failure (AHF) in a small subset of patients. The inflammation results in dysfunction of the heart wall, such as dilation, scarring, valvular pathologies, and reduced ventricular compliance. The placement of a Left Ventricular Assist Device (LVAD) is utilized as a bridge to transplantation or as destination therapy, with an average life expectancy of five years. End-of-life (EoL) care in a patient with AHF with an LVAD placement has complex needs and requires communication and an interprofessional approach that is unique in the hospice setting.

Case: A 75-year-old male diagnosed with CS progressed to AHF stage D ischemic cardiomyopathy. The patient was implanted with a HeartMate II LVAD for ten years. The patient was admitted to the ICU in December 2023 due to a GI hemorrhage secondary to treatment of LVAD pump thrombosis with tPA. Treatment options for pump thrombosis were exhausted, leading to the transition to EoL and home hospice care. Discussions on preferences and wishes for EoL care with the patient and power of attorney (spouse) were met with curiosity and attentiveness. These included curative treatment as tolerated to assist with symptomatic treatment for pain, management of anxiety and dyspnea, and fulfilled wishes allowing consumption of an alcoholic beverage, one-time cigar use, and the support of loved ones and staff. The dynamics of LVAD decommission were addressed through a caregiver-centered approach provided by healthcare professionals, a chaplain, and a social worker. In June 2024, after transitioning from the hospital to an acute care hospice house for three weeks, the patient was decommissioned from their LVAD and died peacefully at hospice in the presence of his loved ones.

Discussion: This case report describes the vitality of effective communication and interprofessional collaboration in optimal EoL care. Unique EoL care for patients with LVAD placement may be made after careful discussion involving the patient and their caregiver, the hospice staff, and the cardiac LVAD team. Personalized physical and psychosocial symptom management for patients with AHF stage D ischemic cardiomyopathy needs to be efficiently addressed. Further research is necessary to understand meeting preferences and wishes of AHF secondary to CS patients with LVAD at the EoL.

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Multidisciplinary Perceptions of Implementation and Sustainability of the Healthy Weight Clinic

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Introduction: In the United States, over 14 million children and adolescents have obesity. The Healthy Weight Clinic (HWC) is a CDC-recognized Family Healthy Weight Program (FHWP) consistent with AAP guidelines for children and adolescents with overweight or obesity.

Methods: This qualitative study evaluates HWC implementation through directed content analysis. Interviews were conducted with multidisciplinary clinic teams following the implementation in 2 health centers in Mississippi (MS) and 2 in Massachusetts (MA) to inform modifications to the HWC implementation package's resources, training, and technical assistance to promote sustainability and dissemination to other clinics nationally. Interview guides were informed by the Consolidated Framework for Implementation Research (CFIR).

Results: Participants (*n*=21) included 8 Pediatricians, 3 Registered Dietitians, 3 Community Health Workers, and 7 Clinic Leadership roles. Perspectives include health center personnel who implemented the HWC in a MS Federally Qualified Health Center (FQHC) (29%), a MA FQHC (24%), and a MA Academic Site (48%). The following themes (and associated CFIR construct) were perceived key factors for effective implementation and sustainability of the HWC: Clearly defined staff roles and readiness for implementation (*Individuals*); A formal standalone clinic structure with administrative support *(Inner setting)*; Flexibility including COVID-19 adaptations, telehealth, hiring, and reimbursement (*Outer setting)*; Dedicated time for provider training and discussion (*Reflecting & Evaluating, Implementation Process)*; A comprehensive HWC Curriculum Guide that is sensitive to equity, inclusion, and belonging *(Relative Advantage, Innovation Adaptability).*

Conclusions: Findings highlight the perceived key factors influencing implementation and sustainability of the HWC and inform future packaging of multidisciplinary training and materials, adoption, and spread of evidence-based FHWPs in the US.

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Gender Difference in Orthostatic Hypotension Test Outcomes: Implications of a Male-Derived Scale

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Introduction: Autonomic dysfunction following concussion often manifests as abnormal heart rate and blood pressure regulation. Research indicates that females are more prone to post-concussion autonomic dysfunction, resulting in extended recovery times. However, many diagnostic scales are based on male data, potentially overlooking key physiological differences between genders. The Sport Concussion Office Assessment Tool (SCOAT6), developed by the Concussion in Sport Group expert panel, is a widely used tool for concussion assessment. This study investigates gender-based failure rates in the orthostatic hypotension test among non-concussed individuals. We hypothesize that diagnostic scales derived primarily from male data may lead to higher failure rates for females, reflecting a gender bias in these diagnostic tools.

Methods: Data was collected from 53 participants (aged 18-25) with no concussion in the past 6 months. Participants attended two sessions, one week apart, completing demographic questionnaires and the SCOAT6, which included orthostatic blood pressure and heart rate assessments. They laid down for at least 2 minutes for baseline measurements, then stood for 1 minute, after which measurements were repeated. Participants were asked about symptoms such as dizziness, light-headedness, fainting, blurred vision, nausea, fatigue, or lack of concentration during both phases. The orthostatic test had five failure criteria: 1) systolic decrease of ≥20 mmHg, 2) diastolic decrease of ≥10 mmHg, 3) any heart rate decrease, 4) heart rate increase of ≥30 beats per minute, or 5) reporting any symptoms. Data were analyzed using chi-square and logistic regression to assess failure rates by gender.

Results: A higher proportion of females (63.6%) failed at least one criterion of the orthostatic test compared to males (36.4%). Although this difference was not statistically significant, descriptive data suggest a trend of higher failure rates among females. Logistic regression results showed that females are 1.81 times more likely to fail the test compared to males ($p=0.33$).

Conclusion: The higher failure rate in females suggests that the SCOAT6 test may not fully account for female-specific physiological differences, potentially reflecting a male-centric bias. Given this disparity, future research should focus on developing gender-sensitive diagnostic tools for orthostatic hypotension to improve diagnostic accuracy in concussion assessments.

Utilizing Machine Learning for the Recognition of Behavior Patterns of Chronic Pain in Mouse Models

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Introduction. Chronic pain is the primary reason for patients to seek medical care and has a higher socioeconomic burden than cancer, cardiovascular disease, and diabetes combined. Chronic pain is poorly treated leading to greatly diminished quality of life in chronic pain patients. Mechanisms underlying chronic pain are still poorly understood, and improved unbiased measures are needed to further our understanding. DeepLabCut is a machine learning tool that utilizes 2D and 3D markerless pose estimation based on transfer learning with deep neural networks. This allows for unbiased automated analyses that improves reproducibility and limits potential experimental errors that can occur due to human bias. Using DeepLabCut, we examined behavioral changes in hindpaw posture across 2 mouse models of chronic pain, cancer-induced bone pain and neuropathic pain.

Methods. Video captured from under the mice for analysis the posture of the injured hindlimb. DeepLabCut analysis of the videos was performed to determine changes in hindpaw postures in mouse models of cancer-induced bone pain or spared nerve injury of the sciatic nerve (SNI). Analysis of variance (ANOVA) was used to compare changes in hindpaw posture in mice with cancer-induced bone pain, SNI and their surgical sham controls. All groups were compared to naïve to determine potential of sham surgery-induced changes.

Results. In both models, distance between the hindpaw center and end of the thumb and between the hindpaw center and end of the 5^{th} finger shortened in the ipsilateral hindpaw compared to contralateral paw, shams, and naïve hindpaws. Distance between the hindpaw center and end of the middle finger shortened in cancer, but not SNI treated mice. Shortened angles were also observed for the thumb - hindpaw center - 5^{th} finger in both SNI and cancer treated mice. These observations suggest contraction of the ipsilateral hindpaw in both models.

Conclusions. Our data indicate that mice with chronic pain contract the hindpaw. This may serve as a novel and accessible measure of ongoing pain. However, further validation is required prior to general use to verify that postural changes are specific to pain and not to other potential factors such as loss of motor control. These advances in machine learning will allow for an accessible, unbiased, and powerful analytical tools to explore mechanisms underlying and screen for potential therapeutics to better manage cancer-induced bone pain.

IACUC protocol 04121-099

Chemotherapy Regimens Impact CD4⁺ T cells and Nerve Loss in Peripheral Tissue in Chemotherapy-Induced Peripheral Neuropathy

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Introduction: Chemotherapy is a life-saving cancer treatment, but the development of chemotherapy-induced peripheral neuropathy (CIPN) is a major dose-limiting toxicity. We have shown that paclitaxel (PTX) promotes anti-inflammatory CD4⁺ T cells (IL-10, IL-4, FoxP3) in the DRG more robustly in estrogen-competent female mice compared to ovariectomized and male mice. In addition to the DRG, CD4⁺ T cells may act in peripheral tissue as IL-4 and IL-10 have been shown to promote nerve regeneration. Although the relationship between CIPN and nerve loss is unclear, nerve loss is positively correlated with higher cumulative doses and is often more pronounced in areas of greatest pain. The clinical presentation of CIPN may be similar, but the mechanism driving the development/resolution seem dependent on hormones and the immune microenvironment. Understanding these complex relationships will better facilitate the development of targeted immunotherapies to treat CIPN. In this study, we sought to determine the extent to which chemotherapy regimens modulate CD4⁺ T cells in the DRG/skin and nerve loss/regeneration in peripheral tissue.

Methods: Male and female C57BL6/J mice were administered PTX at 6 mg/kg on day 0 (HD) or 2 mg/kg on days 0, 2, 4, and 6 (LD). Von Frey was used to assess hypersensitivity, flow cytometry to characterize CD4+ T cells in the DRG, and immunohistochemistry to quantify nerve loss/CD4+ T cells in hind paw tissue.

Results: There was no difference in PTX-induced mechanical hypersensitivity with HD and LD regimens in male or female mice. However, each regimen promoted distinct CD4⁺ T cells in the DRG. HD in females induced IL-10, IL-4, and FoxP3 CD4⁺ T cells at d14 whereas LD induced LAP at d14. HD in males induced LAP at d3 and d7 and IL-4 at d14 whereas LD induced FoxP3 and IL-10 at d7. Female and male mice that received HD were mechanically hypersensitive but had minimal nerve loss in the hind paw at d7 and d14. In contrast, the LD regimen resulted in significantly more nerve loss even though behaviorally the LD and HD mice were similar.

Conclusions: Although there was no difference in PTX-induced hypersensitivity with the HD and LD regimens, there were distinct differences in the types of CD4⁺ T cells in the DRG and nerve loss in the peripheral tissue, suggesting that dosing induces specific responses in a sex-dependent manner. By identifying the mechanisms driving CIPN, we can develop targeted therapies better suited for each individual.

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Cell Signaling in Sensory Neurons

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Introduction: Since 1999, the world has been fighting an opioid epidemic. Prior research on non-addictive alternatives has shown that mitochondrial uncoupling drugs such as 2,4-dinitrophenol and BAM15 have analgesic effects in opioid-induced hyperalgesia in rodents. To determine whether these signaling channels are expressed in humans, we tested immunohistochemical (IHC) stained mouse pain models in isolated dorsal root ganglion (DRG) neurons and human DRG-derived cells (HD10.6). The channel we tested was Nuak1, a kinase related to AMPK that has not been investigated. It is activated by LKB1, a kinase that acts as a master stress sensor and activates AMPK and metabolic pathways that conserve energy in response to stress.

Methods: Cells obtained from HD10.6 DRGs were incubated and stimulated with BAM15 for 10 minutes and fixed in paraformaldehyde (PFA) for 15 minutes. Control HD10.6 cells and injury-model mouse lumbar DRGs were not stimulated with BAM15 and only fixed in PFA. The cells were stained via IHC with Nuak1 diluted 1:250 and TRPV1 diluted 1:1,000 and sat covered overnight. Secondary antibodies were added after 24 hours and the slides were mounted with 4’,6-diamidino-2-phenylindole (DAPI) to be visualized under the microscope.

Results: In the HD10.6 cells, the BAM15-stimulated and control cells demonstrated positive Nuak1 labeling with equal intensity and projections branching off the axons indicating potential subcellular structures. We realized the TRPV1 antibody selected only recognizes mouse cells, so the HD10.6 cells did not show positive TRPV1 labeling. In the mouse DRG cells, there was positive Nuak1 labeling in the TRPV1-labeled neurons.

Conclusion: Nuak1 is a novel kinase channel that has not been previously studied in sensory neurons. We have found that Nuak1 is enriched in nociceptive sensory neurons in both mouse and human cell lines, and likely their nociceptors. Because Nuak1 is part of the AMPK family, as is Metformin, a drug used as an AMPK activator for years, we think Nuak1 may have closely related functions that have not yet been investigated. One limitation of our study was that we could not determine if the HD10.6 Nuak1 staining correlated 100% with the TRPV1-labeled neurons. This can be addressed by using a guinea pig anti-TRPV1. The importance of using human cell lines in pain signaling pathway modeling was a critical step toward developing a highly novel non-addictive analgesic agent for humans.

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Tollip and Cytokine Expression Profile in Doxycycline-Induced Transgenic Tat Mice: A Model of HIV-Associated Peripheral Neuropathy (HIV-PN)

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Introduction: Using doxycycline-inducible HIV-1 Tat transgenic (iTat) mice, it has been observed that the protein Tat, trans-activator of transcription, contributes to the development of HIV-PN, though the mechanism is unknown. The Toll-like receptor (TLR) pathway is a known contributor to neuropathic pain, and the Tollip protein is a key regulator of the TLR pathway. Tollip has been shown to be upregulated in Tat-induced iTat mice. To investigate the underlying mechanism of Tat-induced HIV-PN, we examined the expression of Tollip and TLR downstream cytokines at the protein level via ELISA and multiplex assay respectively. Cytokine profiling may help us to elucidate the involvement of TLR downstream signaling pathways.

Methods: iTat mice (2-4 months old, 3/sex/treatment/time point) received daily intraperitoneal injections of doxycycline hyclate (DOX) at 100mg/kg in sterile phosphate-buffered saline (PBS) or pH-matched (pH=3) PBS (from day 0-13). Lumbar spinal cord (LSC) tissue segments were collected on days 0, 3, 7, 14, 21, 28, and 35 following trans-cardiac perfusion. LSC tissue lysate was prepared and total protein content was quantified via BCA assay. Tollip protein expression was measured using Aviva® Tollip ELISA Kit and cytokine (TNF-α, IL-1β, IL-10, IL-6, IL-12p70, CXCL1, CXCL10, CCL3, CCL4, CCL5, IFN-α, and IFN-β) expression was determined via ProcartaPlex® Immunoassay. All data are expressed in pg/mg protein. ANOVA analyses on Tollip and cytokine data are on-going via IBM SPSS v27. Treatment, Sex, and Day are used as main factors. Preliminary results are shown.

Results: There were no significant differences in LSC total Tollip expression across all groups. ProcartaPlex data has been collected and data analysis is ongoing, though preliminary analysis showed transiently increased expression of most cytokines in female, but not male, Tat-induced iTat mice on day 14 compared to PBS mice.

Conclusion: The expression of total Tollip protein appears stable regardless of Tat induction, which is different from the observed changes in Tollip RNA. Cell-specific Tollip expression is under investigation. Potential sex-dependent changes in cytokine expression may contribute to the previously observed sex-dependent differences on neuropathy-like behaviors.

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Assessing Composition of Gut Microbiota in Patients with Chronic Pancreatitis and Exocrine Pancreatic Insufficiency

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Introduction

A healthy gut flora is largely responsible for maintaining overall health due to its vital role in regulating the function of the immune system and homeostasis. When dysbiosis occurs, development of chronic conditions, such as chronic pancreatitis, will become more likely. Due to a limited understanding of the relationship between the gut microbiome and pancreatic diseases, the aim of this study is to analyze the composition of the gut microbiome in patients with chronic pancreatitis (CP) and exocrine pancreatic insufficiency (EPI) to establish a more thorough understanding of the gut microbiome in this population.

Methods

Stool samples from 46 CP or EPI patients were collected. Bacterial DNA was extracted from fecal samples using a Qiagen DNeasy PowerSoil HTP extraction kit. Golay barcode primers 515 F and 806 R were used for 16S rRNA gene sequencing. Alpha and beta diversity were analyzed using Quantitative Insights Into Microbial Ecology (QIIME) 2 2020.11. Comparison of within-sample diversity (alpha diversity) was performed using Faith's phylogenetic diversity (Faith's PD) and comparison of between-sample diversity, i.e. community composition (beta diversity), was performed using unweighted UniFrac.

Results

The most abundant taxa in CP and EPI patients were Bacteroides, Firmicutes, and Actinobacteria. Facultative pathogenic organisms Streptococcus, Escherichia-Shigella, and other Enterobacteriaceae had relatively high frequencies within this population. Alpha diversity was significantly lower in females ($p=0.0301$), in participants with no alcohol consumption ($p=0.0104$), and in participants with GI diarrheal infections in the last 3 months ($p=0.0333$). No association was found between alpha diversity and use of probiotics or pancrelipase medications.

Conclusion

The high relative abundances of pathogenic bacteria, particularly phylum Proteobacteria, may suggest a correlation between the overgrowth of such bacteria and pancreatic conditions. With other studies supporting this relationship, the abundance of bacterial species could serve as diagnostic markers due to their correlation with intestinal dysbiosis and risk of disease. Furthermore, differences observed in factors such as gender and alcohol use may warrant further exploration to determine their impact on gut biodiversity in CP and EPI patients. This would be beneficial in the refinement of strategies for managing these conditions through targeting of pathogenic gut microorganisms.

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Cooper Medical School of Rowan University, Department of Biomedical Sciences, and Cooper University Hospital, Department of Gastroenterology, Camden, New Jersey

Ethics Approval

Approval was obtained by our tertiary care center's Institutional Review Board (IRB) to conduct this study (IRB number 20-427). As procedures in this study involved human participants, all steps were performed in accordance with the ethical standard of the institutional research committee and with the 1964 Helsinki Declaration and its later ethical standards.

Butterflies in the Field: Introducing POCUS to Paramedics in a Rural Emergency Medical Services and Wilderness Environment

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Introduction
Point of care ultrasound (POCUS) may help paramedics navigate wilderness and rural (WR) environments by providing objective visual data in the field. Evidence suggests training paramedics in prehospital POCUS is effective, but most research has focused on implementation in urban settings. We assessed the use of POCUS in WR Emergency Medical Services (EMS) by strategically training paramedics to perform the extended focused assessment with sonography for trauma (eFAST) and cardiac termination of resuscitation (TOR) exams using tailored clinical questions relevant to their practice location.

Methods
Paramedics from a National Park Service unit and local Fire/EMS agency were trained using online modules and a 1-day course with supervised image acquisition practice. Knowledge acquisition was assessed using pre/post intervention knowledge tests. Knowledge, attitudes, and practice (KAP) towards prehospital POCUS were assessed using pre/post training surveys. The impact of scans on transport/medical decision making was assessed using hand off surveys completed at patient hand off between participants and the receiving physician or air ambulance team. Results were assessed for common themes and analyzed using descriptive statistics and paired/unpaired t-test with p values <0.05 considered significant.

Results
Participants' (n=23) knowledge of POCUS increased by 33% based on pre/post training knowledge tests (52% ± 3.2 to 69% ± 1.5, $p<0.0001$). The pre(n=24)/post(n=21) training KAP survey results did not significantly change, although the average level of agreement (rated 1-5) to questions regarding the perceived usefulness of POCUS in the prehospital setting increased slightly (3.7 ± 0.18 to 3.8 ± 0.15). Data collection for the hand off surveys is ongoing.

Conclusion
Paramedics in WR settings were capable of learning eFAST and TOR ultrasound protocols. While analysis of KAP survey responses was complicated by attrition between pre/post training responses, participants generally endorsed pre-hospital POCUS as a useful tool with the potential to improve their practice. These results suggest that pre-hospital POCUS can be implemented in WR settings and that paramedics working in these settings believe it has the potential to improve patient care. Further research should seek to increase the number of participating agencies to expand the sample size and analyze patient outcome data.

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Artificial Intelligence: A Tool for Augmenting Labor and Delivery Management

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Introduction

Artificial intelligence (AI) is increasingly integral to modern life, using algorithms to integrate imaging, vitals, and other data for enhanced decision-making. In medicine, AI improves patient outcomes by predicting risks, managing intraoperative devices, and monitoring to reduce pain and optimize results (Solanki et al., 2021). Expanding AI use in obstetrics should enhance decision-making, reduce maternal-fetal morbidity and mortality, and prevent postpartum complications. This abstract focuses on AI's current role in managing patient pain and minimizing complications during labor and delivery(L&D).

Methods

A systematic review of peer-reviewed articles published between 2019 and 2024 is presented, focusing on AI's role in labor and delivery management.

Results

Data suggest that AI integration in L&D management enhances decision-making, risk evaluation, and outcome prediction. Machine learning alerts clinicians to early signs of cardiac issues in pregnant patients (Meng & Arent, 2021). Deep learning, a subtype of AI, can compare multiple parameters simultaneously, especially in early pregnancy, to improve prediction accuracy of preterm labor (Singh et al., 2019).

AI enhances ultrasound-guided injections by aiding in obtaining more precise images for regional and neuraxial anesthesia (Bowness et al., 2022; Compagne et al., 2022). Lim (2023) showed that AI improves predictive models for stillbirth and neonatal mortality by integrating post-delivery variables with prenatal data. AI systems also reduce postoperative pain scores by optimizing pain management during surgery (Solanki et al., 2021). Pilot studies indicate that AI-assisted patient-controlled analgesia systems can overcome limitations in pain management by analyzing real-time patient data, including physiological parameters and historical pain management data, for more precise and personalized medication adjustments (Wang et al., 2020).

Conclusion

The multifaceted role of AI in labor and delivery care can reduce human error, enhance predictive accuracy, and improve patient outcomes. By integrating AI with clinical judgment, obstetricians can provide safer and more efficient care. These data support of the need for ongoing research and collaboration between AI specialists and healthcare professionals to fully realize the potential of AI in enhancing optimal labor and delivery outcomes.

Acknowledgment

The University of New England College of Osteopathic Medicine and Rutgers Robert Wood Johnson Medical School

Effect of Antimicrobial Peptides on the Antibiotic-Mediated Killing of Bacterial Biofilms

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Introduction: *Staphylococcus aureus* is a common drug-resistant nosocomial and community-acquired infection. During bacterial biofilm formation, bacterial colonies secrete a slimy, polysaccharide matrix, which becomes crucial to their virulence. Biofilms can form on host tissue or medical equipment like catheters or hip replacements. One strategy for overcoming drug resistance is to use antimicrobial adjuvants, compounds that can help improve antibiotic function. Antimicrobial peptides (AMPs) are an adjuvant and are produced by immune cells to weaken antigens and are thought to have biofilm-permeating properties. Here, we tested AMPs, on the susceptibility of biofilm-resident *S. aureus* USA300 to the antibiotic linezolid. We hypothesized that biofilm susceptibility would increase when treated simultaneously with sublethal doses of antimicrobial peptides and antibiotics.

Methods: *S. aureus* USA300 was used in biofilm viability assays where 24-hour mature biofilms were treated with the antibiotic linezolid in the presence or absence of sublethal doses of individual synthetic AMPs (DIK-8, IDR-1018, WR-12, RI-10). The biofilms were incubated for 48 hours at 37°C before being plated and incubated for another 24 hours at 37°C. Individual colonies were analyzed to measure the effect of each treatment. *S. aureus* USA300 was used in biofilm integrity assays where 48-hour treated biofilms from the viability assays were stained with crystal violet. The stained biofilms were photographed and absorbance was read using a spectrophotometer at 595 nm.

Results: We observed overall greater bacterial killing when established biofilms were treated with the combination of linezolid and a sublethal AMP concentration compared to linezolid alone treatment. There was a significant decrease in the *S. aureus* viability of biofilm-resident bacteria when treated with AMP IDR-1018 (4 ug/mL) with linezolid compared to percent of linezolid alone. No significant differences existed between all groups of AMP treatment and percent linezolid alone for biofilm integrity.

Conclusions: All synthetic AMPs reduced the viability of biofilm resident bacteria in conjunction with linezolid, but only had minimal effect on biofilm structural integrity. This suggests that AMPs play a role in cell death but not in the degradation of the biofilm itself. Further research could study the effect of AMPs using antibiotics of different classes on mature biofilms and testing bacterial resistance to the AMP itself.

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Non-Obese, High-Fat Diet Fed Mice Have Improved Metabolic and Bone Phenotypes Compared to Obese, High-Fat Diet Fed Mice

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Introduction: Prior studies showed C57BL/6J (B6) mice fed a high-fat diet (HFD) have high variation in body composition, despite genetic homogeneity. However, our understanding of this heterogeneity is still limited. Thus, we sought to investigate if the variation in body composition resulted in different metabolic and bone phenotypes in HFD-fed mice.

Methods: At 8 weeks old, B6 mice were fed a HFD (60% kcal fat) or sucrose-matched low-fat diet (LFD; 10% kcal fat) for 12 weeks. Body parameters were used to classify obese, HFD (ObHFD) mice (males: >58% weight increase and >3.3 fold increase in fat mass; female: >38% weight increase and >1.2 fold increase in fat mass). Mice that did not meet these parameters were classified as non-obese, HFD-fed (NObHFD). Body and metabolic phenotyping were measured using NMR, glucose and insulin tolerance testing, and serum ELISAs. Tibial trabecular bone volume was measured through μCT.

Results: Serum leptin levels were decreased in NObHFD mice compared to ObHFD (male: $p=0.0117$; female: $p=0.0001$), which demonstrates NObHFD mice have improved leptin sensitivity, a key regulator for body weight. The average serum adiponectin levels were higher in male NObHFD compared ObHFD (11.6 and 10.5μg/mL). Since lower adiponectin levels are associated with insulin resistance, these results support our findings of better glucose handling and insulin sensitivity in NObHFD mice. Female NObHFD mice showed improved glucose handling, but overall females did not demonstrate insulin resistance like we observed in male ObHFD mice. Previous studies have suggested females have better preservation of pancreatic β-cells, which may explain their protection against insulin resistance. Tibial μCT results revealed ObHFD male and female mice had lower trabecular bone volume compared to LFD ($p<0.0001$ and $p=0.0101$). Male NObHFD showed a significant increase in trabecular bone volume compared to ObHFD ($p=0.0044$) and no difference compared to LFD mice. Both male and female NObHFD mice showed decreased serum levels of the osteoclast activity marker, TRAcP 5b compared to ObHFD. These result suggest NObHFD mice have less bone resorption occurring which supports our findings of improved trabecular bone.

Conclusions: NObHFD mice showed improved glucose handling and less osteoclast activity resulting in better trabecular bone volume. Given these results we believe obesity, but not the high-fat diet, is associated with worsened metabolic and bone phenotypes.

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Geriatrics Education Mentor (GEM) Program: Outcomes from Pairing Students and Older Adults During Medical School

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Introduction: Currently, only 15% of medical schools have mentor programs that educate students to work with older adults and their health. The University of New England College of Osteopathic Medicine Geriatrics Education Mentor (GEM) program is an experiential education component within the 1st and 2nd year curriculum whereby students and older adults are paired to conduct five “home-visit” GEM assignments. A pre/post survey design assessed students’ competence and confidence with older people (assigned GEMs).

Methods: The survey was emailed to first-year medical students before they began GEMs and was sent again upon completion of the program at the end of their second year. This process was carried out through academic years 2020-2021 through 2023-2024 with an average of 174 first-year students per class, and this data was analyzed in RStudio. Results had a 26% response rate that included overall data (N= 133/Pre & N=138/ post), 24 responses were matched assessments.

Results: No significant change in students' interest ($p > 0.4$), perceived readiness and competence ($p > 0.07$), or confidence in working with older adults ($p > 0.5$) was revealed. However, perceived readiness and confidence increased from pre- to post-test, indicating that a larger sample size might reveal significance. Self-reported knowledge of older adult healthcare needs increased, pre- to post-test, with the paired subset showing a significant increase ($p<0.015$).

Conclusion: Although a small sample, these findings provide a foundation for medical schools to consider implementing a mentor type program to augment medical student skill/knowledge in older adult health care to advance age-friendly health care. Future research should address these limitations by using larger samples and incorporating objective measures of knowledge and competence.

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APC I1307K Homozygosity And Colorectal Cancer Risk: A Review Of The Literature

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APC I1307K, a founder mutation in the Ashkenazi Jewish population, is a commonly identified pathogenic variant for colorectal cancer. The mutation is associated with a twofold increase in colorectal cancer risk among heterozygotes, with large numbers of cases having been identified. The risk among homozygotes, who are estimated to be 0.14% of total cases, and sparsely mentioned in the literature, is currently unknown, with the largest group mentioned in the literature being just 13 cases. Performing a review of the literature using PubMed and general internet searches for mentions of *APC* I1307K homozygotes, we aimed to identify more cases, and to investigate the risk of colorectal cancer. Inclusion criteria included any publication that had confirmed cases of homozygosity through genetic testing, and any analysis of the cases or discrete mention of them. Results showed 9 publications, ranging from published papers of community studies and case reports and a position paper, to abstracts and poster presentations from genetics companies of indexed, confirmed cases with analysis. The total number of homozygotes identified was 43. The largest group found was through a community study and subsequent mouse model paired with statistical testing of over 6000 patients, revealing 16 cases. This same study found that there is a dose-response effect observed in homozygous carriers in humans. The second largest cohort identified 14 cases and concluded that *APC* I1307K homozygotes appear to be at an increased risk of colorectal cancer, similar to heterozygotes. Specific phenotypes in this cohort also referenced other publications with similar results, particularly desmoid tumors, with two discrete cases found in the literature. Another publication found that homozygous carriers of the mutation were at an especially high risk of colorectal cancer, as shown by their statistical analysis. Multiple publications were identified that made discrete mentions of the homozygotes but offered no further analysis beyond the current state of the literature. While being one of the most common pathogenic variants, *APC* I1307K is also an actionable mutation that has been shown to confer an increased risk of colorectal cancer in both heterozygous and homozygous populations. With such little data in the literature, more work must be done to identify more homozygote cases and provide more definitive risk analysis for this population. Such data and risk analysis can help guide clinical guidelines, and give peace of mind to patients with this rare mutation.

Differences in Synovial Growth Factor and Immune Cells Between Sexes Contributing to Pain

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Introduction: Osteoarthritis (OA) is a degenerative joint disease-causing severe pain and disability. Due to heterogeneity and complexity of OA pain, targeted treatments are lacking. Most common pain descriptions are mid-stage OA characterized by activity-related pain that dissipates with rest, and advanced OA pain described as development of a constant pain that does not dissipate with rest. Research shows females report more severe advanced OA pain than males despite similar pathology. We propose that differences in immune cell infiltration and associated cytokines and growth factors within the synovial fluid underlie these differences in joint pain. Vascular Endothelial Growth Factor (VEGF) is a growth factor released by macrophages that promotes angiogenesis and contributes to inflammation and pain. We examined the hypothesize that females demonstrate increased levels of immune cells and elevated VEGF-A in the synovial fluid compared to males treated with 16 mg/ml monosodium iodoacetate (MIA), a concentration that produced advanced OA pain in females and mid-stage OA pain in males.

Methods: We induced mid-stage OA in males and advanced-stage OA in females using 16 mg/mL MIA injections. Synovial fluid samples were collected and analyzed with Flow Cytometry to detect immune cell types and by ELISA to measure VEGF levels. Statistical analysis was run using 2-way ANOVA with appropriate post-hoc analyses.

Results: Females treated with 16 mg/ml MIA develop constant joint pain and weight asymmetry indicating advanced OA pain whereas males show weight asymmetry in the absence of constant joint pain indicating mid-stage OA pain. Synovial fluid of females treated with 16 mg/ml MIA showed elevated macrophage and B-cells than controls or males treated with 16 mg/ml MIA. No changes in T-cells, neutrophils, or NK cells were observed. Elevated VEGF-A was observed in the synovial fluid of females but not males treated with 16 mg/ml.

Conclusions: These data indicate elevated levels of macrophages, B-cells and VEGF-A in females but not males treated with 16 mg/ml MIA. This corresponds to sex differences in pain phenotypes, with females showing advanced OA pain whereas males show mid-stage OA pain in response to joint injection of 16 mg/ml MIA.

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Frailty and Adversе Events in Veterans with Newly Diagnosed Multiple Myeloma Initiating Treatment

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Introduction: Cancer-focused guidelines for treatment now recommend geriatric and frailty assessments for older adults with cancer. However, implementation in Multiple Myeloma (MM) has been limited, and the number and nature of adverse events in frail patients is understudied. Here we present our preliminary analysis evaluating the association between frailty and adverse events in U.S. Veterans with newly diagnosed and treated MM.
Methods: We identified in the national VA database (Corporate Data Warehouse) all Veterans initiating treatment for MM with Velcade, Revlimid, and Dexamethasone (VRd)—a standard regimen used for initial MM treatment. Hospital discharge summaries associated with unplanned hospitalizations in the year following the date of treatment initiation were pulled from 2010 to 2023 Content analysis was performed on the clinician documentation in these discharge summaries and associated ICD-9/10 billing codes, coding adverse events according to National Cancer Institutes (NCI's) Common Terminology Criteria for Adverse events V5 and further into categories of (1) MM (2) MM treatment, (3) a non-oncologic condition or (4) an interaction between a nononcologic condition and MM or MM treatment (infection, kidney injury and pain etc.). Poisson regression was used to assess the association of frailty, measured electronically via the VA-frailty index (VA-FI), with the number and etiology of adverse events experienced by Veterans.

Results: We performed content analysis on 159 discharge summaries from unplanned hospitalizations in 250 Veterans with NDMM in the year after initiating treatment with VRd. With 532 total adverse events, rail Veterans (VA-FI ≥ 0.2) experienced substantially more adverse events in the year after starting treatment compared to non-frail Veterans (297 adverse events, 95% Confidence Interval [CI] 264-333) vs. 235 events, 95% CI, 206-267).
Nearly half (130 events, 43.8%) of adverse events in frail Veterans were related to nononcologic conditions or interactions between nononcologic and MM-specific factors, a significantly higher amount compared to nonfrail patients (70 events, 95% CI 55-88).

Conclusion: Preliminary data suggests frail Veterans are at greater risk of adverse events, and this increased risk is mediated by the nononcologic conditions. These adverse events confer a higher risk of unplanned hospitalizations and death through different mechanisms that is not addressed through prescribing the MM treatments alone.

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Research was conducted remotely through the VA network. Jamaica Plains VA hospital was used as a location for background checks and fingerprinting.

IRB Approval: IRB was approved by the VA R&D Committee chair or designee on June 19, 2024. This was then accepted by UNECOM as proof of IRB approval.
IRBnet#1578039

Irisin Deficiency Impairs Weight Maintenance with Voluntary Wheel Running in Mice

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Introduction: Irisin, a hormone released from muscle during exercise, impacts tissues from fat to brain to bone. Elevated irisin via forced FNDC5 expression in mice enhances thermogenesis and energy expenditure, ameliorating diet-induced obesity. Global FNDC5 knockouts show normal musckuloskeletal and metabolic development but are protected against systemic challenges such as ovariectomy and calcium deficiency. FNDC5 expression in bone and disrupted osteogenesis in bone-specific knockouts suggest a para/autocrine role for irisin beyond its endocrine function.

Methods: To assess muscle-derived irisin's role and its endocrine vs. autocrine pathways in exercise, we created a FNDC5-floxed mouse with targeted deletion in striated muscle using human alpha-skeletal actin Cre. We compared wild type Cre-negative littermates (WT) with muscle-FNDC5 knockout (KO) individually housed with or without access to voluntary wheel running (VWR vs. CTL) from ages 8-12 weeks. Mice of both sexes and genotypes (N=6) were weighed and analyzed for body composition and bone density via DXA at 8 and 12 weeks, then sacrificed for tissue collection. Adipose, muscle, and bone tissue were collected for later gene expression analysis, and additional bones were collected for micro-CT, histology, and mechanical testing.

Results: Both WT and KO VWR mice acclimated to running wheels within days, achieving 5-10 km/day. Male KO mice exhibited more daytime running with significantly higher running speed and water intake. All mice significantly increased body and femur bone mineral density from 8 to 12 weeks of age, but with no effect of exercise or knockout. While WT and KO CTL mice gained weight from 8-12 weeks, weight gain was markedly less in male and female WT VWR mice. In females, the percent of weight gained was significantly lower in VWR versus CTL mice, while in males this trend was more dramatic with some WT mice losing weight with running. This trend was absent in KO mice, with both male and female mice demonstrating similar weight increases to non-running controls. Trends in whole body weight were mirrored in soft and lean weight, while no differences in bone microarchitecture were observed at week 12 via micro–CT.

Conclusions: Results support previous findings of irisin’s key role in potentiating beneficial metabolic effects of exercise. Ongoing work will characterize gene expression pathways regulating body composition and further explore potential effects on bone development.

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Navigating the Integration of Generative Artificial Intelligence in Undergraduate Medical Education: Insights from a Survey at University of New England College of Osteopathic Medicine

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Introduction:
Generative artificial intelligence (GenAI), a type of artificial intelligence technology capable of producing text, imagery, and synthetic data, has begun appearing in both healthcare and medical education. To better understand GenAI's presence and potential in medical education we surveyed faculty and students at the University of New England College of Osteopathic Medicine (UNECOM) about their experience with it and their views on its benefits and challenges.

Methods:
The survey was designed in Qualtrics and distributed to the entire student body (712) and full-time (60) and affiliate (~500) faculty via email in October 2023. The survey was self-administered, and all responses were anonymous. Quantitative statistics and thematic analysis were employed.

Results:
Of 241 total responses, 34% of students and 17% of faculty reported that they had used GenAI technology in their role at COM, suggesting that GenAI use may not be as prevalent as initially expected. The free tool GPT 3.5 was reported to be the most used. When asked what their institutions response to GenAI should be, 45% advocated for regulated use of GenAI, with AI users tending to be less restrictive than non-AI users. We found significant differences between users and non-users surrounding the ethics of using GenAI to complete graded assignments ($p=0.0015$), as well as trending differences regarding the benefits and risks of GenAI use in medical education. There were notable differences between faculty and students regarding risks and benefits as well. Over 80% of respondents, indiscriminate of usage patterns, indicated that UNECOM should offer training on using GenAI ethically and responsibly for educational purposes.

Conclusion:
Although only about one third of UNECOM students use GenAI, both students and faculty recognize the potential benefits to enhance learning and risks related to misinformation and ethical misuse. Students generally appraise the benefits higher and the risks lower than faculty. Yet, there is an overwhelming demand for institutional wide education surrounding the responsible and effective use of GenAI. Students are interested in using GenAI as a learning tool, and minimally to complete graded written assignments, as over half of students consider it unethical. This study underscores the need for ongoing research into the effective and ethical integration of GenAI technologies in undergraduate medical education environments.

Acknowledgments: This research was completed at the University of New England College of Osteopathic Medicine.

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Unraveling the Molecular Dynamics of Pain by Investigating Effects of Mitochondrial Uncoupling Drugs on Mouse Dorsal Root Ganglion Sensory Neurons.

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Introduction: Pain is a pervasive and debilitating condition and effective treatment is a major clinical challenge. Dorsal root ganglion (DRG) neurons convey sensory information from tissues of the body trunk and limbs to the CNS and give rise to nociceptive transmission that leads to the sensation of pain. Mouse DRG cultures currently serve as a widely used model for studying the molecular processes underlying pain and analgesic drug development. The Molliver lab recently demonstrated that mitochondrial uncouplers, such as BAM-15, modulate neuronal metabolism by dissipating the mitochondrial membrane potential and provide analgesia in rodent models of inflammatory and neuropathic pain. Our study aims to characterize the molecular mechanisms by which mitochondrial uncoupling by BAM-15 leads to inhibition of nociceptive signaling in cultured mouse DRG neurons. Work to date has involved preparing optimal cultured neurons for patch clamp electrophysiology and the replication of previous work demonstrating inhibitor of sensory neuron excitability, to provide a model system for analyzing the impacts on neuronal excitability of manipulating signaling pathways that may be responsible for the analgesic effects of BAM15.

Methods: DRG neurons were isolated from mice following Avertin anesthetic and perfusion with divalent ion free HBSS. DRGs were digested with papain and collagenase, then resuspended in complete DMEM media before plating on poly-D-lysine -coated coverslips. Electrophysiological recordings were performed using an Olympus microscope with IR-DIC optics, and patch clamp configuration was achieved with borosilicate glass pipettes. Data were collected via Multiclamp 700B amplifier and Digidata 1440A digitizer, with voltage and current clamp protocols and offline analysis using Clampfit.

Results: Preliminary data confirms that BAM-15 treatment decreases resting membrane potential and reduces action potential firing, consistent with its analgesic actions in vivo. Ongoing experiments will use inhibitors of specific cell signaling pathways to block the inhibitory effects of BAM15. A future goal is to extend these studies the HD10.6 human DRG-derived cell line to demonstrate whether similar mechanisms function in mouse and human sensory neurons.

Conclusions: Our current data demonstrates a decrease in mitochondrial membrane potential with BAM-15 treatment, allowing us to begin analyzing signaling pathways mediating this effect. Furthermore, if we can demonstrate similar results in HD10.6 cells, this will provide critical data supporting the translational relevance of mitochondrial uncouplers for pain management and facilitate the development of a novel class of non-addictive analgesic treatments.

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Title: Using network analysis to understand pain and psychological symptoms in cancer patients presenting to the emergency department: The impact of recent surgery

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Introduction: Pain is a common complaint among patients with cancer presenting to the emergency department (ED). This study aimed to examine differences in the relationships among pain and psychological symptoms between patients with cancer who recently had surgery (within 3 months) and those who had surgery greater than 3 months prior to their ED admission.

Methods: In this prospective observational cohort study, patients with cancer presenting to the ED with a complaint of moderate-severe pain completed validated self-report measures assessing sociodemographics, cancer-related treatments, pain severity and interference, medication use, and psychological symptoms (depression, anxiety, pain catastrophizing, and sleep disturbance). Patients self-reported whether they had recently undergone cancer-related surgery (≤3 months). Network analysis included construction of correlation matrices of pain and psychological symptoms, and use of centrality measures to identify key symptoms and their interrelationships among 2 groups of patients: those with recent surgery (<3mo prior) and those with more distant surgery.

Results: Out of the 173 participants enrolled in the study, 120 had previously undergone cancer-related surgery. Abdominal pain was the most frequently reported pain site (n=42), with co-occurrence of lower back and pelvic pain. Network analysis revealed distinct symptom clusters in each group. For patients with recent surgery, sleep disturbance and pain catastrophizing (helplessness subscale) were central in the symptom network, followed by pain interference. However, pain interference and pain catastrophizing (helplessness) were the most central symptoms in patients with more distant surgery, followed by average pain intensity. The network for patients presenting to the ED with recent surgery had a global clustering coefficient of 0.70, while for those presenting to the ED with more distant surgery, it increased to 0.78.

Conclusion: We observed that pain interference and pain catastrophizing (helplessness subscale) played a central role in both networks. Sleep disturbance was more central within the first 3 months for surgical recovery. Symptoms were also more intercorrelated in the group with distant surgery. Careful prospective longitudinal studies are needed to confirm these findings, but

these differences may have implications for the type of interventions that are prioritized among patients according to the timing since their surgery.

Evaluating the Feasibility and Acceptability of a Novel Biological Drug-Checking Model in Emergency Departments: A Pilot Study

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Introduction

Drug checking studies show that people who use drugs (PWUD) often request testing after an overdose and take risk reduction actions when informed of their drugs' contents. Unfortunately, in many areas of the US, drug checking services, remain inaccessible due to legal restrictions, limited equipment, and logistical barriers. In this pilot study, we evaluated the feasibility and acceptability of a novel "biological drug checking" model by providing comprehensive toxicology testing via liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS) at the time of an Emergency Department (ED) visit for non-fatal drug overdoses, directly back to study participants.

Methods

From February 1 - September 1, 2022, research assistants enrolled a consecutive sample of adult ED patients with unintentional non-fatal overdoses at 2 hospitals. Eligible patients were English-speaking, 18 or older, presenting for overdose, and willing to provide blood and urine samples. Baseline surveys collected demographic and substance use data. Blood and urine samples underwent comprehensive toxicology testing via LC-QTOF-MS, alongside standard hospital Urine Drug Screen (UDS). Participants were contacted within 72 hours with testing results, delivered via personalized surveys and were compensated for survey completion.

Results

Of 76 enrolled participants, 62 (82%) completed post-receipt surveys. The study found high levels of participant interest and satisfaction. Over half (51.35%) were "Very Interested" in drug checking, and 62.90% reported the service met "Almost All" their needs. The majority (74.19%) rated the service "Excellent" and 80.65% would recommend it to others. Concern about drug safety was noted from baseline to follow-up, and 82.26% expressed willingness to use the service again.

Conclusion

This pilot highlights the potential of "biological drug-checking" in EDs, showing high participant interest and satisfaction. LC-QTOF-MS testing gave detailed information on substance exposure at the time of overdose, aiding participants in making informed decisions about future drug use. This patient-centered model, combining comprehensive testing and timely feedback to PWUD, addresses a critical gap as standard ED drug testing via UDS fails to account for drug supply changes, including novel psychoactive substances. Expanding these services could reduce overdose deaths and improve public health outcomes, but more research is needed to gauge long-term impacts.

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IRB

This project was granted an exemption from the UNE IRB as this project has External IRB approval. Attached to the submission are external IRB approvals and approved UNE exemption notification.

De Novo Synthesis of High Purity CD3 Epsilon Peptides Utilizing SUMO Expression System in Bacteria

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Cancer is one of the leading causes of death in the United States. Monoclonal antibody drugs became one of the commercially and clinically successful drugs for many diseases. Among the monoclonal antibodies, T cell-dependent bispecific antibodies directly target tumor cells for cancer treatment, they kill tumor cells by activating T cells through binding to the CD3 (cluster of differentiation 3) receptor on T cells. Many anti- CD3 antibodies bind to the surface exposed CD3 γ, δ, ε subunits for T cell activation.
SP34, an anti-CD3ε antibody, specifically binds to the first 27 amino acids of CD3ε. Synthesis of CD3ε peptides proofed to be difficult due to its hydrophobic nature and presence of an N-terminal glutamine that caused many side reactions resulting in very poor peptide quality and purity. For some commercial full-length CD3ε proteins it is unclear whether N-terminal glutamine is present or absent. In cases where N-terminal glutamine is present it is modified to pyroglutamic acid. To study the SP34-CD3ε interaction a reliable and defined source of CD3ε peptide and peptide variants is required. By utilizing the SUMO (Small Ubiquitin-related Modifier) system from yeast, CD3ε1-27 amino acid and a truncated version 2-27 amino acid peptide are expressed in *E. coli* cells with an SMT3 (Mitotic Fidelity Gene 3) tag. Subsequently, SMT3 tag is removed with SUMO protease and the resulting peptide is further purified. This novel *in vitro* approach results in high yields of non-modified peptides with great purity (>95%).

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IRB: No human subject involved in this study

Final Clinical and Biomarker Outcomes of a Phase Ib/II Study of Pre-operative Induction Pembrolizumab with Radiation Therapy in Early-Stage Triple Negative and High-Risk Hormone Receptor Positive Breast Cancer (PEARL)

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Introduction: Breast cancer (BC) is the second leading cause of cancer deaths in women worldwide. Current literature indicates that patients with high-risk BC subtypes may benefit from combination neoadjuvant immunotherapy and chemotherapy. However, 33% of patients do not achieve a pathological complete response (pCR) on this regimen and have a higher risk of recurrence. Adding radiation therapy (RT) may results in synergistic immunogenicity and improved treatment response. Herein, we report the results of the first, phase 1b/II study of preoperative RT with pembrolizumab (anti-PD1) for triple negative BC (TNBC) and high-risk hormone receptor-positive (HR+) BC.

Methods: Between 12/2017 to 12/2021, 66 patients with stage I-III BC (54 TNBC, 12 HR+) were treated with cycle 1 anti-PD1 (200 mg iv), cycle 2 anti-PD1 and RT (200mg iv, 24Gy in 3 fractions) followed by chemotherapy and surgery. Serial tumor and blood specimens were collected pre-treatment, after anti-PD1, and after anti-PD1/RT. Coprimary endpoints were safety and change in tumor-infiltrating lymphocytes (TILs). Secondary endpoints were pCR, residual cancer burden (RCB) rates, and event-free survival (EFS).

Results: The median age of the cohort was 53y (range 26-94) with median follow-up of 32mo. The majority (84.8%) were clinical stage II; 3% stage I and 12.1% stage III. 42.4% of patients presented with clinically node-positive disease. Safety end point was met. Incidence of grade ≥3 toxicities was 41%. In the entire cohort, 54.5% achieved pCR (59.2% TNBC, 33.3% HR+). A total of 77.8% of TNBC and 41.6% of HR+ had a near pCR (RCB score 0-1). The 3-year EFS was 80%. Compared to baseline, PD-L1 expression increased after anti-PD1 (median Combined Positive Score [CPS] 7.49 to 23.20, p=0.044), but there was a nonsignificant change between anti-PD1 and anti-PD1/RT (median CPS 23.20 to 23.41, p=0.28). Baseline TILs correlated with PD-L1 expression and TNF-a. Adding RT to anti-PD1 significantly decreased TILs (28.9% to 17.1%, p=0.014).

Conclusion: Preoperative RT with pembrolizumab and NAC is safe and results in favorable treatment response rates and 3-year EFS. Safety profiles were comparable to current SOC treatment regimens. PD-L1 and TILs may be predictive biomarkers for neoadjuvant anti-PD1/RT response. Although the addition of RT did not change PD-L1 expression, the reduction in TILs after adding RT to pembrolizumab highlights the importance of treatment sequencing to optimize anti-tumor responses.

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Bacterial Metabolic Signaling Drives Neutrophil Responses in Infected Airways

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Introduction: *Pseudomonas aeruginosa* is a bacterial pathogen that chronically infects the lungs of patients with cystic fibrosis. Even in the era of CFTR modulators, *P. aeruginosa* triggers amplified neutrophil recruitment along with pro-inflammatory cytokine and eicosanoid release. This response damages airways and contributes to morbidity and mortality. With increasing antibiotic-resistant *P. aeruginosa* strains, there is a need for novel therapeutic strategies to attenuate airway damage caused by infection. Thus, we screened for, identified, and further characterized a bacterial gene that is likely involved in *P. aeruginosa* induced airway inflammation. We hypothesized that key bacterial genes induce host eicosanoid signaling causing neutrophil influx into infected airways.

Methods: A library of PA14 non-redundant transposon mutants was screened for bacterial genes involved in neutrophil transmigration. Lung epithelial cells grown on the apical side of transwell filters were infected with individual mutants. The number of neutrophils that migrated from the basolateral side to the apical side of the transwell was then measured by myeloperoxidase. Motility, virulence, and adhesion assays were also carried out on an identified mutant. Leukotriene B_4 (LTB_4), an eicosanoid that drives neutrophil migration, was measured by enzyme-linked immunosorbent assay. Neutrophil protein expression and phosphorylation were assessed by western blot.

Results: Mutant PA14 23790::MAR2xT7 with a transposon in the *leuB* gene revealed significantly reduced neutrophil transmigration compared to wild-type (WT) PA14, which was confirmed with an in-frame deletion mutant (PA14Δ*leuB*). Exogenous leucine, the biosynthetic product of the *leuB* gene, restored neutrophil transmigration. Bacterial motility, virulence, and adhesion were unaffected by the *leuB* mutation. However, host production of LTB_4 during transmigration was significantly decreased after infection with PA14Δ*leuB* compared to WT. Furthermore, phosphorylation of ERK, a key pathway in neutrophil transmigration and LTB_4 production, was reduced in neutrophils after exposure to airways infected with PA14Δ*leuB* compared to WT.

Conclusion: These results suggest that the bacterial *leuB* gene plays a key role in driving neutrophil transmigration by inducing neutrophilic LTB_4 release via the ERK pathway. Continued research will focus on further defining neutrophil pathways impacted by *leuB* for identification of future therapeutic targets.

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Patient Perceptions on Opioid Therapy for Acute Pain: A Qualitative Study

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Background: Opioids are highly effective in treating both chronic and acute pain but have various detrimental, non-therapeutic effects that may lead to the development of opioid use disorder (OUD) in certain individuals. This creates a complex landscape of opioid prescribing and use, especially during the opioid epidemic. The present study uses a qualitative research lens to understand the patient experience during opioid therapy for acute pain during the third wave of the opioid epidemic, including perceptions, behaviors, and internal or external influences.

Methods: Patients using opioids for acute pain were recruited from the emergency department and general surgery clinic at a large urban academic medical center in Worcester, Massachusetts. This sample was also part of a larger study involving continuous physiologic monitoring during opioid use. Semi-structured interviews were conducted at hospital discharge or up to 10 days post-discharge. Interviews were recorded, transcribed verbatim, analyzed using NVivo qualitative analysis software, and subjected to applied thematic analysis.

Results: Of 60 subjects from the parent study, 44 completed the semi-structured interviews (mean age 47 years, 50% female). Participants took a mean of 18.8 doses of opioids (range 1-110) over the course of the study, with a mean total MME of 321.9 (range 7.5-3057.0) and a mean duration of 4.4 days (range 1-14). Three main themes emerged from the interviews: 1) Direct effects of opioids, including experiences of analgesia, euphoria, anxiolysis, and withdrawal symptoms after discontinuation; 2) Internal factors, with patients describing varied expectations, goals, and perceptions of the quantity of opioids prescribed for outpatient use; 3) External factors, such as previous experiences with prescription opioids, stigma, and interactions with clinical staff.

Conclusions: Even short-term opioid therapy for acute pain can be complex for patients to navigate. The findings of this study reveal several themes that promote clinical variability in short-term courses of opioids for acute pain. Participants described internal and external factors, in addition to the effects of the opioids themselves, as influencing their behaviors, experiences, and goals of therapy. Both patients and clinicians may benefit from educational initiatives that more thoroughly consider patient perspectives of opioid analgesics, balancing safe opioid prescribing with satisfactory pain control.

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Identity and Inclusive Sex Education Information: Ascertaining What Parents of LGBTQ+ Youth Want to Know (Pilot Study); Maine

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Introduction

The availability and quality of sex education in schools in the U.S. differs greatly by state, city, and even school district, leading to disparities in sexual health education. Prior research has demonstrated the need for more comprehensive sex education, especially for LGBTQ+ youth. While parents have long been a source for providing sex education to their children, there is limited research on how this practice is different for parents of LGBTQ+ youth. There is also limited research on parents' understanding of their LGBTQ+ child's identity, which may play an important role in these conversations. Our goals were to better understand what parents of LGBTQ+ youth wish they knew about their child's identity, about sex education topics, and ultimately how to best deliver this information to parents.

Methods

Qualitative interview research design was implemented. Participants (n=8) were recruited from within York and Cumberland Counties in Maine. Semi-structured interviews were conducted via Zoom and lasted 30-45 minutes. Interview transcripts were edited and analyzed, making notations of significant quotes, themes, and native concepts. Transcripts were uploaded into QSR NVivo 14 software to aid in organization of coding and analysis. Themes were identified using thematic and content analysis.

Results

Ten main themes were identified, with many subthemes. The 3 top themes were: (1) Open Communication: open and proactive communication habits with their children, especially about their identity; (2) Support Systems: internal and external support for parents and their children; and (3) Reactions to Child's Identity: parents' strong desire to educate themselves to better understand and accept their LGBTQ+ child. Responses were varied on the topic of sex education: some parents were very comfortable and progressive in their approach, while others felt uncomfortable broaching the topic (not due to their child's LGBTQ+ identity). Informative resources mentioned by parents included friends, online sources, medical professionals, LGBTQ+ organizations, and their child; however, a significant lack of educational resources specifically for parents was noted.

Conclusion

This pilot project helps to better understand how parents are preparing for and navigating conversations about sex education and identity with their LGBTQ+ children. In the future, the knowledge gained from this project can be used to create an educational resource for parents of LGBTQ+ individuals.

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A Want and a Need: Firearm Harm Reduction Education Should Be Included in Medical School Curriculum

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Introduction: Firearm-related injuries are a major public health crisis in the United States. While physicians can play an important role in educating their patients to prevent future firearm-related deaths, less than 20% of US medical schools offer training surrounding gun violence and patient-centered counseling on firearm safety. Through a one-time pilot educational program on firearm harm reduction for second-year medical students at the University of New England College of Osteopathic Medicine (UNECOM), we aim to provide novel data assessing the knowledge gaps and desire for more education on firearm harm reduction in medical school curricula.

Methods: The second-year medical class of 180 students were required to participate in a mandatory, University- approved, two-hour firearm harm reduction education program on February 28th, 2024. The program consisted of an overview of firearm basics and common injuries, firearm safety and patient counseling, and an overview of relevant local and federal legislation. All participants were invited to complete an anonymous standardized electronic survey before and after attending the program.

Results: Of the 180 students invited to participate in the surveys, 118 completed the pre-education program survey and 52 completed the post-survey. Prior to the educational program, 80% of students agreed or strongly agreed that knowledge of firearms is relevant to their medical education. 72% of students agreed or strongly agreed that firearm risk screening and safety intervention is a responsibility of healthcare providers. Only 53% of students reported feeling comfortable discussing firearm safety with patients and 24% of students reported feeling knowledgeable of local gun laws as they relate to patient safety counseling. Due to the high rate of attrition, we did not compare the pre-and post-survey results to study the effectiveness of the educational program.

Conclusion: There is a significant need and desire for firearm safety education in medical school curricula. Future studies should improve data collection strategies to allow for the evaluation of the effectiveness of firearm harm reduction educational programs for medical students.

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Pde3a Deficiency Plays a Novel Role in Lipolysis

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Background: PDE3A and PDE3B hydrolyze cAMP and cGMP, which are critical second messengers important in cellular function. While PDE3B has been shown to have an anti-lipolytic effect, the role of PDE3A on lipolysis is not known. We have previously found that *Pde3a*$^{-/-}$ mice (3A-KO) have decreased adiposity, histopathologic liver disease, and increased serum-free FA (FFA) levels, while *Pde3b*$^{-/-}$ mice (3B-KO) have no obvious phenotype.

Objective: To elucidate the etiology of high circulating FFA in 3A-KO mice and their effects on the liver.

Design/Methods: 3-5 wk-old C57bl/6J (WT), 3A-KO and 3B-KO mice were sacrificed (n=3 per gender). White adipose tissue (AT) was protein quantified for PDE3A, PDE3B, hormone-sensitive lipase (HSL), adipose triglyceride lipase (ATGL), adiponectin, and b-actin by Western blot. Pre-adipocytes were isolated from WT mice, differentiated, and transfected with scramble, PDE3A (siPDE3A), or PDE3B (siPDE3B) siRNA. Media was collected and FFA measured. Hepatocytes were isolated from WT mice and transfected with scramble siRNA (WT) or siPDE3A. Scramble-WT hepatocytes were incubated for 48 hours with media from the siPDE3A-transfected adipocytes (WTCM). Protein was quantified for fatty acid synthase (FAS), sterol regulatory element binding transcription factor 1 (SREB1c), cleaved and total caspase-3, diacylglycerol O-acyltransferase 2 (DGAT-2), pyruvate dehydrogenase kinase (PDK) 1-4, and b-actin by Western blot. Hepatocyte intracellular cAMP levels were measured.

Results: PDE3A protein was increased in 3B-KO AT and siPDE3B adipocytes, whereas PDE3B was decreased in the siPDE3A adipocytes ($p < 0.001$). PDE3A deficient AT and adipocytes had increased HSL and ATGL and decreased adiponectin ($p < 0.001$) compared to PDE3B-deficient AT/cells. FFA levels in the media were significantly higher in siPDE3A, and lower in siPDE3B adipocytes than in scramble-WT. FAS and SREB1c were decreased, while DGAT-2, PDK 1-4, caspase 3 protein levels and intracellular cAMP levels were increased in both the scramble-WT-CM and siPDE3A compared to scramble-WT ($p < 0.01$).

Conclusion: These data suggest that the liver findings and potentially other organs affected in 3A-KO mice may be due to elevated cAMP levels in AT, thereby activating lipolysis to cause excess circulating FFA. We hypothesize that the FFA overwhelm the cells housed in organs highly utilizing FA oxidation and produce lipotoxic metabolites that cause tissue damage and mitochondrial dysfunction.

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Recurrence or Persistence of Atrial Fibrillation is Associated with Frailty Phenotype, as well as Adverse Clinical Outcomes: Data from the SAGE-AF Cohort Study

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Introduction: Atrial fibrillation (AF) is a prevalent arrhythmia in older adults in the United States. While traditional risk factors are well-established, the role of frailty, a marker of biological aging, in the course of AF over time remains underexplored. This investigation focuses on the hypothesis that frailty or pre-frailty captures residual risk for AF progression beyond traditional CV risk factors.

Methods: We utilized data from 854 older adults (≥ 65 years) and a CHA2DS2VASc score ≥ 2, enrolled in the Systematic Assessment of Geriatric Elements (SAGE-AF) prospective cohort study, who had electrocardiograms (ECGs) available at both a baseline and two-year follow-up visit. Participants were classified as having AF recurrence if baseline ECG showed sinus rhythm and year-two ECG showed AF, and as having AF persistence if AF was present at both time points. Frailty was assessed using the Cardiovascular Health Study frailty scale. Multivariate analyses adjusted for baseline demographic and cardiovascular risk factors were performed to determine associations between frailty and AF recurrence or persistence, and whether this AF status was linked to adverse outcomes.

Results: We included 773 older adults in our analysis (mean age 76±7, 52% male, 92% white). AF recurrence or persistence was detected on ECG in 379 (49%) of participants at two-year follow-up. Baseline frailty or pre-frailty was significantly associated with higher odds of AF recurrence or persistence (aOR 1.63, 95%CI 1.11–2.39). Participants with recurrent or persistent AF had a higher incidence of major bleeding events, even after adjusting for anticoagulation use, age, and other demographic and cardiovascular risk factors (aHR 1.87, 95%CI 1.01–3.45).

Conclusion: Frailty or pre-frailty increases odds of AF recurrence or persistence at two years, underscoring its potential role in influencing the course of AF over time. AF recurrence or persistence is associated with increased risks of major bleeding, even after adjusting for key clinical factors. This may suggest that certain unmeasured health behaviors contribute to bleeding risk in this population, warranting confirmation in future studies.

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Telmisartan is a Cardiac Sodium Channel Gating Modifier: Potential Mechanism of Action

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Introduction

Sudden cardiac death (SCD) and Brugada Syndrome remain among the leading causes of death both regionally and globally. Many efforts to reduce these conditions have focused on anti-arrhythmic therapy but they have returned disappointing results. Recent findings have shown that modulation of inward sodium current plays a crucial role in cardiac conduction and that defects in the kinetics of this current can contribute to cardiac arrhythmias.

Pharmacological regulation of sodium channel inactivation may represent a novel strategy for treating cardiac arrhythmias. The angiotensin receptor blocker, Telmisartan, displays a secondary effect on inward sodium current by delaying sodium channel inactivation, identifying this drug as a promising treatment for cardiac arrhythmias. However, the mechanism of telmisartan action on sodium channels is not well understood.

Method

Cardiac and neuronal voltage-gated sodium channels, along with cardiac/neuronal channel chimeras, were ectopically expressed in N2A cells and channel gating properties were assayed by voltage patch clamp electrophysiology in the presence or absence of telmisartan. In some experiments, channel-binding FHF proteins were coexpressed. Additionally, computational experiments with a human-like cardiomyocyte model and ring-shaped cardiac fiber model were conducted to understand how telmisartan may overcome reentrant arrhythmia.

Results

Telmisartan was found to delay the inactivation of cardiac Nav1.5 channels, causing a prolonged open state conformation and enhanced inward sodium current. Neuronal channels Nav1.6 and Nav1.7 were not similarly affected. The cytoplasmic C-terminal cytoplasmic domain (CTD) of Nav1.5 was sufficient to impart telmisartan responsiveness to an otherwise wildtype Nav1.6 channel, and FHF binding to the Nav1.5 CTD was also required for telmisartan modulation. Suboptimal telmisartan concentrations resulted in the modulation of only a fraction of expressed Nav1.5 channels, suggesting that telmisartan acts via stoichiometric binding to the cytoplasm-facing Nav1.5 CTD:FHF complex. Additionally, computational modeling showed that telmisartan increases excitability and conduction velocity, in addition to rescuing conduction block and preventing reentry.

Conclusion

Novel findings showed the direct effect of telmisartan on delaying sodium channel inactivation and enhancing inward sodium current, highlighting telmisartan as a promising treatment for cardiac arrythmias.

Substance Use Disorder Education in New England Medical Schools

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Introduction: The overdose crisis in the New England region underscores the need for healthcare providers to be trained to address substance use disorder (SUD). Medical schools often neglect SUD education, leaving many physicians feeling unprepared to care for people who use drugs (PWUD). Some medical schools have revised curricula to prepare future physicians to manage PWUD, but often, educators fail to provide comprehensive learning experiences for students. SUD education can reduce stigmas that limit the care provided to PWUD. This study aimed to determine how many hours of SUD education are provided to medical students in the New England region, the perceived level of preparation, and what curricula is provided on SUD.

Methods: This is a qualitative and quantitative mixed research study conducted via an anonymous survey on RedCAP. 10 survey questions were designed by the authors and asked how many hours of SUD education students received and how prepared they felt treating PWUD. Recruitment efforts included email invitations to participate in the survey to all 11 medical schools in the New England region. The University of New England agreed to participate and distributed the survey to currently enrolled medical students. The survey was also advertised on Reddit via forums such as r/takemysurvey, r/emergencymedicine, and r/SampleSize. Students from University of Vermont, Quinnipiac University, Yale University and Brown University accessed the survey via Reddit.

Results: We obtained data from 29 respondents (41% MS-I, 14% MS-II, 34% MS-III, 7% MS-IV, 3% undisclosed), including participants from University of New England, University of Vermont, Quinnipiac University, Yale University, and Brown University. The average time of SUD education received was 6.09 hours. The average level of preparedness students felt treating patients living with SUD on a scale of 1 to 100 was 45.83. 62% of respondents reported having some form of experience treating patients living with SUD prior to entering medical school. 24% of respondents reported not having any form of didactic education of SUD while in medical school. Respondents frequently mentioned a need for more events and opportunities to hear directly from people living with SUD.

Conclusion: This study highlights gaps in knowledge about SUD and a need for more didactic and hands-on exposure for medical students. The data could be used as baseline information for future evaluations.

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This work received an exemption by UNE's IRB.

Deep Lumbar Muscle Activation During Core Stabilization Exercises in Healthy Subjects

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Introduction: Musculoskeletal low back pain is a common condition that is often characterized by reduced strength and atrophy in the lumbar extensors, most notably the multifidus (MF). Superficial MF fibers cross 3 to 5 segments and primarily function as extensors, while deep MF fibers cross 2 segments and are more ideally positioned for intervertebral stability. Following injury, deep MF fibers are most prone to atrophy and fatty infiltration. Although exercises are commonly prescribed to improve MF activation, size, and strength, limited studies have investigated independent activation of deep and superficial MF fibers. This study aims to identify exercises that may preferentially activate deep MF fibers, compared to the synergistic lumbar erector spinae (LES) and superficial MF.

Methods: LES and deep and superficial MF activity was compared across three isometric exercises (trunk extension, reverse hyperextension, and weighted trunk extension) in seventeen healthy individuals (11 males, 6 females). LES activity was recorded with a surface electrode and indwelling electrodes were used to record superficial and deep MF activity. Muscle activity was normalized to a maximal voluntary isometric contraction. Rates of perceived exertion (RPE) from 0 (resting) to 10 (maximal exertion) were collected following each exercise. A one-way repeated measures analysis of variance with a post-hoc Bonferroni correction was used to detect significant differences. Cohen's effect sizes were used to describe the magnitude of change.

Results: For LES activity, the weighted back extension (54.3 ± 19.0%) was significantly greater than body weight back extension (29.2 ± 9.9%, $p < 0.001$, $d = 1.66$) and reverse hyperextension (38.0 ± 13.6%, $p = 0.002$, $d = 0.99$). Superficial MF activity was not significantly different between exercises. For deep MF activity, weighted trunk extension was significantly greater compared to trunk extension (54.6 ± 42% versus 37.4 ± 21.2% ; $p = 0.028$, $d = 0.52$). RPE for weighted trunk extension (6.1 ± 1.3) was greater than trunk extension (3.3 ± 1.3, $p < 0.001$, $d = 2.15$) and reverse hyperextension (3.9 ± 1.4, $p < 0.001$, $d = 1.63$).

Conclusion: Our findings show that activation of the LES and deep MF increased with mechanical loading, while this did not occur for superficial MF. This data suggests that loaded trunk extension exercises may preferentially activate the LES and deep MF and suggests differential activation between superficial and deep MF fibers.

Acknowledgments: The University of New England College of Osteopathic Medicine. This work has been supported by the Peter Morgane Student Research Fellowship. IRB approval was granted by the University of New England (IRB # 0423-21).

Analysis of Maladaptive Behaviors in Relation to Pain and Illness in Minimally Verbal Individuals with Disabilities

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Introduction: Current treatment for maladaptive or socially impairing behaviors in neurodevelopmental disorders focuses on altering environmental factors to change consequences rather than addressing physiological causes. Alternative approaches consider medical treatment for challenging behaviors, though the link between physiological changes and behavior is unclear. While illness and pain often worsen behaviors, no clear relationship exists between medical diagnoses, treatments, and behavioral outcomes. Additionally, the impact of illness onset on maladaptive behaviors remains unexplored. This study aims to examine how medical treatment for physiological issues affects pain.

Methods: The study included 21 participants (13 males and 8 females). During a primary care visit, participants were assessed using the Non-communicating Children's Pain Checklist-Revised (NCCPC-R) and prescribed a treatment for their presenting illness. The NCCPC-R was re-administered two weeks post-treatment, and pre- and post- treatment pain scores were compared.

Results:

The mean total pain score before the intervention was 13.7 (SD = 10); after the intervention, it decreased to 11.3 (SD = 10). Non-normally distributed pain score data necessitated the use of non-parametric methods for analysis. Pre-intervention to post-intervention total pain scores reflect an overall decrease. Specifically, 62% (n=13) of participants experienced a reduction in their pain scores, 5% (n=1) reported no change, and 33% (n=7) showed an increase.

Conclusion: Cohen's d-effect size of 0.484 indicates a medium impact of the intervention on reducing pain. A Wilcoxon Signed Rank Test evaluating the statistical significance of the pre- and post-intervention pain score differences yielded a statistic of V = 154 and a p-value of 0.0681, indicating a marginally significant reduction in pain scores post-intervention warranting further investigation.

Acknowledgements: A special thanks to the Center for Discovery. This work has been funded by the Peter Morgane Student Research Fellowship.

IRB Study Registration: The Center for Discovery granted an IRB exemption, which approved this project under protocol #0424-12.

Exploring Success in Early Breastfeeding at EMMC: A Retrospective Cohort Study on Factors Affecting Exclusive Breastfeeding at Hospital Discharge up to 2 Months of Life

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INTRODUCTION: Exclusive breastfeeding for the first 6 months of life has been shown to be beneficial for the child and the mother. Current newborn nutrition recommendations by the American Academy of Pediatrics, Dietary Guidelines for Americans 2020-2025, and the World Health Organization are that infants should be exclusively breastfed for the first 6 months of life. The CDC reports nationally that 19.2% of breastfed infants receive formula in the first 48 hours of life and in Maine overall only 16.9% do (CDC Breastfeeding Report Card, United States 2022); early formula supplementation may affect long-term success at exclusive breastfeeding. Over a recent 8-month period at EMMC less than 50% of newborns had received exclusively breastmilk at hospital discharge, despite over 90% initiating breastfeeding.

STUDY DESIGN: Retrospective Observational Cohort Study. POPULATION: Singleton infant/mother dyads born at 36 weeks gestation or more at Northern Light EMMC during February and March of 2024 whose documented feeding plan was “exclusive breastfeeding”.

METHODS: Following IRB approval, chart extraction was completed into a secure data file reviewing cases from monthly infant feeding reports meeting inclusion criteria. The population was divided into groups by whether they received any supplementation or not during the newborn period. Infants who received supplemental feedings were compared to those who did not for preexisting variables such as maternal health factors and hospital events. For a subset with available outpatient follow-up data, we report rates of exclusive breastfeeding at 1-3 day and 2-month follow-up visits.

RESULTS: Percentage of infants in each group who were exclusively breastfeeding at hospital discharge. RESULTS: A total of 99 infant/mother dyad charts were reviewed after one was excluded for not meeting the inclusion criteria. 28 (28.3%) received supplementation and 71 (71.7%) did not. The average age for first supplemental feeding was 12 hours (range 1-38 hours). With mothers with greater than 1 para, there was a statistically significant decrease in the use of formula supplementation during the newborn period, $\chi 2$ (2, N=99)=4.0689, p = 0.044.

CONCLUSIONS: Hospital policy for supplementing newborns whose mother's plan was exclusive breastfeeding may need to be reviewed to improve the performance of exclusive breastfeeding at hospital discharge for this population, particularly for first-time mothers.

Assessing Parasympathetic Function and Hypoalgesia Induced by Noxious Electrical Stimulation

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Introduction
Noxious Electrical Stimulation (NXES) has been shown to induce hypoalgesia in both healthy and clinical populations. Unlike traditional electrical stimulation, which uses non-painful electrical currents, NXES delivers higher intensity, painful stimuli that trigger natural pain inhibition mechanisms. These mechanisms include Diffuse Noxious Inhibitory Control (DNIC) in animals and Conditioned Pain Modulation (CPM) in humans. The autonomic nervous system (ANS), particularly parasympathetic activity, plays a critical role in pain processing, and can be assessed via Heart Rate Variability (HRV). The aim of this study was to examine whether parasympathetic activity during NXES influences pain inhibition.

Methods
Nineteen healthy participants (10 females, age 19-27) were recruited for this study. NXES was applied for 20 minutes using electrical pulses at a frequency of 100 pulses per second. Pain perception was assessed with Heat Temporal Summation (HTS), which measures the degree of pain facilitation from repetitive heat stimuli, and Pressure Pain Threshold (PPT), which measures the minimum force that induces pain. Electrocardiogram data were collected before and during NXES to calculate HRV, including time domain measures such as the root mean square of successive R-R interval differences (RMSSD) and frequency domain measures such as the high frequency percent power (Hf%Pwr), which represents parasympathetic activity.

Results
NXES significantly increased PPT ($t=-2.69$, $p=0.015$), indicating reduced pain sensitivity, and decreased HTS ($t=4.9$, $p<0.001$), suggesting reduced pain facilitation. HRV analysis showed a significant reduction in Hf%Pwr during NXES ($t=2.94$, $p=0.009$), indicating reduced parasympathetic activity. There was no significant relationship between baseline parasympathetic activity and the degree of pain inhibition. However, participants who experienced a greater increase in RMSSD during NXES also had a greater reduction in HTS ($r^2=0.244$, $p=0.044$), suggesting that parasympathetic activity plays a role in modulating pain facilitation after NXES treatment.

Conclusions
This study suggests that NXES induces hypoalgesia through mechanisms involving the autonomic nervous system, and that parasympathetic activity during NXES is related to the degree of pain modulation. Further research is required to determine how these findings extend to individuals with chronic pain and how changes in parasympathetic activity relate to clinical improvement.

Acknowledgement
Special thanks to The University of New England College of Osteopathic Medicine and The Westbrook College of Health Professions Department of Physical Therapy for making this research possible. Additional thanks to the Kahn Family Research Fellowship for helping to fund this research. Final thank you to all the participants who volunteered their time to help gather data for this project. This research was approved by the University of New England IRB # 0423-06.

Impact of demographics and social determinants of health on chronic pain in Maine

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Introduction: Chronic pain is a major healthcare problem. The prevalence of chronic pain tends to be higher among older adults, females, and veterans. There is a lack of studies on the impact of social determinants of health (SDOH) on chronic pain and lack of data regarding pain in Maine. Little is known about educational disparities in pain and there is conflicting research on racial impacts on pain. We aim to understand the characteristics of those with pain in Maine as well as explore the relationships between selected demographics and SDOH factors and pain related-measures.

Methods: Data from the PainRegistryforME were used. Individuals living in Maine who are ≥ 18 years with any type of recurrent or frequent pain are eligible to participate in the registry. Pain characteristics were measured via the NIH Patient-Reported Outcomes Measurement System (PROMIS) -29+2 Profile/Battery v2.1 (PROPr). This measures pain co-morbidities in 8 domains: anxiety, depression, fatigue, pain interference, physical function, sleep disturbance, ability to participate in social roles/activities and cognitive function. The first 109 subjects were included in the data analysis via Multivariate Analysis of Variance (MANOVA) using SDOH factors as independent variables and pain-related measures as dependent variables.

Results: Biological sex (76 females/109), veteran status (9 veterans/109), and race (95 white only/109) did not significantly affect any pain domain. Both age, with two peaks between 25-29 (12/109) and 55-59 (12/109), and education level (83/109 with Bachelor's degree and above) significantly affected participants' levels of anxiety, depression, and cognitive function. Being younger and having lower education degrees were associated with worse pain-related outcomes, including anxiety ($p=0.013$ and $p<0.001$, respectively), depression ($p=0.007$ and $p<0.001$, respectively) and cognitive function ($p=0.008$ and $p=0.007$, respectively).

Conclusion: The experience of pain is multifactorial. Patient reported pain-related outcomes seemed to be affected more by age vs. sex. Lower education levels tend to correlate with lower socioeconomic status that is known to negatively affect pain outcomes. Small sample size may be attributed to the lack of effects from veteran status and race. Continued data collection and analysis will help to further understand the relationship between SDOH and pain, which may inform future research and public health strategies for pain management in Maine.

Acknowledgements: This work was supported by the Peter Morgane Student Research Fellowship (to PO). The PainRegistryforME was established through a pilot grant from the Northern New England Clinical & Translational Research Network (NNE-CTR), in collaboration with MaineHealth (to Cao). IRB exemption was granted by the University of New England Office of Research Integrity (protocol # 0224-03).

Exploring Metabolic Vulnerabilities in Tuberous Sclerosis Complex: The Role of Tryptophan and the Kynurenine Pathway in Macropinocytosis

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Introduction

Tuberous Sclerosis Complex(TSC) is a genetic disorder presenting as cysts and tumors in the kidneys and in the lung. TSC is caused by loss of function mutations in the *TSC1/2* genes, resulting in mTORC1 hyperactivation. This triggers macropinocytosis(MPC), a process by which tumor cells engulf extracellular material to acquire nutrients and sustain proliferation. This study aims to identify the role of extracellular nutrients in TSC and identify metabolic vulnerabilities that could be therapeutically targeted. More specifically, we hypothesize that tryptophan(Trp) and the kynurenine(Kyn) pathway play a role in MPC in TSC-dc cells.

Methods

We used flow cytometry and epifluorescent microscopy to quantify dextran uptake(70kDa). Immunofluorescence and epifluorescence microscopy were done to evaluate the localization of AHR, and its target gene, IDO1. Cell proliferation was assessed by crystal violet staining, and apoptosis was quantified by cleaved caspase 3 levels in cells treated with Kyn pathway inhibitors. We performed an *in vivo* xenograft experiment by subcutaneously inoculating C57/BL6 mice with $2.5x10^6$ TSC2-dc. Mice were treated with AHR inhibitor SR1(200ug/kg/M-F) or Rapamycin(3mg/kg/MWF) for 29 days. Student unpaired T tests were performed for normally distributed data, and multiple comparisons were made using one way and two way ANOVA.

Results

We found that Trp increases MPC 3-fold($p<0.01$) in TSC2-dc but not in TSC2-expressing cells. Trp is metabolized via the Kyn pathway, which activates AHR and promotes cell growth. Importantly, AHR was localized in the nucleus of TSC2-dc, indicating that there may be an active transcriptional program regulating MPC. Treatment with Kyn pathway inhibitors TDO2(LM-10), IDO1(Linrodostat), or AHR(SR1) strongly decreased MPC in TSC2-dc(20-70%; $p<0.0001$), and selectively inhibited the proliferation of TSC2-dc by 50%($p<0.001$). Our *in vivo* studies showed that SR1 limited the growth of TSC2-dc tumors(75%, $p<0.001$), indicating that AHR and the Kyn pathway may be potential therapeutic targets in TSC.

Conclusion

We have shown that the Kyn pathway is intimately linked with MPC, thus supporting a key role of Trp in the induction of MPC, which is necessary for the survival of TSC2-dc. Future studies will focus on determining the molecular mechanism by which Trp induces MPC in TSC. These findings are crucial to elucidate the metabolic mechanism behind TSC tumorigenesis and the development of therapies that could reverse the disease process in patients.

Acknowledgements

This study was initiated at Brigham and Women's Hospital and is ongoing at the University of New England College of Osteopathic Medicine. This work was supported by the The LAM Foundation and a UNE Mini Grant (to HF).

Military Exposure to Trichloroethylene and Risk for Parkinson's Disease in New Hampshire: Camp Lejeune and Beyond

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Introduction

Background: Parkinson's Disease (PD) is a neurodegenerative disorder that affects the dopaminergic neurons of the substantia nigra, which is responsible for the initiation and coordination of voluntary movement. PD is one of the world's fastest growing neurodegenerative disorders, with an incidence of 90,000 cases annually. A study published in May 2023 identified that patients have an increased risk of PD associated with exposure to a degreasing solvent called trichloroethylene (TCE).

Rationale: Military service members have a significantly greater occupational exposure to TCE.

Objectives: Our study aims to investigate the prevalence of occupational TCE exposure and a diagnosis of PD in military service members who are treated at Wentworth-Douglass Hospital in New Hampshire.

Hypothesis: The environmental exposure and outcome are linked beyond the cases observed at Camp Lejeune U.S. Marine Corps Base.

Methods: Participants are identified through physician referrals from current neurologists at Wentworth Douglass Hospital, and through medical chart review in EPIC. Eligible patients include adults (>18yo) diagnosed with Parkinson's Disease, parkinsonism, or atypical parkinsonism with a history of military service, and occupational exposure to TCE. All data is registered in the MGB REDCap database.

Results: To date, 40 patients have been screened, 12 met eligibility criteria and 5 consented to enroll in the study. Patient age ranges from 50-83; diagnoses include Young Onset PD, PD without dyskinesia, or Parkinsonism, unspecified type. Patients enrolled served in Camp LeJeune, Biloxi Mississippi, South Carolina, and Sumter, Germany. All patients report no protective equipment use while working with TCE degreasing agents.

Conclusion: It is crucial that we identify more cases that demonstrate the association between TCE exposure and a diagnosis of PD beyond Camp LeJeune. This will enable physicians to support policy that will protect the public's health from this preventable environmental contaminant and potentially reduce the prevalence of this devastating neurodegenerative disease.

Acknowledgements: Our team gives special thanks to Dr. Samuel Goldman for his thoughtful consultation for this research. All research activities are conducted at MassGeneral Brigham Wentworth-Douglass Hospital in NH. We are also grateful to the Khan Family Foundation for funding this research project through their Student Research Fellowship.

IRB: Obtained study approval from MassGeneral Brigham IRB, Protocol #2024P000889, on April 24, 2024.

Can Medical Students Learn to Code?

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Introduction

Teaching billing and coding during medical training is neglected. Yet, proper billing and coding practice is necessary from regulatory, ethical, and financial perspectives and should be embedded in curricula[1,2]. As of 2019, the Centers for Medicare and Medicaid Services (CMS) passed major revisions that allowed evaluation and management (E/M) codes to streamline and focus primarily on medical decision-making (MDM) or time[5]. This simplification of the billing process makes coding more accessible and MDM more relevant to all, including medical students[7]. It is logical to train students in proper coding and billing practices as habits are formed[8]. What is the efficacy of a 35-minute educational intervention designed to teach E/M coding to third-year medical students?

Methods

Current UNE COM 3rd-year medical students were recruited to participate in an educational intervention consisting of a pretest questionnaire, a 20-minute prerecorded PowerPoint presentation, a post-test questionnaire, and the Kirkpatrick model of evaluation. The presentation included contextual information about U.S. healthcare which corresponded to the systems sections of the Level 2 and Step 2 board exam blueprints. The remainder focused on the elements of medical decision-making. A paired *t-test* was used to analyze differences in the number of correct responses between the pre and post-test questionnaires. The Kirkpatrick model of evaluation was used as a validated measure of participant perspective to further examine the efficacy of the intervention.

Results

Of 12 submissions, only three included all parts of the questionnaire and Kirkpatrick evaluation making quantitative interpretation impossible. The Kirkpatrick evaluations indicated a positive reaction, that learning occurred, that participant behavior was changed after the intervention, and that the presentation aligned with the learning objectives.

Conclusion

Despite an inability to interpret the quantitative results of the pre and post-test, the Kirkpatrick evaluation makes it possible to cautiously say that a 35-minute educational intervention given to third-year medical students is efficacious for teaching E/M coding. This study is undergoing minor content revision and will be redistributed with gift cards to aid participation in the class of 2026 for another round of data collection.

Acknowledgment

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TITLE: Modern Trends in Receipt of Adjuvant Chemotherapy From a Single Institution

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Radical Cystectomy (RC) is a standard of care for Muscle Invasive Bladder Cancer (MIBC). For eligible patients (pts), guidelines recommend adjuvant chemotherapy (AC) for pts at high risk of recurrence. Since 2021, multiple immune checkpoint inhibitors (ICI) were approved for AC. As our group provides >80% of RC care in a rural state, we examined contemporary trends in utilization of AC and subsequent outcomes at a single, high-volume center, following ICI approval.

313 pts were identified from a prospectively maintained database of pts undergoing RC for bladder cancer from 2015-2023. All pts were navigated to medical oncology perioperatively. Pts eligible for AC were selected based on final pathology in accordance with current guidelines with high-risk pathology defined as (y)pT3-T4 or (y)pN+. Trends of AC regimens were evaluated. Chi-square analysis was performed to compare the groups. Kaplan-Meier analysis was performed to assess for overall survival (OS).

Overall, 48/313 (15.3%) received AC and 168/313 (53.7%) received a complete course of neoadjuvant chemotherapy (NAC). For pts who received a complete course of NAC, 18/168 (10.7%) received AC. 9/18 (50%) received ICI, 7/18 (38%) received cisplatin, and 1/18 (12%) received cisplatin + ICI. In the non-NAC group 127/313 (40.6%) that received AC, 20/25 (80%) received ICI, 4/25 (16%) received cisplatin, and 1/25 (4%) received carboplatin (Table 1). Following approval of ICI in 2021, there was a 23% increase in use (Figure 1). AC pts were younger, with a mean age of 66.5 ± 10.0 vs 69 ± 10.3, p=.11, and had a lower mean BMI, 26.3 ± 5.6 vs. 28.1 ± 6.1, p=.45, compared with pts not receiving AC. 166 pts were considered to be high risk for disease recurrence. On Kaplan Meier analysis, there was an OS advantage in pts who received any AC (p=.075) (Figure 2). There were insufficient patients to assess for AC outcomes with ICI vs. chemotherapy.

We noted an overall increase in use of AC for high-risk urothelial cancer pts following RC, particularly ICI utilization increased since its approval. This illustrates the importance of multidisciplinary care and involvement of medical oncology. Pts with high risk for disease recurrence that received AC had improved OS compared to those not receiving AC, although not statistically significant. Future studies with a larger number of patients receiving AC will allow for assessing patient factors associated with OS and which pts receive adjuvant AC.

Acknowledgements
Research Conducted at Maine Medical Center and Funded through the Maine Health Institute for Research.

IRB Approval
This research has received exemption from the MaineHealth IRB (IRB# - 1728828-2) and from the UNE IRB (IRB # 0824-16)

Decreased Dose-Response to Fibrinogen Concentrate in Patients Experiencing Postpartum Hemorrhage: A Retrospective Dose-Response Study

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Introduction: Postpartum hemorrhage (PPH), defined as >1L of blood loss after delivery, is the leading cause of maternal morbidity and mortality worldwide. A fibrinogen level <200mg/dL is a leading predictor of PPH progressing to severe PPH, and early administration of fibrinogen concentrate (FC) has been shown to decrease complications and death. The manufacturer's equation for FC dose-response was derived from a 2009 study of 14 non-pregnant patients with afibrinogenemia and no active bleeding. However, our prior work showed a lower FC dose-response in pregnant patients with hypofibrinogenemia during labor. In this retrospective study, we compared the observed fibrinogen change (oFC) to the manufacturer's expected fibrinogen change (eFC). We also examined the clinical predictors of fibrinogen dose-response in PPH.

Methods: The patient database was examined for all parturients from 2015-2024 who received FC within 24h of delivery with documented pre- and post-dose fibrinogen levels. Patients who had a history of congenital fibrinogen disorders, chronic abruption, or intrauterine fetal demise without PPH were excluded. The primary outcome utilized a paired t-test to compare oFC versus the manufacturer's eFC after each dose. Additionally, fibrinogen change was compared between the acute PPH (aPPH) phase (bleeding onset through final red blood cell transfusion) and the recovery phase (the first 24 hours after the final blood product transfusion postpartum).

Results: In the final analysis of 162 FC doses, the overall mean oFC was 18.8 (6.6-30.9) vs mean eFC of 41.9 (37.1-46.6) (p=0.0005). The discrepancy was further pronounced in the aPPH group with an oFC of 7.0 (-5.9-19.9) vs eFC of 42.4 (36.8-48.1) (p<0.0001). There was no difference in the recovery group. The manufacturer's dose-response is 1.8 mg/kg. Our observed dose-response in the aPPH group was significantly less at 0.74 [-1.67-2.39] compared to the recovery group 2.42 [1.14-4.60] (p=0.0005). This resulted in 42% of patients experiencing a negative fibrinogen change in response to a FC dose during aPPH.

Conclusion: This study demonstrates a substantial discrepancy in oFC compared to the manufacturer's eFC in patients experiencing aPPH. The results suggest a near 3-fold higher dose requirement of FC during the aPPH phase than predicted based on the manufacturer's dose-response equation. Understanding the dose-response of FC during PPH is critical for rapid correction of coagulopathy and may improve PPH outcomes.

Acknowledgement: I would like to express my gratitude to the Brigham and Women's Hospital & Harvard Medical School, Department of Anesthesiology, for providing mentorship, access to resources, and facilities crucial for conducting this study. I appreciate the opportunity and financial support provided by the Foundation for Anesthesia Education and Research (FAER), through the Medical Student Anesthesia Research Fellowship (MSARF). Lastly, I would like to thank the University of New England College of Osteopathic Medicine for their support and education. This study was granted IRB exemption by both Mass General Brigham IRB committee (protocol #2023P002495) and University of New England Office of Research Integrity (protocol # 0924-09).

Assessing the Effect of Baseline Parasympathetic Nervous System Activity on Pain Inhibition by Sex

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Introduction: The nervous system can facilitate and inhibit pain, measured by temporal summation (TS) and conditioned pain modulation (CPM), respectively. The autonomic nervous system (ANS) responds to acute stressors, including pain, leading to a reduction in parasympathetic nervous system (PNS) activity. Observation of males and females indicates a difference in the processing of pain by the PNS. This study investigates the influence of parasympathetic activity on pain modulation in males and females.

Methods: Nineteen participants (age 19-34) have been tested. PNS activity was assessed using HRV measures collected during a 10-minute period of quiet rest. Pain inhibition was assessed with CPM using cold water immersion (CWI) as the conditioning stimulus and pressure pain threshold (PPT) as the test stimulus. Heat Temporal Summation (HTS) was measured by applying 10 heat pulses to the medial knee. Pain inhibition was measured after the CWI and after 20-min noxious electrical stimulation (NXES). Participants completed the DASS-21 (Depression Anxiety and Stress Scale) and PSQ (Pain Sensitivity Questionnaire).

Results: Across participants, PPTs were higher during CWI (♀: p=.060, ♂: p= .000), indicating pain inhibition. HTS was attenuated after (♀: p=.042, ♂: p= .376) CWI. No interaction effects were observed by sex. In response to NXES, inhibition of PPTs (♀: p=.170, ♂: p= .054), and attenuation of HTS (♀: p=.004, ♂: p= .010) were observed, but no interaction effects of sex. HRV measures did not correlate with inhibition of pressure pain, attenuation of HTS, pain sensitivity measures or depression, anxiety, or stress scores. However, prior to CWI, no relationships were observed between the HRV measures (PNN50, RMSSD, HF%PWR) and PSQ or DASS21 scores in females, but DASS21-Sum correlated with HF%PWR (r=-.886, p=.019) and PNN50 (r=-.771, p=.072) in males. In females, HRV prior to NXES showed relationships between anxiety (r=-.661, p=.038) and depression (r=-.614, p=.059) and RMSSD. In males, DASS21-Sum correlated with PNN50 (r=.771, p=.072) and DASS21-anxiety score with HF%PWR (r=-.675, p=.046).

Conclusion: Both CWI and NXES produced lower HTS, but CWI did not produce inhibition of pressure pain while NXES did. NXES may utilize a different inhibitory mechanism than CWI. Although HRV measures did not relate to the amount of PPT inhibition or HTS attenuation, relationships between HRV measures and DASS21 scores indicate that further study is warranted.

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IRB Study Registration: This project was approved by the UNE IRB under protocol #0423-06.

Continuing Quality Improvement and the Implementation of MRI targeted Prostate Biopsy at a Regional Medical Center

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Abstract:

This study aims to evaluate the effectiveness of Multiparametric MRI (mpMRI) and fusion biopsy technology adoption at Maine Medical Center. The utilization of mpMRI technology allows for more accurate detection of clinically significant prostate cancer (PCa) by combining a radiologically scored lesion of interest with a traditional 12-core biopsy template. The implementation of mpMRI began in 2016 and data was collected for the current study until the end of 2021; this research will assess potential areas of improvement over time. Data collection using mpMRI and subsequent biopsy using the Phillips UroNav system were implemented in 2016. The PI-RADS scored lesion(s) of interest were biopsied in addition to the traditional 12-core biopsy template. The data was then analyzed with a heightened focus on the probability of cancer detection (PCD) of intermediate to high clinical significance of PCa in PI-RADS 3, 4, 5 lesions. We defined the false-negative rate as the percent of patients who had negative biopsies using the fusion method but had clinically significant PCa using the traditional 12-core biopsy. We also collected urology-specific and general demographic information. Data from 390 patients was analyzed (9.5%, 49.2%, 40.3% PI-RADS 3, 4, 5 respectively). Overall, the diagnosis of clinically significant disease (CSD) increased over the five years of the study (≥ Gleason 3+4=7) = 65.1%. In addition, PCD increased yearly across PI-RADS 3, 4, and 5 scores, from 39% in 2016 to 64.1% in 2021. The false-negative rate declined from 52.4% to 27.0% throughout the study. Our findings exemplify the benefits of longitudinal initiatives to decrease false negatives and increase the PCa detection rate. Our institution increased its detection of CSD over the study period while having an overall prominent decreasing trend in false negatives across all PI-RADS scores. In addition, the rate of detection of CSD associated with PI-RADS 5 lesions increased over the study period. This accuracy can be attributed to familiarity with the fusion biopsy technique, radiologists' ability to score PI-RADS lesions correctly, and intense efforts for quality improvement.

Acknowledgements: This research was conducted at Maine Medical Center and was an investigator initiated, unfunded study.

A Systematic Review of Risk Factors and Diagnostic Measures of Postpartum Depression among Military Personnel

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Objectives: In recent years, there has been an increased recognition of mental health conditions among people who currently serve or have served in the armed forces. In particular, as the number of females occupying careers in the DOD grows, it is becoming more critical to screen for and treat female-specific mental health conditions such as postpartum depression (PPD) in this subpopulation. Per the available literature, the prevalence of PPD among female military personnel is significantly higher than that of the general U.S. population. That said, we hypothesize that there is a gap in the literature which characterizes the disparity that is seen between these populations in their presentation of PPD. It is critical to identify the unique risk factors military personnel have which may predispose them to this condition. This qualitative review aims to further describe the nuanced determinants of PPD in military females by isolating unique risk factors and screening measures.

Methods: A literature review including observational surveys, cohort studies, and scoping reviews from 2006 to 2024 was performed across databases such as: AccessMedicine, ClinicalKey, JSTOR, PsycInfo, PubMed, and ScienceDirect. A MeSH database-built search around key terms: “postpartum depression” and “military” was used to gather 19 sources that fit our inclusion criteria in evaluating our hypothesis. Assessment of screening techniques was performed on a subset of the articles that specified their screening tools and metrics in their methods.

Results: Out of the 19 sources referenced, 16 explicitly identify one or more of the following risk factors for the development of PPD in a military sample: active-duty status, deployment (self or spousal), race, history of depression, and social support. Out of the 10 survey publications that specified the screening tool(s) they used to evaluate for PPD: 7 used the Edinburgh Postnatal Depression Scale (EPDS), 1 used the Postpartum Depression Screening Scale (PDSS), while 2 used both.

Conclusion: Females in the military have exposure to novel risk factors for PPD within their role in the service, not experienced by U.S. female civilians. It is important to identify these risk factors to better facilitate diagnostics and care for PPD in this population. Consistent qualitative findings in our review suggest that early detection via widespread screening using any of the above screening tools leads to better disease outcomes and treatment usage.

Acknowledgement: The University of New England College of Osteopathic Medicine. A special thanks to the University of New England Library Services Department for their assistance in medical database utilization.

Deletion of 11β-HSD1 Prevents Craniofacial Bone Loss Caused by Caloric Restriction

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Introduction: With the rising prevalence of obesity in the U.S., calorie restriction (CR) has become an increasingly popular method for individuals to reduce body weight. It is well documented that CR helps in effective weight loss, however, there is also an associated loss in volume in appendicular long bones such as the femur or tibia. There is currently a lack of data showing bone loss effects of CR on craniofacial bones such as the mandible, which is imperative in speech and mastication. In these previous calorie restriction studies, there has been an increase in cortisol levels that is responsible for bone loss. 11β-Hydroxysteroid dehydrogenase type 1 (11β-HSD1) is an enzyme that works to convert glucocorticoids such as cortisone to cortisol in humans. In this study, we implemented a 11β-HSD1 knock out mouse model to observe for a protective effect on mandible bone loss found in CR.

Methods: 80 Male and female control and 11β-HSD1 KO mice at 8 weeks old were acquired. They were randomly assigned to either the ad libitum (AL) diet or a 30% calorie-restricted diet for 8 wks. Mice weight was measured every week. After 8 weeks of CR treatment, mandibles were isolated before being processed for microcomputed tomography (micro-CT) imaging and histology. The trabecular and cortical bone microarchitecture, volume, and mineral density of mice mandibles were evaluated.

Results: After 8 weeks, micro-CT showed a significant decrease in trabecular bone volume fraction (BV/TV) and bone marrow density (BMD) between the AL and CR diets in female mice. There was a significant protective effect on BV/TV and BMD between the calorie restricted control and calorie restricted 11β-HSD1 KO groups. These effects were not statistically significant in female cortical bone, but followed a similar trend. Male mice did not see a significant decrease in BV/TV and BMD between the AL and CR diets in both trabecular and cortical bones. There was also no significant protective effect on BV/TV and BMD between the calorie restricted control and 11β-HSD1 KO male groups.

Conclusions: 11β-HSD1 KO female mice saw protective effects in mandible trabecular BV/TV and BMD loss under caloric restriction. We found sex-dependent effects of 11β-HSD1 KO under caloric restricted diets as male mice did not experience similar effects. The improved bone morphology in 11β-HSD1 KO female mice suggests a way to protect against bone loss found in caloric restriction diets.

Acknowledgements: The Maine Health Institute for Research and the University of New England College of Osteopathic Medicine. Special thanks to the Rosen Lab for their support. IACUC approval was granted by the Maine Health Institute for Research IACUC committee (protocol # 2209).

Investigating Postoperative Urinary Retention (POUR): Risk Factors and Post-Surgical Outcomes in Total Joint Arthroplasty

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Abstract:

Introduction

Postoperative urinary retention (POUR) is a known complication after total joint arthroplasty (TJA), though it lacks consensus regarding its diagnostic criteria, prevalence, and risk factors. This study aims to quantify the rate of POUR, identify risk factors, and measure complication rates associated with catheterization.

Methods

Utilizing a prospectively collected institutional database, a single-center TJA cohort was retrospectively reviewed between April 2014 and March 2023. POUR rates were quantified utilizing three different diagnostic criteria. Variables of interest included age, sex, operative joint, body mass index (BMI), American Society of Anesthesiologists (ASA) score, Charlson Comorbidity Index (CCI) classification, and anesthesia type. Complications and urinary tract infections (UTIs) within 90 days of surgery were compared. Using overall complication rates among POUR patients, utilization and type of catheterization was evaluated.

Results

Among the 17,220 TJA patients identified, POUR incidence rates based on diagnostic criteria varied from 20% (based on presence of catheterization), 25% (based on >500 ml in postoperative bladder scan), to 29% (catheterization and/or bladder scan). Advanced age, male gender, lower Body Mass Index (BMI), moderate Charlson Comorbidity Index (CCI) scores, undergoing Total Knee Arthroplasty (TKA), and receiving spinal anesthesia were significantly more prevalent among POUR patients. The number of POUR patients who developed complications or UTIs within 90 days of surgery was not significant compared to patients without POUR. Among POUR patients, those who received a straight and indwelling catheterization were twice (OR=2.02, 1.09-3.74) as likely to develop complications compared to no catheterization ($p<0.05$).

Discussion

The diagnosis of POUR across a variety of diagnostic criteria remains high following TJA. Patients who underwent catheterization for the management of POUR were twice as likely to develop complications in the postoperative period compared to those who were not catheterized. Implementing protocols to reduce catheterization and risk stratification tools may provide a viable prevention strategy.

Acknowledgements: University of New England College of Osteopathic Medicine, Dr. Matthew Grosso, St. Francis Hospital Orthopedics Department, and Connecticut Joint Replacement Institute

IRB: IRB Approval for Waiver or Alteration of Consent and Individual Authorization for Disclosure of Protected Health Information. **IRB#:** SFH-23-30

Functional Connectivity Analysis of the Default Mode Network Using Self-Report of Spontaneous Cognition

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Introduction: Resting-state neuroimaging (rsfMRI) studies have deepened our understanding of cognitive alterations in clinical populations. In particular, functional connectivity (FC) of the default mode network (DMN), including the posterior cingulate cortex (PCC) – whose functions pertain to memory, attention, and internally-directed cognition – can show alterations within participants with mood disorders, perhaps related to rumination. However, it remains unclear the extent to which such alterations reflect ongoing cognition during the scan.

Methods: Eighty young adults (66% female; age: mean=23.49/SD=2.86) with varying psychiatric diagnoses underwent resting-state functional MRI using a multi-echo sequence. Spontaneous cognition during the scan was measured by the Amsterdam Resting-State Questionnaire (ARSQ) 2.0. Data were processed using a multi-echo independent components analysis package (TEDANA) and normalized into MNI space using fmriprep. Seed-based FC analysis was performed for each participant using a PCC seed, including denoising using motion and white matter/CSF data. Separate whole-brain regressions with all 10 ARSQ subscales, including motion/demographic covariates, were performed, using cluster corrected p_FWE=0.0025.

Results: Higher scores on the ‘Self’ subscale were associated with reduced PCC-left posterior insula FC (T=4.84, k=355); ‘Planning’ with reduced PCC-left mid insula FC (T=4.92, k=258; trend level on right); and ‘Verbal Instructions’ with increased PCC-right cerebellum FC (T=4.30, k=223).

Conclusion: These findings indicate a role for ongoing cognitive state in the interpretation of resting state neuroimaging findings, suggesting that the content of cognition during rest may be linked to altered patterns of FC between the PCC and insula/cerebellum. Such findings have implications for the development of rsfMRI biomarkers of mental illness, especially if clinical groups are expected to differ in their cognitive state while resting.

Acknowledgements: This research was completed at the University of Pittsburgh with the support of the National Institute of Mental Heath (Grant No. R37MH100041 [to MLP]). The study was granted IRB approval prior to the start of the project.

Intracranial Hemorrhage After Excessive Licorice Candy Consumption: A Case Report

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Case Description:

A previously healthy, athletic 65-year-old female with a history of bipolar disorder, migraines, and hypertension admitted for spontaneous right frontal ICH with subarachnoid hemorrhage extending into the superior temporal lobe, in an atypical area. Further workup for underlying conditions returned negative.

Assessment/Results:

Her initial functional levels upon admission to IRF were moderate to maximum assistance for ADLs with mobility at wheelchair level. She remained without neuropsychiatric behavioral issues and was very motivated. Further exploration of the cause led to questioning of the patient's dietary intake with findings that she consumed an excessive amount, 10-15 bags of licorice daily. She made tremendous progress, discharging home modified independence with a quad cane in 11 days.

Discussion (relevance):

A literature review found limited examples of licorice related hemorrhagic stroke, but did speculate that one of the major components is glycyrrhizin, which when hydrolyzed to glycyrrhetinic acid, possesses significant hypertensive effects. This patient also serves as an example of the important role physiatry plays in acute care in addition to delving further into the nature of otherwise atypical causes of certain diseases. The ability to focus on the patient's lifestyle, including dietary health, served as a way to find the atypical cause of this hemorrhagic stroke.

Conclusion:

Two important aspects we hope to shed light on through this case report are that there is still gpas in the literature between isolated, but similar events of excessive licorice consumption and spontaneous ICH and the importance of exploring further possible causes of otherwise unexplainable major life events of patients in IRF setting. Further exploration can help expand our understanding of processes that may benefit patients in the future.

Using Hands-on Culinary Medicine Education to Increase the Confidence and Ability of Medical Students to Address Lifestyle and Nutrition-related Disease.

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Introduction
Culinary medicine utilizes the approach of educating learners about food by active involvement in food preparation, quality, and consumption. In our study, we assessed the impact of culinary medicine intervention on medical students' nutrition knowledge and counseling skills.

Methods
Two cohorts of second-year UNECOM medical students were included in this study. In the first cohort, 15 students were randomly assigned to a control group (n=6) or an experimental group (n=9). The experimental group participated in a culinary medicine educational session which involved watching 4 modules, each focused on a medical condition (diabetes, cardiovascular, cancer, and pediatrics). Students then cooked meals aligned with each condition and discussed incorporating these meals into patient care. The effectiveness of nutritional counseling skills were assessed using Standardized Patient Exams (SPEx), with a main complaint of weight changes, hyperlipidemia, or poorly controlled diabetes. In the second cohort, 13 students participated in the SPEx before and after completing all of the culinary education sessions. Blinded grading was used on the recorded patient encounters (n=36) using a standardized rubric. The rubric consisted of 6 domains, (Assess, Advise, Agreement, Assistance, Arrange, and General Counseling Performance) with multiple questions to each domain. Questions were scored with a Likert scale ranging from 0 to 3.
Student T-test was used to evaluate the outcomes in both cohorts. Cohen's Kappa was used to assess inter-grader reliability.

Results
In the first cohort, the experimental group scored higher across the 5 A's than the control group on average. Some improvements were seen in Assess (1.55 to 2.10), Agree (1.32 to 1.98), and Assist (1.36 to 2.17). The second cohort demonstrated similar results with higher post-education score averages versus the pre-education score. Improvements were seen in Assess (1.72 to 1.95), Agree (1.46 to 1.88), and Arrange (0.77 to 1.59). Both cohorts also demonstrated an increase in the students' counseling scores (General Counseling Performance).

Conclusion
Culinary medicine education improved medical students' nutrition counseling skills, as reflected by higher rubric scores in the intervention groups. These results support the integration of interdisciplinary culinary medicine education in medical programs. Future studies should explore the long-term retention of these skills and their impact on patient outcomes.

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Molecular Basis for the Interaction of Phafin2 with the Actin Network During Macropinocytosis

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Introduction: Macropinocytosis is a vesicle-mediated process that allows for the uptake of extracellular fluid and molecules. Its failure contributes to cancer growth and inflammation. Phafin2 has been shown to play a critical role in macropinocytosis by interacting with phosphatidylinositol 3-phosphate (PI3P) and phosphatidylinositol 4-phosphate (PI4P). Phafin2's PH domain binds PI3P and PI4P, while the FYVE domain is specific for PI3P. Macropinocytic vesicle maturation depends on the actin network, specifically the cross-linking protein Filamin A, which binds to the PH domain of Phafin2. The aim of this study is to characterize the binding between the recombinant Filamin A Phafin2-binding region (PBR; residues 186-368) and to explore whether Filamin A binding enhances Phafin2's affinity for phosphoinositides, which facilitates progression of macropinocytosis.

Methods: To characterize the association, we purified Filamin A PBR using conventional protein purification procedures such as overexpression in *E. coli* bacteria and affinity chromatography. SDS-PAGE and Fast Protein Liquid Chromatography (FPLC) techniques were used to confirm the purity of the protein. Utilizing isothermal titration calorimetry (ITC), we measured the binding affinity, enthalpy, and stoichiometric ratio between the Filamin A PBR and Phafin2. Nuclear magnetic resonance (NMR) spectroscopy will be obtained to identify the specific binding site of Filamin A on the PH domain of Phafin2.

Results: ITC analysis revealed that Filamin A PBR binds to Phafin2 with a dissociation constant (Kd) of 1.08 ± 0.40 μM which is evident of a strong interaction. The analysis yielded a Gibbs free energy of -34.1 kJ/mol, indicating an exothermic reaction. A stoichiometry ratio of 1:1 is observed which suggests that for every 1 molecule of Phafin2, 1 molecule of Filamin A PBR is bound.

Conclusion: The data suggests an interaction between Phafin2 and Filamin A which is critical for macropinocytosis. Filamin A is dependent on Phafin2 and likely regulates the process through its interaction with the actin network. NMR resonance assignments are being conducted to determine the specific site of interaction of Filamin A PBR on the Phafin2 PH domain. Future work will examine if Filamin A binding to Phafin2 is dependent on concentrations of phosphoinositides within a cell. Further studies will focus on minimizing a fragment of Filamin A PBR needed for effective binding with Phafin2.

Acknowledgments: This research was conducted at Virginia Tech, Protein Signaling Domains Laboratory.

IACUC/IRB Compliance: N/A (this study does not involve human or animal subjects).

Title: The Impact of Telecommunicator CPR Program on Out-of-Hospital Cardiac Arrest Outcomes in Rhode Island: A Pilot Study

Authors:
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Introduction:
Out-of-hospital cardiac arrest (OHCA) is a leading cause of death worldwide, with survival rates dependent on the quality and timing of resuscitation. Rhode Island implemented a telecommunicator CPR (T-CPR) program in 2022, to improve the return of spontaneous circulation (ROSC) and neurologically intact survival rates by focusing on early initiation of CPR and minimizing interruptions during pre-hospital care. This study evaluates the effectiveness of T-CPR on outcomes in OHCA patients in Rhode Island.

Methods:
This multicenter, retrospective cohort study analyzed OHCA data from three hospitals in a single Rhode Island healthcare system (Lifespan Corporation) between May 2022 and September 2022. Patients treated under the T-CPR program were compared to those treated under the prior model in which bystanders were not provided CPR instruction in real-time. Data was sourced from EMS run sheets and hospital electronic medical records. The primary outcomes were the rates of bystander CPR, ROSC, survival to admission, 24-hour survival, and functional outcomes measured using the Cerebral Performance Category (CPC) score.

Results:
142 OHCA cases met inclusion criteria and baseline characteristics were similar between the groups. For the primary outcome of bystander CPR, the rate was 24% for the T-CPR group and 26% (p=0.31) for the previous program. Rates of ROSC (pre 39%, post 37%), survival to admission (pre 28%, post 30%), 24-hour survival (pre 25%, post 30%) and favorable CPC score (pre 7%, post 5%) were not significantly different. There was a non-significant (p=0.41) trend towards increased automatic defibrillator device (AED) use in the T-CPR group (10% pre, 16% post).

Conclusion:
This pilot study did not demonstrate a significant change in rates of bystander CPR/ROSC/CPC scores with the advent of a T-CPR program. The data did show a trend toward increased use of AEDs by bystanders, which may represent an impact of T-CPR instructions. These results are potentially limited by the heterogeneity of participating EMS agencies and a lack of statistical power demonstrated by a small sample size and short time intervals. Ultimately, a longitudinal, multi-year analysis would be needed to examine more definitively the degree to which the statewide T-CPR program implementation affects bystander CPR rates and OHCA survival in Rhode Island.

Acknowledgments:
Research was conducted in the Department of Emergency Medicine at the Alpert Medical School of Brown University. Funding was provided by the Peter Morgane Research Fellowship and the Alpert Medical School Summer Research Assistantship.

IRB Approval:
This study was approved by the Lifespan IRB, Providence, Rhode Island.

Regulation of Wnt Signaling Genes in Dexamethasone-treated Human Trabecular Meshwork Cells

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This study was conducted under UCLA's IRB oversight and was determined to be Non-Human Subject's Research by UCLA's Institutional Review Board.

Introduction

Glaucoma is the primary cause of blindness worldwide and is characterized by a gradient progression toward vision loss from damage to the optic nerve usually related to increased intraocular pressure (IOP). The common ophthalmological drug Dexamethasone (Dex) has been shown to impede the trabecular meshwork's (TM) functions and elevate IOP, which is a major risk factor for glaucoma. In recent studies, the use of Wnt signaling inhibitors has been shown to negate the Dex-mediated phenotype of the TM, suggesting abnormal Wnt signaling as a mechanism for steroid-induced glaucoma.

Methods

RNAseq data of 26 human TM cells assays treated with Dex versus vehicle was obtained using Illumina HiSeq 3000. FASTQ file was converted to raw counts data file and normalized using the DESeq2 package in RStudio. Differential gene expression analysis was further conducted to investigate the gene expression changes of Dex on Wnt signaling markers in TM cells. Ggplot2 package was used to create better visualization of Wnt activity.

Results

Dex-treated TM cells relative to the vehicle exhibited a statistically significant decrease in differential expression across markers for canonical and non-canonical Wnt signaling activity: DVL2, DVL3, FZD7, FZD8, LRP11, LRP12, SFRP4. While Dex-treated TM cells exhibited a decrease in expression across a few markers of Wnt signaling activity, exploratory data analysis revealed that the Axin2 gene, which is widely regarded as a general indicator for Wnt signaling pathway activity, was associated with upregulation post-Dex treatment.

Conclusion

Overall, changes in Wnt signaling activation are observed and the finding suggests abnormal Wnt signaling as a mechanism for Dex-induced increased IOP. Further investigation with RT-qPCR to confirm data is suggested along with analysis of publicly available microarray data to understand the specifics of the Wnt pathway further. Future study will also use differential gene expression data from results to investigate potential drugs to reverse gene expression. Candidate list of drugs will be obtained utilizing large-scale visualization of drug-induced gene expression database (L1000FWD).

Acknowledgements

University of California, Los Angeles and the Stein Eye Institute. I would like to acknowledge principal investigator Dr. Jie Zheng and mentors Dr. Chi Zhang and PhD candidate Luis Sanchez for their guidance. This research was supported in part by NIH grants GM100909.

Bone Marrow Adipose Tissue is Distributed Similarly in the Anterior to Posterior Plane in the Murine Tibia

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Background: Bone marrow adipose tissue (BMAT) is located in the marrow cavity of long bones, and impacts bone homeostasis. Increased BMAT can raise fracture risk, and BMAT increases with age, menopause, and metabolic disease. The amount of BMAT and its unsaturated to saturated lipid ratio varies spatially from the proximal to distal tibia. With increased age, BMAT in the proximal tibia decreases in size, whereas BMAT in the distal tibia remains unchanged. Spatial differences in BMAT distribution between anterior and posterior planes have not previously been explained. In this study, histologic images of the proximal tibia in 9- and 12-month-old male and female mice were analyzed to evaluate the differences in distribution and size of BMAT in the anterior to posterior plane. We hypothesized BMAT size and distribution would vary spatially in the anterior/posterior plane, and expected increased BMAT in females.

Methods: Hematoxylin and Eosinophil-stained images of the proximal tibia were obtained from 9- and 12-month old C57Bl6 mice (n=4-5/group). Using ImageJ software, the proximal region of the marrow cavity within the tibia was segmented into anterior, posterior, and central regions. Images were thresholded, noise removed, and adipocytes identified. Adipocyte size and number were recorded within each region. Adipocyte size was normalized to the area analyzed, and the percent of area occupied by adipocytes was calculated. 9- and 12-month-old mice were analyzed as separate cohorts. Differences in adipocytes per area, adipocyte size, and percent area covered by adipocytes of each region were compared via 2-way ANOVA using factors of region and sex.

Results: In 9- and 12-month-old cohorts, anterior, central, and posterior regions had similar numbers of adipocytes per area, adipocyte size, and percent area occupied by adipocytes. Females had more adipocytes per area and a greater percent area occupied by adipocytes in the marrow sites than males. No sex difference was identified in adipocyte size.

Conclusion: BMAT distribution is similar across the anterior to posterior regions in male and female mice. However, females had more adipocytes per area and greater percent area occupied by adipocytes. These sex-dependent findings are consistent with other BMAT studies, which may indicate a hormonal influence on marrow adiposity. This study emphasizes the importance of understanding how BMAT can be affected throughout the lifespan, especially in aging women.

Acknowledgements: This research was supported by MaineHealth Institute for Research. Animal work was approved by the MaineHealth Institute for Research IACUC Committee (Protocol #2209, previously Protocol #1914). Histology was performed at the University of New England Histology and Imaging Core, funded by NIGMS P20GM103643.

Community-Engaged Co-Design of Strategies for Family Caregiver Engagement during Inpatient Stays

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Introduction:
Progressive chronic diseases diminish quality of life, often requiring family caregivers (FCGs) to offer daily support. FCG engagement becomes essential during hospitalizations, especially for caregivers from underserved backgrounds who face competing demands like inflexible work hours, childcare, transportation, and healthcare literacy. Equity in Caregiving (EIC) is a 5-year NIH funded project addressing barriers faced by FCG and improving equitable caregiver engagement during a family member's hospitalization. As part of this project, we collaborated with community members and leaders at a local safety-net hospital to plan a series of convenings designed to foster collaboration between caregivers and clinicians. The March 2024 hybrid (in-person/online) EIC convening focused on enhancing FCG engagement within the hospital setting.

Methods:
The convening included a panel of FCGs and clinicians with real-time audience polling. FCGs addressed the following questions: "What makes an encounter with the [hospital] caregiving team rewarding? Please share your loved one's story and the barriers encountered in your engagement with clinicians. What could the clinicians have done in those interactions to better understand your experience?" Clinicians addressed the following questions: "What makes an encounter with FCGs rewarding?" The convening was videorecorded. Two research team members independently analyzed the recorded video using qualitative methods, classifying recommendations for improving FCG engagement.

Results:
Four domains emerged and highlighted barriers faced by FCGs and clinicians: caring for caregivers, enhancing communication, building trust, and setting realistic expectations for hospital care. Caregivers primarily addressed the healthcare system treating care as transactional, while clinicians spoke about time constraints as a significant stressor. Major recommendations from caregivers stemmed from providing tools for healthcare system navigation and hospital procedure while clinicians spoke about the need for systems to adopt an empathetic approach to care and provided practical tips to utilize interdisciplinary collaboration in helping FCGs.

Conclusion:
The March 2024 convening produced valuable recommendations that can foster collaboration between FCGs and clinicians. These insights offer a foundation for equitable caregiver engagement in hospitals and can inform future healthcare practices, policies, and subsequent convenings.

Acknowledgements: University of Massachusetts Chan School of Medicine, Worcester, MA. This work is supported by a NIH 5-year grant (2022-2027). IRB approval was obtained from UMass Chan School of Medicine's IRB in January 2022.

A Case of Aicardi Syndrome

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Abstract:
Aicardi Syndrome was first defined in 1965 by Dr. Jean Aicardi as a classic triad of infantile spasms, chorioretinal lacunae, and partial or full agenesis of the corpus callosum (AS) (Aicardi, 1965). Aicardi proposed a broader diagnostic criteria in 1999 to capture emerging evidence of a spectrum of severity. In addition to the classic triad the new criteria allows for diagnosis with at least 2 of the following: cortical malformations, periventricular and subcortical heterotopia, cysts around the 3rd ventricle and/or choroid plexuses, papillomas of choroid plexuses, optic disc/ nerve coloboma (Aicardi, 1999, King et al., 1998). AS is a very rare condition with estimates placing its world-wide prevalence between 400 and 4000 cases (National Organization for Rare Disorders, 2023, Kroner et al., 2008). AS is widely considered to be a de-novo X linked mutation that is only present in XX or XXY individuals; though no specific mutation has been identified to date. (Van den Veyver 2002, Donnenfeld et al., 1989). It is thought to be lethal in XY children with the three reported examples in XY individuals being largely dismissed (Chappelow et al., 2008, Curatolo et al., 1980, Aicardi, 1980, Hunter, 1980). People with AS demonstrate a range of cognitive disability. In addition to the CNS findings, AS is frequently associated with gastrointestinal problems. Glasmacher et al., 2007 reported 94% of respondents had recurrent episodes of constipation, 56% had reflux, 42% had abdominal pain and 85% had gastric feeding tubes. 55% of patients with AS had scoliosis and 33% had costoverterbal malformation including butterfly vertebrae. Glasmacher et al. further reported that 42% reported onset of puberty at a median age of 9.3 years and they suggest precocious puberty maybe an associated feature of AS.

This case study presents the story of 14 year old female with Aicardia who's seizures have been recalcitrant to pharmacotherapy requiring trial of 16 different medications. During the course of this management DD has stopped taking her medication either due to patient refusal or physician directed taper and both times DD's cognition, affect, and eating mechanics improved. In addition to detailing a very rare condition, this case highlights the need to balance the dangers of repeated seizures with the negative effects of anti-epileptics.

Acknowledgments:
This condition is so rare that the diagnosis alone is identifying. In public presentations I would be hesitant to provide information regarding the site of research.

Chartercare Medical Associates, Greenville, RI
Dr. Gary King - Mentor

The Effects of Arrow mRNA Knockdown On The Dendritic Arbor of Primary Nociceptors of *Drosophila melanogaster*

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Introduction: The Wnt/Wg pathway, which is well conserved across animal taxa, has been implicated in the regulation of abnormal pain, which 51.6 million US adults currently experience. However, the genetic components of this pathway have not been thoroughly explored to determine what their exact pain modulatory effects may be. Given this consideration, the hypothesis that Wnt/Wg co-receptor Arrow (mammal homolog: LRP6) plays a role in regulation of pain sensitivity was tested and led to further questions regarding mechanisms for the observed results. A secondary hypothesis formulated in response to this is underexpression of Arrow plays a role in regulation of pain sensitivity through control of the dendritic arbor morphology in *Drosophila melanogaster*.

Methods: Gal4/UAS and RNA interference genetic technology was used to precisely control gene expression of Arrow, allowing for underexpression specifically in the nociceptor. Experimentation using a 45°C thermal stimulus on manipulated *Drosophila* larvae allowed for measurement of escape behaviors which are triggered upon the detection of painful stimuli by the larvae. Dendritic length and branching were analyzed by ImageJ and Photoshop and Morphometric values were compared via t-test.

Results: Analysis of behavioral results suggest that larvae with underexpression of Arrow exhibited hyposensitivity to the thermal stimulation when compared to the normal controls. Arrow underexpressors displayed escape behavior responses at a significantly lower frequency than the normal controls. Underexpression of Arrow specifically in the nociceptor was associated with nominal neuromorphological reductions in dendritic length and branching. However, unpaired t-test showed the observed differences were not statistically significant.

Conclusion: Reduction of Arrow expression within the nociceptor is associated with decreased levels of nociceptive sensitivity, suggesting drugs treating these genetic components may be effective in treating abnormal pain in humans. However, the hypothesis that Arrow regulates dendritic morphology was not supported by these results. This may suggest that the observed behavioral hyposensitivity is not related to morphological changes in the dendritic arbor as a result of reduction of Arrow expression. Alternative hypotheses include that Arrow's control over sensitivity is accomplished by mechanisms intrinsic to the nociceptor, such as control of membrane excitability.

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Impact of CFTR Modulators on Pancreatic Function in Pediatric Cystic Fibrosis Patients: A Retrospective Analysis of FE-1 Levels

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Introduction:

Cystic Fibrosis (CF) is a genetic disorder resulting from mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene, leading to reduced Cl- transport and subsequent dehydration of mucus, and contributing to pancreatic insufficiency (PI). Around 85% of people with CF (PwCF) experience impaired pancreatic function due to obstructed pancreatic ducts. Pancreatic damage occurs in-utero and was previously thought to be irreversible in most cases. CFTR modulators, which enhance CFTR protein function, have shown efficacy with improved lung function in PwCF, but it remains unknown if pancreatic exocrine function is recoverable. Fecal-elastase-1 (FE-1) levels serve as a reliable marker for pancreatic exocrine function, with values below 200 mcg/g indicative of PI. This study aims to provide additional insights into the impact of CFTR modulators on pancreatic function for PwCF.

Methods:

We retrospectively analyzed electronic medical records (EMRs) of 60 CF patients age <19 years, treated with CFTR modulator therapy from 2019 to 2024. FE-1 values were assessed to determine pancreatic sufficiency status before and after modulator use. In 8 patients, a FE-1 value prior to modulator start time was not available. These subjects were previously classified as PI through clinical and genetic indications. The primary outcome was the percentage of patients who had converted their status from PI to pancreatic sufficient (PS). This study was deemed exempt by the MaineHealth Institutional Review Board.

Results:

Of the 60 patients who met criteria to have FE-1 repeated, 20 patients had repeat values available at the time of this analysis. Of the patients analyzed (N=20), 20% (N=4) exhibited a transition from PI (FE-1 <200 mcg/g) to PS (FE-1 >200 mcg/g) following CFTR modulator therapy. The median time to PS conversion in these 4 patients was 382.5 days from the start of

modulator therapy (range 243-1091 days). The age at conversion to PS ranged from 6 years to 15 years.

Discussion:

These results suggest that CFTR modulators may facilitate the conversion from PI to PS in some CF patients. The variability in response highlights the need for further research to elucidate factors influencing modulator efficacy such as genetic variability, co-morbidities, and patient age at the time of therapy. Further investigation is required to fully understand the impact of CFTR modulators on pancreatic function and to optimize therapeutic strategies.

Resource Constraints and Disease Management: A Case Study of Disease Progression in La Sabana, Panama

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Introduction: Healthcare access remains a topic of contention within Latin American indigenous communities. A significant portion of Panama's population is composed of the Ngäbe people, who lack access to healthcare due to the geographic isolation. Illness is poorly managed due to limited medical providers' ability to travel, inadequate monetary resources, and language barriers. Floating Doctors (FD), a non-governmental healthcare organization, provides services to remote populations in Panama and has addressed some healthcare gaps of the Ngäbe people.

Description: This case presents a 25-year-old Ngäbe woman from La Sabana, Panama, diagnosed with severe inflammatory joint disease. Presumed onset was at age 15 when she was unable to ambulate due to severe joint stiffness. FD first met her at the age of 19, when her disease progressed, and only symptomatic management was feasible. Her recent follow-up in the family's single-room hut, June 2024, exhibited new axial involvement, as well as bilateral ankylosis-like joint stiffness severely limiting her ROM. She remains by her window to watch her community with few verbal interactions. Support from her family (parents, siblings, and cousins) includes providing care. She relies on intense assistance in ADLs (toileting, bathing, transferring, and dressing). Due to language barriers and poor record keeping, an accurate family history was not acquired, though no similar familial conditions were noted. Physical examination revealed pressure sores on her right lateral malleolus, skin plaques on her knees bilaterally, and severe malnourishment secondary to decreased appetite and limited food accessibility.

Discussion: FD providers prescribed a 3-month supply of corticosteroids and antihistamines for inflammation, paracetamol for pain relief, and soap to maintain hygiene for her pressure sores. Further diagnosis requires imaging, MRI, and blood tests, which are not available. Lack of longitudinal medical intervention, nutritional support, and health education has exacerbated this patient's chronic condition. An accurate prognosis was not possible.

Conclusion: In alignment with the World Health Organization's Sustainable Development Goals (SDG), this case exemplifies the critical need for mobilizing healthcare resources (SDG 1.a) and addressing the malnutrition crisis (SDG 2.2) among the Ngäbe people. Achieving these goals is essential to ensuring healthcare access to bolster health outcomes within these communities.

Food Insecurity in University of New England Medical Students

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Introduction: Food insecurity is defined as the limited or uncertain availability of nutritionally adequate and safe foods or the limited or uncertain ability to acquire acceptable foods in socially acceptable ways by the USDA. Food insecurity is a growing problem and affecting nearly 30% of college students. The purpose of this study was to examine food insecurity in students at the University of New England College of Osteopathic Medicine (UNECOM).

Methods: A survey adapted from the US household Food Security Survey made by the United States Department of Agriculture (USDA), was distributed by email to osteopathic medical students enrolled and recently graduated from UNECOM. In addition to the quantitative scoring of the survey, open ended questions were included to qualitatively characterize the unique experiences of and challenges encountered by osteopathic medical students. The US household survey was quantitatively analyzed based on prescribed metrics developed by the USDA, which use affirmative answers (Yes and often) and score responses on a scale of zero to six. Scores of 0-1 are food secure households, 2-4 are low food insecure households and 5-6 are high food insecure households. Qualitative data was reviewed and categorized in most common challenges and barriers for medical students.

Results: The survey adapted from the USDA was scored based on affirmative answers. 70 students from UNECOM classes of 2024-2028 completed the survey. Preliminary results revealed that more than 41% of those who completed the survey have experienced food insecurity. Of those who completed the survey, 24% have experienced low food insecurity and 17% have experience high food insecurity. The survey also included short answer questions with qualitative data concerning the biggest challenges the participants faced. The challenges mentioned by students in the survey lack of time, stress and financial strain due to the demands of medical school.

Conclusion: The results of this study demonstrate that medical students at UNECOM struggle with food insecurity at higher rates than the general population across the United States. Medical students experience high levels of stress regularly through the course of their academic pursuits and clinical training. While many stressors are addressed and minimized through wellness and resiliency training offerings, food insecurity is a significant stressor for medical students. Interventions in this area would improve student wellness and may also improve academic, clinical and personal successes during osteopathic medical training.

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IRB: The University of New England IRB committee deemed this project exempt (Project # 0424-14)

Investigating Regional Sensory Distribution of the Saphenous Nerve in Tibial Periosteum

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Background: Osteoporosis significantly increases fracture risk and mortality, with 19% of osteoporotic fractures in adults over 65 resulting in death within a year. A greater understanding of factors influencing bone mineral density and fracture risk can aid in the development of novel therapeutic strategies to reduce adverse outcomes. Recent research examines the role of sensory innervation in regulating bone remodeling. Sensory neurons in the peripheral nervous system directly influence bone formation in skeletal development and fracture healing. Disruptions in sensory innervation result in reduced bone regeneration and increase fracture susceptibility. This highlights sensory nerves as potential therapeutic targets for osteoporosis and bone-related disorders.

The saphenous nerve is a terminal branch of the femoral nerve with both sensory and sympathetic fibers but no motor fibers. Its location in the lower extremity makes it vulnerable to injury in surgeries such as saphenous vein harvesting for CABG, as well as ACL and meniscus repairs. It is unclear whether injury to the saphenous nerve can increase the risk of osteoporotic fractures. Preliminary research from the Becker lab found that saphenous nerve transection (SNT) results in a 45% reduction in nerve fibers in the proximal lateral-most tibial periosteum. We hypothesize that SNT will cause even greater denervation in the medial tibial periosteum, given the nerve's anatomical course.

Methods: Experiments were performed in 8-week-old Nav1.8-Cre; TdTomato mice where sensory nerves were fluorescently labeled with a TdTomato reporter. Either a sham procedure or SNT was performed, where a 1-mm section of nerve proximal to the knee was removed to prevent re-ligation. Proximal transverse tibial sections (300 μm) of the right tibiae were cleared using SHIELD-fDISCO, stained with antibodies against β_3-tubulin, and imaged using confocal microscopy.

Future Directions: We will use Imaris to quantify total (β_3-tubulin+) and sensory (TdTomato+) neurons of the medial and lateral-most proximal tibial periosteum in sham and SNT mice (n=5/group/sex). A reduction in nerve fiber density in SNT mice compared to sham control mice would indicate saphenous nerve injury-induced denervation of the medial and lateral periosteal regions. These results will help us understand whether saphenous injury differentially affects regional innervation in the tibial periosteum, which will be further evaluated for impacts on bone health.

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Probability of Concurrent Incidence of Medial Meniscus Injuries with Anterior Cruciate Ligament Tears: A Literature Review.

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Introduction: In patients with anterior cruciate ligament (ACL) tears, there is reason to believe that the instability of the knee may lead to or indicate concurrent injury to the medial meniscus. The purpose of this study is to investigate the probability of concurrent incidence of medial meniscus injuries with ACL tears.

Methods: A literature review of pubmed and associated grey literature was performed. Searched key words included 'concurrent medial menical tears', 'ACL tears', and 'incidence of concurrent meniscus tears'. The articles selected were all English-language articles that examined common similarities within the epidemiology, biomechanics, and clinical impacts that influences a potential relationship between Medial Meniscus injuries and ACL tears. Factors such as patient age, gender, activity level, concomitant procedures, cause of injury, return to sport prior to surgery, and duration of time before ACL reconstruction were observed and analyzed.

Results: A total of 12 studies were analyzed with a total of 1939 patients suffering from an ACL tear. Within this subject pool, 65% of the subjects were male, 35% female, with an average age of 28.6 y/o (range: 17 – 66 y/o). A total of 50.95% (n = 988 patients) of the patients suffered a concomitant medial meniscus injury along with an ACL tear, 277 of these patients also had a lateral meniscus injury. Of the 1939 patients, 24.8% (n=481) were considered as chronic injuries (greater than 6 months between injury and surgery) indicating that a prolonged amount of time with knee instability can increase the chance of meniscus injury. It was also found that the medial meniscus ramp injuries were hard to diagnose using Magnetic Resonance Imaging and needed an exploratory knee arthroscopy to officially diagnose during the time of ACL reconstruction indicating that patient pre-surgery diagnoses are not always completely accurate.

Conclusion: ACL ruptures are a prime predictor of meniscus injuries. This implies that with an improved ability to diagnose ACL injuries with concurrent meniscus damage has the potential to also improve the success of the reconstruction procedure as well as the future quality of life for patients who suffer from these injuries. Influential factors such as premature return to sport, delayed ACL reconstruction, and age all play a role in the probability of a meniscus injury, primarily to the medial meniscus.