



Department of
Critical Care Medicine
Calgary



Thursday, October 24, 2024
8:00am - 4:00pm
Health Sciences Centre (Theatre 3)

17th Annual DCCM Research Day



UNIVERSITY OF CALGARY
CUMMING SCHOOL OF MEDICINE



Alberta Health
Services

Guest Speaker:

Dr. Keith Walley

OC, MD, FRCPC



Dr. Walley received his MD from the University of Manitoba in 1981, trained in Internal Medicine at McGill University, and subsequently trained in Critical Care Medicine at the University of Chicago. He has been a practicing Intensivist at St. Paul's Hospital ICU and investigator at the Centre for Heart Lung Innovation since 1988.

The focus of Dr. Walley's research is to investigate 1) the mechanism of decreased left ventricular contractility and other organ failure during sepsis and 2) the impact of genotype on patient outcomes in sepsis and systemic inflammatory states. Dr. Walley translates basic discoveries into clinical practice in the ICU. Together with Drs. Russell and Boyd, he recently demonstrated that blocking the function of PCSK9, an enzyme that inhibits the clearance of endogenous cholesterol from blood, is associated with increased pathogen clearance via the LDL-receptor, a decreased inflammatory response, and improved septic shock outcome. This important discovery facilitated the emergence of anti-PCSK9 therapies as one of the most promising treatments for sepsis. This discovery has led to further investigation into the role of lipoproteins in sepsis.

Training the next generation of clinician scientists is the other passion in my career. I led a multicentre CIHR Strategic Training in Health Research project over the course of 12 years. This led to over 50 postdoctoral trainees launching prominent academic and industry careers.

Event Schedule

Department of Critical Care Medicine Research Day October 24, 2024	
8:00am – 8:20am	Registration / Breakfast (in Lobby of HSC Theatre 3)
8:20am – 8:30am	Welcome / Opening Remarks Miriam and Arnold Winston Lectureship Introduction – Braedon McDonald
8:30am – 9:30am	Keynote Address – Keith Walley [<i>introduced by Braedon, moderated by Braedon</i>]
9:30am – 9:35am	Introduction to Presentations [<i>Braedon McDonald</i>]
<i>Session 1: Moderated by Natalia Jaworska</i>	
9:35am – 9:50am	<i>Sungki Park</i> ^T – Pilot Study of ECG Pattern Recognition Using Deep Learning Algorithms
9:50am – 10:05am	<i>Nicole Cho</i> ^T – Manipulation of a Microbiota-Immune Metasystem Dysbiosis Using Precision Microbial Therapy Reduces Gut Pathogen Number and Function and Improves Immune Function
10:05am – 10:20am	<i>Colin MacKenzie</i> ^T – Rapid Point-of-care Microbiome Sequencing from Critically Ill Patients for Precision Medicine Microbial Therapeutics
10:20am – 10:35am	<i>Jason Waechter</i> – A Longitudinal Clinical Reasoning Curriculum Reduces Cognitive Errors using Computer Algorithms to provide Feedback. Additionally: A Longitudinal Multi-Site Curriculum providing Deliberate Practice in Clinical Reasoning Reveals Patterns of Misdiagnoses among Pre-Clerkship Medical Students.
10:35am – 10:50am	<i>Jason Waechter</i> – Validation that a Longitudinal Multi-Site Clinical Reasoning Curriculum in Clinical Reasoning Improves Diagnostic Justification and Hypothesis Guided Data Collection. Additionally: A Longitudinal Multi-Site Curriculum providing Deliberate Practice in Clinical Reasoning Reveals Factors Associated with Reducing Rates of Misdiagnoses.
10:50am – 11:10am	Break – Snacks (in Lobby of HSC Theatre 3)
<i>Session 2: Moderated by Ken Parhar</i>	
11:10am – 11:25am	<i>Nicole Gilbert</i> ^T – Early Enteral Nutrition in Critically Ill Children: A Systematic Review and Meta-analysis
11:25am – 11:40am	<i>Kathryn Strayer</i> ^T – Cross-kingdom Potentiation of Bacterial Pathogens by Airway Candida Promotes Ventilator-associated Pneumonia
11:40am – 11:55pm	<i>Matthew Stephens</i> ^T – AptaPore: A Rapid, Cost-effective, and Scalable Aptamer Development Platform for Precision Medicine
11:55pm – 12:10pm	<i>Eric Pimentel</i> ^T – Metabolomics Insights into COVID-19 Severity

12:10pm – 1:00pm	Lunch (in HSC HMRB Atrium)
<i>Session 3: Moderated by Dan Niven</i>	
1:00pm - 1:15pm	<i>Victor Dong</i> – Outcomes of Acute Liver Failure Patients Not Listed for Liver Transplantation: A Cohort Analysis
1:15pm - 1:30pm	<i>Sampson Law</i> ^T – Evaluating the Appropriateness of Red Blood Cell Transfusions in Patients Admitted to Critical Care Units in Alberta
1:30pm – 1:45pm	<i>Jessica Jenkins</i> – Supporting Child Visitors in ICU
1:45pm – 2:00pm	<i>Bethany Trotter</i> ^T – Exploring Public Expectations of Care and Communication in Intensive Care Units: A Cross-sectional Web-based Survey
2:00pm – 2:15pm	<i>Theophany Eystathioy</i> – Facilitators and Barriers to Optimizing Sedation Practices in Critically Ill Adult Patients: A Qualitative Study
2:15pm - 2:30pm	<i>Karla Krewulak</i> – Patient and Family Centered Outcomes on Vasopressor Use in the ICU
2:30pm - 2:45pm	Break – Snacks (in Lobby of HSC Theatre 3)
<i>Session 4: Moderated by Victor Dong</i>	
2:45pm - 3:00pm	<i>Erica McKenzie</i> ^T – Cardiac Manifestations in High-Grade Subarachnoid Hemorrhage: A Single-Center Retrospective Cohort Study
3:00pm - 3:15pm	<i>Andreas Kramer</i> – Neuroimaging Findings Complement DCD-N Score in Donation after Circulatory Death
3:15pm - 3:30pm	<i>Mohammad Banoei</i> ^T – Utilizing Metabolomics to Investigate Primary and Secondary Injuries, Diagnosis, and Severity in Severe Traumatic Brain Injury (sTBI)
3:30pm – 3:45pm	<i>Amanda Roze des Ordons</i> – The Landscape of Trauma Experiences Among Resident Physicians
3:45pm – 4:00pm	<i>Katherine Kissel</i> – Understanding Intensive Care Unit Nursing Knowledge, Perceived Barriers, and Facilitators of Sepsis Recognition and Management: A Cross-Sectional Study
4:00pm	Wrap up and thank you – Dan Zuege

Note: ^T = Trainee

We would like to express our sincere thanks to Dr. Keith Walley for graciously agreeing to be a speaker at our 17th Annual DCCM Research Day.

The event would not have been possible without the generous donation from the Winston family in memory of Miriam and Arnold to establish an endowment with the Canadian Intensive Care Foundation.

This event is an Accredited Rounds activity (Section 1) as defined by the Maintenance of Certification program of the College of Physicians and Surgeons of Canada.

Abstract Presentations

Pilot Study of ECG Pattern Recognition Using Deep Learning Algorithms

Sungki Park¹, Chel Hee Lee^{2,3}, Christopher Doig^{2,4}, Christopher Grant^{2,5}, Jason Waechter^{2,6}, Paul McBeth^{2,7,8}

Affiliations:

- ¹ Master of Data Science and Analytics, University of Calgary
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Background: Detecting abnormalities on an electrocardiogram (ECG) is vital for timely and effective heart health management since ECG provides a detailed map of the heart's electrical activity related to arrhythmias, myocardial infarctions, and other cardiac disorders. Deep-learning algorithms have been explored to classify different rhythms; however, the distinct features of different rhythms have not been well explored for real-time abnormality detection.

Objectives: As a pilot study, our first aim is to establish and optimize our deep-learning model and discuss its diagnostic accuracy. The second aim is to exercise feature engineering to identify which rhythmic characteristics are differently associated with abnormal conditions.

Methods: We mixed CNN and LSTM algorithms using Python Keras. Half-hour samples of two-lead continuous ECG recordings from 48 patients collected in the MIT-BIH arrhythmia Laboratory were used. The diagnostic accuracy of testing samples is discussed using correctness, sensitivity, and specificity. We also visually examined random test samples with the trained signal. Finally, we identified the key features, PR, QRS, and QT intervals.

Result: We found 98% accuracy (Se:98%, Sp: 99%) for the normal ECG and 95.2 % (Se: 99% and Sp: 95.2%) for abnormal conditions on average. We confirmed the normal has reasonable approximation: $125 \pm 144\text{ms}$ (PR ref, $160 \pm 40\text{ms}$), $92 \pm 42\text{ms}$ (QRS ref, $100 \pm 20\text{ms}$), $421 \pm 59\text{ms}$ (QT ref, $400 \pm 40\text{ms}$). We found Left/Right Bundle Branch Block conditions have a shorter QT interval ($222\text{ms} \pm 60\text{ms}$) than the normal signal, and atrial premature conditions have shorter PR and QT intervals.

Conclusion: Constructing a reference normal ECG signal provides benefits such as real-time identification of abnormalities. We believe it is also applicable to validating machine-suggested diagnosis and developing an evaluation module of ECG reading. However, this study is based on the labeled data, which is believed to have no labeling errors.

Manipulation of a Microbiota-Immune Metasystem Dysbiosis Using Precision Microbial Therapy Reduces Gut Pathogen Number and Function and Improves Immune Function

Nicole A. Cho^{1,2}, Jared Schlechte^{1,2}, Braedon McDonald^{1,2}

¹Department of Critical Care Medicine, University of Calgary

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Background: Up to 50% of critically ill patients in the intensive care unit experience nosocomial infections, which are associated with a very high risk of in-hospital death. We have recently demonstrated that this high risk of nosocomial infections in critical illness is associated with dysbiosis of a microbiota-immune metasystem, whereby expansion of Enterobacteriaceae in the gut is coupled with systemic neutrophil dysfunction and impaired defense against infections.

Hypothesis: Metagenomic-guided design of a microbial consortia can be used to reverse gut Enterobacteriaceae overgrowth and associated innate immune dysfunction.

Methods: Metagenomic analysis of the fecal microbiota of 34 ICU patients was used to construct a therapeutic consortium (probiotic) of anaerobic bacteria that were prominently depleted from the microbiota of ICU patients. We utilized a humanized microbiota associated (HMA) mouse model in which germ-free (GF) mice were gavaged with fecal samples from an ICU patient with high Enterobacteriaceae. We tested the impact of our therapeutic consortia by gavaging with our probiotic for 5 days on Enterobacteriaceae colonization in the gut and systemic neutrophil function.

Results: The probiotic anaerobic consortium suppressed Enterobacteriaceae growth in an ex vivo co-culture assay. Administration of the therapeutic consortia to humanized microbiota mice colonized with Enterobacteriaceae-high ICU patient microbiota led to reduced Enterobacteriaceae in the small intestine, reduced AI-2 cell communication signaling, and improved neutrophil extracellular traps production and phagocytosis capacity by bone marrow-derived neutrophils.

Conclusion: Metagenomic-guided design of a precision microbial therapeutic targeting microbiota-immune metasystem dysbiosis in critical illness effectively suppressed Enterobacteriaceae growth and function and may improve systemic neutrophil function, which may improve outcomes in the ICU.

Rapid Point-of-care Microbiome Sequencing from Critically Ill Patients for Precision Medicine Microbial Therapeutics

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Background: Pathological changes in the gut microbiota of critically ill patients have been linked to the development of hospital acquired infections in the ICU, leading to exploration into microbial therapeutics for these patients. A limitation of current approaches is its “one size fits all” approach to patients rather than considering each patient’s microbiome. Previous work from our lab identified specific characteristics of the microbiome linked to an increased risk of infection (reduced biodiversity and expansion of Enterobacteriaceae), creating an opportunity to individualize microbiome-targeting therapy towards patients with this signature of gut dysbiosis.

Objective/Hypothesis: Long-read sequencing (Oxford Nanopore Technology) coupled with real-time data analysis can be used to achieve point-of-care microbiome analysis from critically ill patients in the ICU, in a manner that is rapid, accurate, cost-effective, user friendly, and feasible to guide microbiome-based treatment.

Methods: Utilizing fecal samples, we developed a rapid sequencing workflow with an optimized real-time data processing pipeline. We will determine the ability of rapid metagenomics to identify patients with signatures of gut dysbiosis to enable future clinical trials of individualized microbial therapeutics.

Results: Originating from a fecal swab, we can sequence the entirety of the gut microbiome from a critically ill patient for the total cost of ~\$150CAD. This complete pipeline, from swab to clinically relevant microbiome metric, is completed in approximately 3 hours, with clinically relevant microbiome profiles within 30 minutes of sequencing.

Conclusions: This work seeks to overcome a major barrier in the field of personalized microbiome interventions by delivering an innovative strategy to characterize an individual’s microbiome rapidly at the point of care, with no advanced expertise, for a fraction of the cost of conventional sequencing. This work has the potential to transform the field of microbiome medicine, and its application towards the important clinical problem of hospital-acquired infections in the ICU.

A Longitudinal Clinical Reasoning Curriculum Reduces Cognitive Errors Using Computer Algorithms to Provide Feedback

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²Department of Mathematics and Statistics, University of Calgary

Background: Cognitive errors are important contributors of diagnostic errors. To date, no educational intervention has demonstrated a reduction in cognitive errors, such as premature closure, failure to rule out, anchoring, or confirmation bias.

Objective: Our study aimed to define and measure the change in frequency of these cognitive errors during a longitudinal clinical reasoning (CR) deliberate practice curriculum.

Methods: In a prospective multi-site 2-year observational study, first- and second-year pre-clerkship medical students completed between 13 and 19 self-directed online simulated CR diagnostic cases. CR skills assessed included: creation of the differential diagnosis (Ddx), diagnostic justification, ordering investigations, and identifying the most probable diagnosis. Student performances were compared to expert-created scorecards and students received detailed individualized feedback for every case. Specific algorithms were created to identify premature closure, failure to rule out, anchoring, or confirmation bias. When cognitive errors were identified, students were provided immediate feedback with explanations of their errors.

Results: We analyzed 6,318 cases completed by 406 students at 3 medical schools; 22% of cases were misdiagnosed. Cognitive errors were common: at the start of the curriculum, 60% of students demonstrated at least 1 cognitive error per case and the average number of errors per student was 1.5. This was reduced to 20% of students with a similar 1.5 errors per student at the end of the curriculum ($p < 0.001$).

Conclusions: Cognitive errors are widely recognized as contributing to diagnostic errors. We identified cognitive errors in real time using computer algorithms and provided this feedback to students. This educational strategy for diagnostic clinical reasoning appears to reduce cognitive errors, including premature closure, failure to rule out, anchoring, and confirmation bias. To our knowledge, this is the first report of an educational intervention that has succeeded in reducing diagnostic cognitive errors.

A Longitudinal Multi-Site Curriculum Providing Deliberate Practice in Clinical Reasoning Reveals Patterns of Misdiagnoses Among Pre-Clerkship Medical Students

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Background: Understanding patterns of diagnostic errors among medical students could guide the development of diagnostic clinical reasoning curricula.

Objective: Our study aimed to categorize and quantify patterns of misdiagnoses.

Methods: In a prospective multi-site 2-year observational study, pre-clerkship medical students completed online simulated CR diagnostic cases. CR skills assessed included: creation of the differential diagnosis (Ddx), diagnostic justification, ordering investigations, and identifying the most probable diagnosis. We defined and measured the frequency of two misdiagnosis categories: 1) “failure to build the Ddx” when the correct Dx was never added to the Ddx, and 2) “failure of Dx justification” when the correct Dx was in the Ddx but not chosen. We hypothesized strategies to mitigate them. In both categories, students self-reported either a knowledge deficit or a reasoning error as the cause of their misdiagnosis.

Results: We analyzed 1.55 million data from 12,202 cases completed by 1,083 students (83% consent rate) at 5 medical schools; 2,493 (22%) cases were misdiagnosed. Two categories of misdiagnosis were identified: the correct Dx was either never added (75%) or was added (25%) to the Ddx. Deficits in knowledge and reasoning data are still being analyzed and will be available at the time of the conference.

Conclusions: Failure to add the correct Dx to the Ddx occurred in 75% of all misdiagnoses; therefore, strategies to mitigate this error are important. We hypothesize that thorough pertinent negative diagnostic justification could create awareness that the correct Dx is missing from the Ddx by ruling out all incorrect Dx's, thus leading to Ddx revision. Failure to identify the correct Dx within the Ddx comprised the other 25% of misdiagnoses. Diagnostic justification also differentiates the correct Dx from the incorrect Dx's and can potentially reduce all misdiagnoses in both categories. Diagnostic justification should be a focus of diagnostic clinical reasoning education.

Validation That a Longitudinal Multi-Site Clinical Reasoning Curriculum in Clinical Reasoning Improves Diagnostic Justification and Hypothesis Guided Data Collection

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Background: Clinical reasoning education is an important intervention to improve clinical reasoning skills and reduce misdiagnoses. We have previously published single-site data showing that students score poorly in diagnostic justification but can improve their diagnostic justification skills as well as hypothesis generated data collection with a longitudinal deliberate practice curriculum. This project aimed to confirm and validate those results with multi-site data.

Objective: This project aimed to confirm and validate previously published results with multi-site data.

Methods: In a prospective multi-site 2-year observational study, first- and second-year pre-clerkship medical students completed between 13 and 19 self-directed online simulated CR diagnostic cases. CR skills assessed included: creation of the differential diagnosis (Ddx), diagnostic justification, ordering investigations based on their Ddx and case details, and identifying the most probable diagnosis. Student performances were compared to expert-created scorecards. Individualized and detailed feedback was provided to every student for every case completed relating to their diagnostic justification and ordering of tests.

Results: We analyzed 6,318 cases completed by 406 students (83% consent rate) at 3 medical schools. Scaled scores for diagnostic justification significantly improved from 2.5 to 4.5 ($p < 0.001$). Scaled scores for ordering tests increased from 4.1 to 7.0 ($p < 0.014$).

Conclusions: This multi-site study confirms our previous single site results that a longitudinal clinical reasoning curriculum with deliberate practice improves diagnostic justification and hypothesis guided data collection skills. Clinical reasoning curricula should explicitly develop these skills because improved performance of these skills is associated with reduced rates of misdiagnoses.

A Longitudinal Multi-Site Curriculum Providing Deliberate Practice in Clinical Reasoning Reveals Factors Associated with Reducing Rates of Misdiagnoses

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Background: Diagnostic errors cause significant patient harm and improving clinical reasoning (CR) education could contribute to reducing these errors. It is imperative to understand which components of clinical reasoning have the biggest impact on reducing misdiagnoses so that a curriculum can focus on these aspects.

Objective: This project aimed to measure the association of different components of diagnostic reasoning with misdiagnoses

Methods: In a prospective multi-site 2-year observational study, first- and second-year pre-clerkship medical students completed between 13 and 19 self-directed online simulated CR diagnostic cases. CR skills assessed included: creation of the differential diagnosis (Ddx), diagnostic justification, ordering investigations, and identifying the most probable diagnosis. Student performances were compared to expert-created scorecards and students received detailed individualized feedback for every case. A 3-tiered multi-variate logistic regression was used to determine strength of association between the components of CR and rates of misdiagnosis.

Results: We analyzed 6318 cases completed by 406 students at 3 medical schools; 22% of cases were misdiagnosed. Variables that predicted a reduction of misdiagnoses included: practicing more cases, spending more time analyzing the history, better performance of diagnostic justification, better performance of ordering tests, avoiding cognitive errors, and spending less time ordering tests. All p values are < 0.0001. The R2 coefficient of determination for our regression model was 0.52.

Conclusions: We hypothesize that more time spent on the history indicates appropriate data analysis, while more time spent ordering tests indicates guessing or “fishing”. Our data informs that educational strategies for diagnostic clinical reasoning skill development need to focus on: diagnostic justification, ordering tests and identifying cognitive errors. Additionally, the data supports a longitudinal curriculum that provides multiple practice cases with detailed feedback, which is aligned with well accepted theories of skill development for competence and expertise.

Early Enteral Nutrition in Critically Ill Children: A Systematic Review and Meta-analysis

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²Community Health Sciences, University of Calgary

³Faculty of Medicine, University of Calgary

Background: Guidelines for feeding critically ill children recommend the use of early enteral nutrition (EEN).

Objective: To use systematic review methods to synthesize and evaluate evidence for EEN in pediatric intensive care units regarding mortality and clinical outcomes compared to delayed enteral nutrition (DEN).

Methods: We searched MEDLINE, EMBASE, CINAHL, and CENTRAL databases up to October 2023. Studies were included if they assessed clinical outcomes in critically ill children who received EEN compared to DEN. Screening, extraction and risk of bias assessment was conducted in duplicate by two reviewers using discussion to resolve differences. Data was pooled in the meta-analysis of mortality using random-effects models. Secondary outcomes were examined for the directions of associations and reported qualitatively. PROSPERO (CRD42021286271).

Results: Mortality meta-analysis: Thirteen studies (1 RCT, 12 cohort studies) reported mortality outcomes, however, only four appropriately adjusted for confounders including severity of illness. In the meta-analysis adjusted for confounders, receiving EEN was associated with reduced mortality (adjusted OR 0.45 (95% CI: 0.25, 0.82), I² 45.0%, n=6059). Stratification by quality, EEN definition and mortality definition resulted in non-significant associations, signaling that between study heterogeneity and residual confounding may be present. **Qualitative review:** Eighteen studies (1 RCT, 17 cohort studies) of 9829 subjects were included. Positive associations with EEN or no differences between groups was found for length of stay and invasive respiratory support, a positive association with EEN for nutritional adequacy and infectious complications, and no difference between groups for hemodynamic support and gastrointestinal complications. After adjusting for confounding, no harmful effects of EEN were reported.

Conclusion: Evidence suggests there may be a beneficial effect of EEN over DEN, however; study heterogeneity and residual confounding reduces confidence in pooled effect estimates. Importantly, no harmful effects of EEN were found across multiple domains, supporting guideline recommendations to feed early.

Cross-kingdom Potentiation of Bacterial Pathogens by Airway Candida Promotes Ventilator-associated Pneumonia

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Background: The lungs harbour a distinct community of microorganisms that are important in lung health and homeostasis. In chronic lung diseases the lung microbiome shows significant alterations (dysbiosis) which is associated with adverse outcomes. Similarly, patients with acute lung injury in intensive care units (ICU) who require mechanical ventilation also suffer dysbiosis of the lung microbiome, which has been linked with adverse outcomes, including hospital-acquired infections and increased mortality. Most of the work has focused exclusively on the bacterial microbiome and ignored the fungi that also colonize the lungs. In particular, *Candida* is commonly found in the lungs of ICU patients, and its presence is associated with an increased risk of bacterial ventilator-associated pneumonia (VAP) for unclear reasons.

Objective/Hypothesis: We hypothesize that lung colonization by *Candida* potentiates the development of bacterial VAP by augmenting the growth and virulence of bacterial pathogens and promoting airway inflammation and damage.

Methods: Endotracheal aspirate samples were collected from 49 ICU patients at the FMC ICU. DNA was extracted for 16S and ITS2 amplicon sequencing to characterize the bacterial and fungal microbiome. Human airway epithelial cell lines were used for in vitro analysis of patient *Candida* isolates.

Results: Approximately 60% of the patients have *Candida* colonization in the lungs, which is associated with an increased risk for bacterial VAP or all-cause mortality. *Candida* colonization is also associated with higher relative abundance of common bacterial VAP pathogens (*S. aureus*, Enterobacteriaceae, *Pseudomonas*, *Acinetobacter*). In vitro co-culture of *Candida albicans* with these bacterial VAP pathogens demonstrated that *Candida* potentiates pathogen growth. Co-culture of *Candida* and bacterial pathogens induces more epithelial cell death than the *Candida* or the bacteria on their own.

Conclusions: We see that in ICU patients on mechanical ventilation, airway colonization by *Candida* spp. results in pathological cross-kingdom interactions to potentiate the growth and virulence of bacterial pathogens, culminating in an increased risk of bacterial VAP.

AptaPore: A Rapid, Cost-effective, and Scalable Aptamer Development Platform for Precision Medicine

Matthew Stephens¹, Colin MacKenzie^{2,3}, Jared Schlecht^{2,3}, Kathryn Strayer^{2,3}, Pierre-Yves von der Weid¹, & Braedon McDonald^{2,3}

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Background: Aptamers, refined from vast collections of random oligonucleotide sequences, can bind to a wide range of targets, including important clinical proteins. While they are as effective as monoclonal antibodies, aptamers offer distinct advantages such as easier modification, smaller size, and better scalability. However, their use in diagnostics and clinical settings is still limited, mainly due to lengthy selection processes (taking 3 to 7 weeks) and high sequencing costs (around \$3000).

Objectives: To establish a platform for the rapid and cost-effective identification of single-stranded DNA (ssDNA) aptamers targeting clinically relevant proteins using Oxford Nanopore technology.

Hypotheses: We hypothesize that Oxford Nanopore technology can be utilized to sequence ssDNA aptamers more rapidly and cost-effectively than previously reported methods.

Methods: Aptamers targeting recombinant Candidalysin (ECE1) from *Candida albicans* were isolated using SELEX (Systematic Evolution of Ligands by EXponential enrichment). This process involved 7 rounds of positive selection against the target peptide and 3 rounds of counterselection against non-specific compounds. SELEX was conducted over 3 days, with library preparation and Nanopore sequencing taking place on the 4th day. After 24 hours of sequencing, the abundant sequences were compiled and analyzed using the web-based APptamer analysis pipeline. The top candidate, named "AptCandi," was then synthesized for further testing.

Results: ELISPOT assays confirmed that AptCandi detected recombinant Candidalysin and Candidalysin from both wild-type and clinical *C. albicans* isolates, but not from ECE1 knockout strains, highlighting its specificity.

Conclusion: Although Candidalysin is a critical clinical target, resources for its detection are limited. Here we demonstrate that this Nanopore-based workflow can generate specific ssDNA aptamers in just 5 days at a cost under \$300. Future work will explore the platform's multiplexing capabilities and aim to develop aptamers for microbial and human targets where reliable antibodies are unavailable, advancing both diagnostic tools and potentially therapeutic development.

Metabolomics Insights into COVID-19 Severity

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Background: In 2019, SARS-CoV-2, the novel coronavirus, entered the world scene presenting a global health crisis with a broad spectrum of clinical manifestations, significant morbidity and mortality. Recognizing the significance of metabolomics has become a useful tool for predicting clinical outcomes. Metabolomic studies have indicated variations in the metabolome corresponding to different severities of COVID-19, highlighting the potential of metabolomics to unravel crucial insights into the pathophysiology of SARS-CoV-2 infection.

Methods: We undertook a scoping review following the PRISMA guidelines and involved a systematic search of three major scientific databases – PubMed, Directory of Open Access Journals (DOAJ), and BioMed Central – covering studies published between 2020 and 2024. The search yielded 2,938 articles, which were screened according to predefined inclusion and exclusion criteria. From this, 42 relevant articles were identified for further review, and 11 studies were selected for analysis of recurrently identified metabolites. Severity of disease was assessed wherever possible using the NIH definitions of mild, moderate, severe, and critical COVID-19 disease.

Results: Phenylalanine, glucose and glutamic acid increased with severity, while tryptophan, proline and glutamine decreased, highlighting their significant roles in COVID-19 severity. Metabolites that increased with higher degrees of severity include leucine, phenylalanine, tyrosine, lactate, glucose, glutamic acid, kynurenine and C10:2. Metabolites that decreased with progressing severity of COVID-19 include tryptophan, proline, glutamine, citric acid, citrulline, and isoleucine. Additionally, pathway analysis revealed that phenylalanine, tyrosine and tryptophan biosynthesis, along with arginine biosynthesis were the most significantly impacted pathways with COVID-19 severity.

Conclusion: The metabolic alterations highlight disruptions in amino acid metabolism, energy production, immune response modulation and redox balance. Pathway analysis revealed significant disruptions in phenylalanine, tyrosine, tryptophan and arginine biosynthesis, highlighting the importance of these pathways in managing immune response and inflammation.

Outcomes of Acute Liver Failure Patients Not Listed for Liver Transplantation: A Cohort Analysis

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Background: Acute liver failure (ALF) is a rare condition leading to morbidity and mortality. Liver transplantation (LT) is often required but patients are not always listed for LT. There is lack of data regarding outcomes in these patients.

Objective: Our aim is to describe outcomes of ALF patients not listed for LT and to compare them with those listed for LT.

Methods: Retrospective analysis of all non-listed ALF patients enrolled in the Acute Liver Failure Study Group (ALFSG) registry between 1998 and 2018. Primary outcome was 21-day mortality. Multivariable logistic regression was done to identify factors associated with 21-day mortality. Comparison was then made with ALF patients listed for LT.

Results: 1672 ALF patients were not listed for LT with 1564 having outcome data. Median age was 42 [Interquartile Range (IQR) 30-54]. 362 (29.8%) patients were too sick to list for LT. Most common etiology was acetaminophen (APAP) toxicity (53.9%). 558 (35.7%) patients died at 21 days. After adjusting for relevant covariates, King's College Criteria (KCC) [adjusted odds ratio (aOR) 3.17, CI 2.23-4.51], mechanical ventilation (aOR 1.53, CI 1.01-2.33), and vasopressors (aOR 2.10, CI 1.43-3.08) ($p < 0.05$ for all) were independently associated with 21-day mortality. Compared to listed patients, non-listed patients had higher mortality (35.7% vs. 24.3%). Patients deemed not sick enough had greater than 95% survival while those deemed too sick still had greater than 30% survival.

Conclusion: Despite no LT, majority of patients were alive at 21 days. Survival was lower in non-listed patients. Accurate prognostication is important in this patient population and clinicians are highly accurate at predicting those who are not sick enough to need a LT (spontaneous survival rate of over 95%). Prognosticating patients deemed too sick to survive however still remains somewhat of a challenge (spontaneous survival rates of over 30%).

Evaluating the Appropriateness of Red Blood Cell Transfusions in Patients Admitted to Critical Care Units in Alberta

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Background: Using a hemoglobin threshold of 70g/L in non-bleeding patients, studies have identified that upwards of 60% of red blood cell (RBC) transfusions in intensive care units (ICUs) might be unnecessary. However, critically ill patients often present nuanced circumstances whereby a threshold of 70g/L might not always be suitable. We examined blood product utilization as mapped to appropriate utilization guidelines developed through systematic evidence review and expert consensus. This report focuses on RBC utilization.

Objective: Evaluate the appropriateness of RBC transfusions in critical care units in Alberta between July 1, 2023, and June 30, 2024.

Methods: This was a retrospective observational cohort study among patients admitted to critical care units in Alberta – 15 adult ICUs, 2 adult cardiovascular ICUs, 13 adult coronary care units and 2 pediatric ICUs. Appropriateness guidelines were developed through systematic evaluation of existing guidelines and Provincial expert consensus. From these guidelines, detailed data definitions were developed to identify appropriate RBC transfusions. Alberta Health Services Data and Analytics department provided source data from the EPIC electronic information system. RBC transfusions with a reference hemoglobin result within 12 hours before the RBC order were considered appropriate if the hemoglobin was below the appropriateness threshold.

Results: During the study period, 6,664 RBC transfusions were administered to 2,169 patients. Using a hemoglobin threshold of 70g/L, 31.3% (n=2,089) of RBC transfusions given to non-bleeding patients were identified as unnecessary. Using scenarios and thresholds defined within the evidence-based appropriateness guidelines, 9.4% (n=625) of RBC transfusions were potentially unnecessary. RBC transfusions flagged as unnecessary using a hemoglobin threshold of 70g/L that were then identified as appropriate using guideline-specific algorithms were among patients that had acute ischemic cardiovascular disease, acute neurologic injury, and following cardiac surgery.

Conclusions: Commonly used hemoglobin thresholds may overestimate the number of potentially unnecessary RBC transfusions. To obtain more accurate estimates, analyses should be considerate of detailed appropriateness thresholds.

Supporting Child Visitors in ICU

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Background: Healthcare providers (HCP) in the intensive care unit (ICU) are often faced with supporting child visitors in crisis situations. Visiting family is critical to the psychological well-being of children faced with serious illness or loss of loved ones (Lamiani et al., 2021). The absence of studies exploring the experience of child visitors in ICU perpetuates the assumption that ICU is an unsafe place for children. Indigenous families have expressed concerns that children will be apprehended by child services when a parent is admitted (Bowker et al., 2022) which may impact their decision to allow children to visit. To provide safe, developmentally appropriate patient and family centered care (PFCC), we are embarking on a multi-phase project aimed at improving support and access to ICU for children.

Objective: To describe the facilitators and barriers to child visitors in Calgary Zone ICUs.

Methods: We have developed a survey with interdisciplinary HCP, Indigenous community members, PFCC representatives, and adults who experienced ICU as children to explore facilitators and barriers to child visitors in ICU. The survey will be distributed electronically to HCP in ICU who provide direct support to families.

Results: Without the proper tools to provide evidence-informed interventions to support child visitors there may be unaccounted impacts on children, including fear, anxiety, and long-term adjustment issues that impact their well-being. Operational barriers (restricted visiting hours, infection control policies, or general restriction of child visitors) prevent meaningful visits. Non-operational barriers (lack of healthcare provider education to support children with emotional distress or discomfort with communicating based the developmental understanding of the child (Brauchle et al., 2023) may negatively affect children faced with a critically ill family member.

Conclusion: Through the understanding of barriers and facilitators of child visitors in ICU, we hope to create lasting interdisciplinary collaborations to support families facing critical illness.

Exploring Public Expectations of Care and Communication in Intensive Care Units: A Cross-sectional Web-based Survey

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Background: Explaining critical illnesses to family members or support persons of patients admitted to an Intensive Care Unit (ICU) is a sensitive and challenging duty for healthcare providers (HCPs). Current literature indicates that families often report insufficient and inadequate communication from critical care staff, leading to stress, anxiety, and sometimes even post-traumatic stress disorder (PTSD). Inaccurate media portrayals of ICU care and healthcare further contribute to unrealistic expectations, resulting in a mismatch between family expectations and the reality of care in ICUs.

Objective/Hypothesis: This study aimed to identify and understand the public's expectations of ICU care and communication if they were a family member or support person of an ICU patient.

Methods: A 36-question online survey of the Canadian public (n=489) was conducted to explore their expectations should they have a family member admitted to an ICU. The currently used and validated Family Satisfaction in the ICU (FSICUR-24) tool was used as a basis for the survey in this study, with the questions amended to be public facing. Participants were recruited through social media. The inclusion criteria required participants to be Canadian citizens or residents, aged 18-65 years, and could not have had any previous exposure or experience in ICUs.

Results: Participants expressed high expectations for substantial emotional support, frequent and clear communication from all specialties of HCPs, compassionate care, and a supportive physical environment. Recommendations for practice based on these findings include improving family conversations by managing expectations, expanding ICU HCP education, and procuring organizational support.

Conclusions: The public holds high expectations of ICU care, particularly regarding communication and support. Understanding these expectations can help improve families' experiences, foster better communication, and improve patient and family-centred care in ICUs.

Facilitators and Barriers to Optimizing Sedation Practices in Critically Ill Adult Patients: A Qualitative Study

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Background: Sedation is a common intervention used to support critically ill patients, but suboptimal sedation can lead to prolonged mechanical ventilation and increased delirium incidence. Sedation practices in the intensive care unit (ICU) are complex and present several challenges.

Objective: The objective of this study is to systematically explore relevant factors influencing sedation practices among ICU healthcare professionals.

Methods: We conducted qualitative semi-structured interviews with critical care healthcare professionals including physicians, nurses, pharmacists, respiratory therapists, and physiotherapists to understand sedation practices and define the key factors that limit the opportunity for sedation optimization.

Responses were analyzed with deductive thematic analysis using the Theoretical Domains Framework (TDF) to identify and describe constructs within the relevant domains.

Results: Twenty-five semi-structured interviews were conducted virtually from April to June 2024 comprised of 12 physicians/nurse practitioners, 5 respiratory therapists, 4 nurses, 3 pharmacists and 1 physiotherapist. Preliminary analysis identified eight relevant TDF domains across healthcare professional groups including Behavioral regulation, Belief about capabilities, Emotion, Memory, attention and decision processes, Social influence, Belief about consequences, Environmental context and resources, and Social/professional roles. Participants reported use of sedation for multiple purposes including patient and staff safety, unit culture practices and various challenges (e.g., night shift, patient care efficiency) among the health care professionals. Participants reported several strategies for optimizing sedation delivery to critically ill patients including available sedation recommendations for specific patient populations (e.g., alcohol withdrawal) and for weaning sedation as well as clear sedation indications. Participants reported that recommendations would need to be flexible, nursing-driven, evidence-based and include multidisciplinary perspectives.

Conclusion: Health care professionals working in the ICU reported several factors that influence sedation practices. Interventions designed to optimize sedation practices should address these contributing factors in as part of their implementation strategies.

Patient- and Family Centered Outcomes on Vasopressor Use in the ICU

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Introduction: While vasopressors are essential in managing some life-threatening conditions, they come with potential risks and side effects that can impact patient outcomes.

Objective: To elicit perspectives from patients and families regarding the use and benefits/risks of vasopressor therapy in the ICU.

Methods: We conducted a qualitative interview-based study. We recruited ICU survivors and family members of ICU patients through ongoing research studies and pre-existing patient and family partner groups. Prior to participating in an interview, participants received orienting educational materials and a recorded slide presentation to explain vasopressor use in the ICU. The interviews explored factors that influence their willingness to undergo vasopressor therapy, focusing on perceived benefits, concerns about risks, and the importance of specific patient outcomes. Interviews and focus groups recordings were transcribed verbatim and analyzed using inductive content analysis.

Results: Participants included 25 individuals: 9 ICU survivors (36%), 8 family members of ICU patients (32%), and 8 members of the public without ICU experience (32%). We identified three key contextual factors influencing their views on vasopressor use in the ICU: illness trajectory, pre-existing health conditions or medications, and routine intervention. A willingness to undergo vasopressor therapy was shaped by three main factors: trust in the healthcare team, perceived low probability of risks, and belief that side effects could be monitored or managed. Participants were generally willing to accept the risks of vasopressor therapy when they believed that the benefits, such as maintaining stability and supporting survival, outweighed the risks.

Conclusions: ICU survivors and family members highlighted several factors that influence their comfort and willingness to undergo vasopressor therapy in the ICU particularly when focusing on immediate goals such as stabilization and survival. The findings highlight the importance of acknowledging these contextual factors in clinical discussions, emphasizing the routine nature of vasopressor use.

Cardiac Manifestations in High-Grade Subarachnoid Hemorrhage: A Single-Center Retrospective Cohort Study

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Background: Cardiac injury is a frequent complication of aneurysmal subarachnoid hemorrhage (aSAH). Manifestations include electrocardiogram (ECG) changes, echocardiographic abnormalities, and shock. High-grade aSAH may be associated with higher rates and severity of neurocardiac injury, however, few studies have focused on cardiac manifestations in high-grade aSAH.

Objective/Hypothesis: We characterized the incidence, echocardiographic features, and clinical severity of neurocardiac injury among aSAH patients with World Federation of Neurological Surgeons (WFNS) grade 3-5 aSAH, hypothesizing higher-grade patients would have more frequent and severe neurocardiac injury.

Methods: We retrospectively evaluated WFNS grade 3-5 aSAH patients admitted to the intensive care unit at a neurosurgical referral center in Alberta, Canada between 2009-2019, excluding patients who did not have an echocardiogram within 7 days of admission. We performed descriptive statistical analysis to characterize neurologic sequelae, cardiac features, and mortality.

Results: Among 242 patients with WFNS grade 3-5 aSAH admitted 2009-2019, 95 (39%) underwent echocardiography within 7 days of admission. 38 (40%) had a reduced ejection fraction (EF); 11 (12%) had severe involvement with EF < 30%. Univariate analysis showed lower presenting Glasgow Coma Score (GCS), elevated troponin T, and T-wave inversion were associated with reduced EF. Classic Takotsubo apical wall motion abnormalities were associated with anterior SAH aneurysm location ($p = 0.03$) and moderate-to-severe LV dysfunction ($p = 0.04$). ICU mortality and neurologic outcome on were not significantly different between patients with reduced and preserved EF (mortality 50% vs. 37%, $p=0.20$, neurologic outcome 70% vs. 65%, $p=0.63$).

Conclusions: Predictors of neurocardiac injury in high-grade aSAH included troponin elevation, T wave inversion and lower presenting GCS. Aneurysm location was associated the pattern of wall motion abnormalities and severity of cardiac dysfunction. Among high-grade aSAH patients, ECG findings, troponin elevation and aneurysm location can help identify patients who warrant echocardiography.

Neuroimaging Findings Complement DCD-N Score in Donation after Circulatory Death

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Background: Controlled donation after circulatory death (DCD) is feasible only if circulatory arrest occurs soon after withdrawal of life-sustaining measures (WLSM). When organ recovery cannot occur because the time interval is too long, negative implications include prolongation of end-of-life care, perceptions of “secondary loss” for patients’ families, and substantial resource consumption.

Objective: The DCD-N score is a validated tool for prediction of death within 60 minutes following WLSM. We hypothesized that the DCD-N score would (1) similarly predict death within 2-3 hours; and (2) perform better with addition of neuroimaging findings.

Methods: DCD-N scores were prospectively determined in consecutive patients where consent for DCD had been obtained. The most recent neuroimaging was reviewed by one of the investigators and perimesencephalic cisterns classified as normal, partially effaced, or completely effaced. The outcome of interest was time from WLSM to death. Logistic regression was used to assess the ability of DCD-N score and radiographic findings to predict death within 2 hours of WLSM.

Results: Of 115 consecutive potential DCD donors, 81 (70%) died within 2 hours of WLSM. DCD-N score and effaced basal cisterns were highly predictive of time from WLSM to death. When basal cisterns were patent, the chance of death within 2 hours of WLSM was 48%, compared with 90% for both partially and completely effaced cisterns ($p < 0.0001$). In a multivariable model, the odds ratio for prediction of death within 2 hours was 6.2 (2.6-14.8) for each incremental DCD-N score and 12.7 (3.6-45.1) for the presence of either partially or completely effaced cisterns. Results were similar for prediction of death within 1 or 3 hours.

Conclusion: The presence of cerebral edema with effaced perimesencephalic cisterns strongly predicts rapid death following WLSM in potential organ donors and improves upon performance of the DCD-N score alone.

Utilizing Metabolomics to Investigate Primary and Secondary Injuries, Diagnosis, and Severity in Severe Traumatic Brain Injury (sTBI)

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Background: Traumatic brain injury (TBI) is a significant global public health issue, leading to high rates of injury-related death and disability. Severe traumatic brain injury (sTBI), representing only 10% of all TBI cases, results in a mortality rate of 30-40%. This study investigated the potential of metabolomics to aid in the diagnosis of sTBI and to assess primary and secondary brain injuries in sTBI patients.

Methods: Serum samples were collected from 59 adult sTBI patients and 35 age- and sex-matched orthopedic injury (OI) controls. These samples were analyzed using quantitative metabolomics, to measure and identify metabolites at days 1 and 4 post-injury. Advanced analytical techniques were employed to identify metabolite patterns related to sTBI diagnosis and those potentially linked to primary and secondary brain injuries.

Results: Univariate and multivariate analyses revealed distinct serum metabolic profiles between sTBI and OI controls, with significant metabolite alterations observed between days 1 and 4 post-injury. The number and magnitude of altered metabolites were greater on day 4, suggesting a progression from primary to secondary brain injury. Patients at high risk of secondary injury, indicated by treatment to lower intracranial pressure (ICP), showed notable similarities in their sequential metabolite alterations from day 1 to day 4. Discriminant models using metabolomics data demonstrated high sensitivity and specificity in distinguishing sTBI patients from OI controls. On day 1 post-injury, energy metabolism-related metabolites were significantly altered. By day 4, metabolites related to neurotransmission, catecholamine activity, and excitotoxicity, showed increased levels. Some metabolites were associated with injury severity on day 4, while others correlated with injury severity on day 1.

Conclusion: This study demonstrates that serum metabolomics hold promise for the diagnosis of sTBI and offers insights into the molecular mechanisms of primary and secondary brain injuries. The findings underscore the need for further research and validation of sTBI metabolite biomarkers in larger cohorts.

The Landscape of Trauma Experiences Among Resident Physicians

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Background: Many residents experience trauma in their personal and professional lives. This carried trauma can impact their well-being, relationships, learning, and performance. Previous research has had an epidemiological and biomedical focus and has failed to describe the experience of residency training with carried trauma.

Objective: The purpose of my research was to explore the phenomenon of trauma to inform approaches to resident support.

Methods: The study used a combined phenomenological and phenomenographic methodology. All residents at the University of Calgary and those providing support to them were invited to participate. Semi-structured individual interviews were conducted to explore lived experiences and understandings of trauma and its impacts. The audio-recorded interviews were transcribed verbatim and analyzed using a hermeneutic phenomenological lens.

Results: Thirteen residents and three support professionals participated. Their stories were encapsulated by five core domains, each with multiple subdomains (indicated in parentheses): the experience of trauma (individualized, internal reactions, layered judgments), the impact of trauma (unfavourable, favourable, tensions), adaptations to trauma (cognitive, behavioural), healing from trauma (acknowledging, triggering, finding meaning, spectrum of healing), and moderators of trauma (previous life experiences, internal resources, environmental factors). Three metanarratives were identified that intersected these domains: complexity, sociocultural influences, and existential tensions.

Conclusions: Trauma experienced by residents can carry forward over time and across contexts. The in-depth understanding of residents' experiences of trauma developed through this study draws attention to how supports and structures might be adapted in ways that could support individual residents and address problematic aspects of the learning environment.

Understanding Intensive Care Unit Nursing Knowledge, Perceived Barriers, and Facilitators of Sepsis Recognition and Management: A Cross-Sectional Study

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Background: Early sepsis recognition and priority management remain a health priority. Numerous factors, including workforce challenges, translation of evidence, and systems-level barriers may impact nursing sepsis recognition and management within the intensive care unit (ICU).

Objectives: To (1) evaluate current ICU nursing knowledge of sepsis recognition and management, (2) explore individual and environmental/organizational factors impacting nursing recognition and management of sepsis utilizing the Theoretical Domains Framework (TDF), and (3) describe perceived barriers and facilitators to nursing recognition and management of patients with sepsis.

Methods: A survey, comprised of single/multiple choice, true-false, Likert-based, and open-ended responses was distributed to ICU nurses working in four general system ICUs from October 2023 to January 2024. Survey results were analysed using descriptive statistics and effect modification through modelling of an interaction term. Open-ended questions exploring barriers and facilitators to sepsis recognition and management were analysed using qualitative content analysis according to the Theoretical Domains Framework (TDF).

Results: A total of 101 nurses completed the survey. Effect modification was noted between years of ICU nursing experience and the prioritization of cultures over antibiotics (odds ratio 1.09 [95% confidence interval: 1.01-1.17]). Amongst Likert-based statements eliciting agreement, and classified by TDF domains, highest agreement was noted for the questions: early sepsis detection saves lives (n=98, 97%, TDF Domain Beliefs About Consequences) and nursing care can improve patient outcomes (n=97, 96%, TDF Domain Optimism). Barriers and facilitators to sepsis recognition and management were commonly identified across the TDF domains of Knowledge, Skills, Environmental Context and Resources, and Social Influences, which included workload/staffing, knowledge/competency, equipment/resource availability, and collegial support.

Conclusion: Sepsis recognition and management amongst ICU nurses is influenced by factors at individual and environmental/organizational levels. Future research and quality improvement initiatives are required to address the complex barriers to sepsis identification and management.