



Critical Care Canada Forum 2020 Abstracts

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A New Provincial-Level ICU Database in Nova Scotia

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Introduction: The intensive care unit (ICU) is a complex environment with high rates of resource utilization, patient morbidity, and mortality¹. The medical data of ICU patients is essential to measure and improve patient care in the ICU, and thus has the potential to impact the healthcare system². In Nova Scotia (NS), there are 14 adult ICUs that vary in size from small community ICUs to regional or tertiary care ICUs. The only ICU-related data available in NS until 2018 was provided by the Canadian Institute of Health Information (CIHI). Deficiencies in CIHI data on ICU visits led to an incomplete picture of ICU care in NS. Therefore, a dedicated database was needed to collect data on ICU visits in NS.

Objectives: To describe the steps taken to design, develop, test, and implement a provincial-level database to collect and store data on patients admitted to adult ICUs throughout NS.

Methods: The steps taken were as follows: (1) the scope of the project and the stakeholders to be involved were identified; (2) administrative approval was obtained, and funding secured; (3) data elements to be collected and stored in the database were identified; (4) an online data-entry program was developed; (5) the developed ICU database was rolled out to 12 adult ICUs in NS, and staff trained on its usage; (6) reports were created to summarize data entered into the database; (7) a governance committee was established for ongoing oversight, and a process for sharing data with research projects was established.

While the steps are presented chronologically, parts of one-step were often needed to complete other steps, and some steps were revisited after others were completed.

Results: The process resulted in three separate categories of datasets to accommodate significant variations in the needs of different levels of ICUs, namely, community (level-3), regional (level-2), and tertiary (level-1). A graphical user interface for the database was created. Users can view and enter data elements determined by their login credentials associated with their ICU. Data elements are prospectively entered while patients are still admitted to the ICU. Data is entered by bedside nurses in community ICUs, and by dedicated data entry staff at tertiary care or large community centers. Reports summarizing collected data can be generated dynamically by users for selected ICUs and time-periods using the BusinessObjects program. Data entered into the database up to the beginning of the previous calendar day are reflected in reports, which can viewed within the BusinessObjects program or exported in multiple file formats.

Building and implementing this database took two years, and it is currently operational in 12 adult ICUs in NS.

Conclusion: We have built a province-level ICU database for use in NS to facilitate informed decision-making about resource utilization and to identify areas that require improvement. In particular, the ICU database has been used as part of provincial COVID-19 planning. Also, the database is contributing to several research projects in identifying new patient patterns not previously understood. The methods and resources shared here will aid other jurisdictions in developing local, regional, or provincial databases.

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Aligning Critical Care Resources in Response to COVID19: Anticipating the Worse, Responding with the Maximum Ventilator and Critical Care Capacity at Humber River Hospital

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Introduction: Early 2020, the Novel Coronavirus (COVID-19) overwhelmed healthcare systems. Inadequate critical care resources, including supplies and ventilators to support the volume of anticipated patients suggested we needed to prepare immediately.

Objectives: The decision to prepare was three-fold: evaluate current state preparing to expand space and care delivery by 58% immediately; maximize critical care, ventilator capacity and resources to create 106 beds; develop a monitoring system for capacity, equipment and supplies.

Methods: Over 8 weeks, administrative leadership, professional practice, practice leads; infection prevention & control (IPAC) and supply chain specialists held daily video meetings to coordinate immediate needs. A Critical Care dashboard was created, providing a twice daily snapshot of beds available, ventilators, dialysis availability, critical drugs and supplies; and the number of COVID-19 positive patients. A new chronic ventilation unit (CVU), on a respiratory ward was created with support of Registered Respiratory Therapists (RRT). Ward nurses were trained over a three-week period on ventilation, using a multi-modal approach. RRTs working as pulmonary function technologists were re-deployed and trained to manage chronic ventilators, daily tracheostomy care and maintenance of critical care respiratory equipment. Logistically, the Post Anaesthetic Care Unit (PACU) space was outfitted with an additional Omnicell for medication management, and equipment and supplies to support an ICU patient population. Operating rooms (OR) remained operational for emergent cases, and patients recovered in ORs to prevent contamination from satellite ICU patients. Nurses from PACU, Same Day Surgery (SDS), and ORs received critical care education and utilized a “team” nursing model led by an ICU lead. Anesthesia assistants (AA) were re-deployed to work alongside RRTs. RRTs were trained on Anaesthetic Gas Machines (AGM) by AAs. Critical supplies were monitored with a threshold for re-ordering and twice weekly reporting. Simulation exercises on donning and doffing of personal protective equipment, protected intubations and extubations,

code blue and proning were ongoing.

Results: Mobilization of resources to support 106 Critical Care beds was completed. Two phases planned, an increase to 60 beds, with a plan to add 46 more. Capacity was created by operationalizing a CVU, a satellite ICU, and 4 additional monitored non-ventilated beds on a Cardiology unit. To mitigate the risk, critically ill COVID-19 suspect or positive patients remained in the main ICU. Of the 48 critically ill COVID-19 cases, 58% were from the ward, 42% were from the Emergency Department. Seventy six to ninety percent of all ICU patients required ventilation, maintaining a high ventilator and supply demand.

Conclusions: Capacity was planned for 106 patients, 60 beds were utilized. Patients requiring ventilation remained high increasing a need for respiratory therapists by almost 20%. Additionally, ICU, PACU, OR and SDS nurses worked collaboratively to provide care to critically ill patients in a satellite ICU. Adaptability, resilience and enhancement of newly formed inter-professional and inter-unit teams were unexpected outcomes. Partnerships, efficiencies, and processes in safety and IPAC measures were strengthened maximizing resources. Humber River Hospital is well positioned to maintain a readiness to respond to expected waves in the future.

An Analysis of ICU Transfers in Nova Scotia – Does the transfer of Critically Ill Patients in Nova Scotia Between ICUs Improve Outcomes?

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Introduction: Critically ill patients are often transferred from lower acuity ICUs to higher acuity ICUs with more specialized care with the hopes of improving outcomes. However, the impact of inter-facility transfer of ICU patients on outcomes has not been well defined. A number of studies indicate poorer outcomes for these patients,¹⁻⁴ while others suggest equivocal or improved outcomes.⁵⁻⁷ Nova Scotia (NS) is an ideal setting to investigate the effect of inter-facility transfer on ICU as it has a single tertiary care adult ICU that receives regular transfers from 11 regional and community ICUs.

Objective: The objective of this study is to estimate differences in case-mix adjusted hospital mortality between adult ICU patients in NS that are transferred during their ICU visit compared to those that are not transferred.

Methods: All visits to 12 adult medical-surgical ICUs in NS between April 1, 2018 and March 31, 2020 were analyzed. For each visit, data on patient demographics, transfer status, APACHE IV score, ventilation, delirium, mortality, and length of stay was obtained from the NS Provincial ICU database. The NS Provincial ICU database has prospectively captured data since April 1, 2018 for all patients admitted to one of the 12 adult ICUs in the province. A generalized linear mixed effects model was used to estimate differences in the case-mix adjusted hospital mortality between patients that are transferred between ICUs during their ICU visit and those that are not transferred. A generalized linear mixed effects model was chosen as it controls for differences in case-mix via fixed effects while also controlling, via random effects, for random variability present in ICU care at different centers. Fixed effects used to control for case-mix included Acute physiologic and chronic health evaluation (APACHE) IV predicted mortality, APACHE IV admit diagnosis category, location prior to ICU admission, pre-ICU length of stay (hrs), ventilation in the first 24 hours, age, gender, and transfer during ICU stay. Odds ratios (OR) were calculated to determine differences in hospital mortality between patients that were transferred and those that were not.

Results: A total of 10,028 ICU visits were recorded from April 1, 2018 to March 31, 2020. 395 ICU visits (3.94% of all ICU visits) involved transfers between ICUs. In patients that **were transferred** during their ICU stay, hospital mortality was 25.3% (100 of 395), APACHE IV predicted hospital mortality was 28.4%, and standardized mortality ratio (SMR) was of 0.89. In patients that **were not transferred** during their ICU stay, hospital mortality was 18.2% (1758 of 9633), APACHE IV predicted hospital mortality was 16.05%, and SMR was of 1.13. Generalized linear mixed effects modelling showed that ICU stay was associated with a 0.2 percent decrease in the relative odds of hospital mortality (OR = 0.998) at fixed levels of the remaining covariates, but this association was not statistically significant at level 0.05 ($p = 0.99$).

Conclusions: Our analysis showed that the transfer of critically ill patients between ICUs in NS does not result in lower hospital mortality after correction for differences in case-mix. Further analysis is required to determine if transfers result in mortality benefit in certain sub-groups of ICU patients. Greater scrutiny may be needed to determine which ICU patients warrant transfer between ICUs in order to balance the risks of transfer with any potential benefits.

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An Assessment of Barriers and Facilitators to Prone Positioning Mechanical Ventilation in Severe ARDS Using the Theoretical Domains Framework

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Background: Use of prone position invasive mechanical ventilation (PPV) in moderate to severe ARDS is associated with life saving benefit. Its use is also recommended in guidelines. Despite this, several observational studies have demonstrated that it is underutilized, suggesting a gap between evidence-based research and implementation in the real world. Barriers to the implementation and use of prone positioning in ARDS remain undefined.

Objective: Our aim was to describe the barriers and facilitators to the use of PPV in adult intensive care units across the province of Alberta using the Theoretical Domains Framework (TDF).

Methods: A survey questionnaire was created, and pilot tested. The questionnaire included assessment of 1) knowledge of ARDS and PPV (5 questions) and 2) barriers and facilitators to the use of PPV exploring all 14 domains of the TDF (5-point Likert scale with 26 questions). The questionnaire and survey were conducted through email invitation to 15 medical-surgical adult ICUs and 2 cardiovascular adult ICUs (n=17) in Alberta and data was collected through a secure web-based electronic platform (Qualtrics). Physicians, nurses and respiratory therapists were eligible to participate and respond.

Results: A total of 536 health care professionals participated in the questionnaire and survey, including nurses (52%), Respiratory therapists (28%), Intensivists (8.8%) and Critical care fellows (1.9%). The majority of respondents were from tertiary hospitals (61%) and had receive specific training on PPV within the past year (51%). When interrogated about ARDS and PPV, the majority answered correctly on questions pertaining to the Berlin definition of ARDS (77%), the benefits of PPV (99%), the minimal duration of PPV (61%) and contraindications to PPV (99%). However, only a minority of participants (43%) were able to correctly identify the PaO₂/FiO₂ ratio cut-off where PPV has been shown to save lives. For the TDF survey segment, respondents felt strongly about beliefs about capabilities (mean scores of 4.45 and 4.56 (out of 5) and optimism (4.59) regarding PPV. In contrast, when surveyed about presence of anxiety (Emotion domain), respondents reported anxiety about performing prone positioning (2.89). Additionally, significant risks of was identified as a possible negative social influence (3.69). Availability of decision support tools as a memory aid for PPV, as well as the presence of a periodic review of PPV practice were both modestly supported (3.76).

Conclusion: Among ICU health care providers, self-perceived knowledge of PPV and ARDS was better than objective assessment of knowledge. In order to increase rates of appropriate PPV in moderate-severe ARDS patients, future implementation science interventions tools to improve positive emotions and social influences, as well as increase behavioral regulation and environmental context and resources could prove useful.

An Examination of the Use and Interpretation of P-Values in Pediatric Critical Care RCT's with Mortality Outcomes

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Introduction: Misinterpretation of null-hypothesis statistical testing (NHST) prevents recognition of high false positive rates (FPR), and may account for poor reproducibility of studies.

Objectives: We aimed to determine the implications of reported p-values and statistically significant findings in pediatric critical care randomized controlled trials (RCT's).

Methods: The EPICC database reports abstracts of all 444 published pediatric critical care RCT's from 1980-2019. We searched EPICC separately for 'mortality' (n=135) and 'more than 1 center' (n=80) studies. We excluded studies with 1 or no deaths, not reporting on deaths, having pilot feasibility or short-term physiologic outcomes only, or non-obtainable publication (only n=2). This generated 120 RCT's with a mortality outcome. Reverse Bayesian implications from the publications were obtained, including FPR (defined as a statistically significant finding that is due to chance alone).

Results: Of 120 studies, 73 (61%) were single center, sample-size/group was median 40 [IQR 22, 80], patients often had sepsis (22%) or were ventilated (36%), and mortality was the primary outcome in 16%. Reported p-values were ≤ 0.005 in 1.7%, 0.0051-0.05 in 8.3%, and 0.051-0.10 in 10.8% of studies. Reverse-Bayesian analysis of the 10% of studies reporting p-value ≤ 0.05 found the i) prior probability of the alternative hypothesis [$Pr^P(H1)$] would need to be median 76% [IQR 54, 80] in order to have FPR 5%; ii) minimum FPR was 14.4% [IQR 5.8, 17.1] assuming a $Pr^P(H1)$ 50%, and 59.9% [IQR 34.5, 64.9] assuming a more realistic $Pr^P(H1)$ 10%; iii) Bayes Factor Bound (upper bound on the likelihood ratio for H1 relative to Ho) was 4.0 [IQR 3.4, 8.5]; and iv) probability that a replication study would find a $p \leq 0.05$ was 60.9% [IQR 57.9, 73.9]. By calculating post-hoc power for medium effect sizes, and assuming $Pr^P(H1)$ 50%, in the field of pediatric critical care, the PPV and NPV of studies using $\alpha \leq 0.05$ can be expected to be 64.3% [IQR 28.6, 86.5] and 51.1% [IQR 49.2, 58.3] respectively. Assuming a more realistic $Pr^P(H1)$ 10%, the PPV and NPV can be expected to be 28.6% [IQR 8.2, 55.0] and 91.2% [IQR 89.9, 95.0].

Conclusions: Pediatric critical care RCT's with *statistically significant* mortality outcomes have a high FPR, much higher than the misinterpretation that a p-value ≤ 0.05 implies a FPR of 5%. In this field, as in many others, most published findings can be expected to be false. We agree with recent recommendations to design RCT's with $\alpha = 0.005$, and to report the FPR of study findings assuming $Pr^P(H1)$ 10%.

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An Observational Pilot Study Investigating the Role of Coagulation in the Diagnosis of SEPSIS in the Emergency Department (SEPSIS-ED)

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Introduction: Between 75-80% of patients with sepsis arrive through the emergency department (ED). Early recognition and diagnosis are important to alter patient prognosis. We have shown that coagulation markers are important for prognosis in the intensive care unit. Inflammation and coagulation are linked in the innate immune response. The role of coagulation markers to aid in sepsis diagnosis in the ED has had limited investigation.

Objectives: The primary objective is to identify the changes in the coagulation biomarkers occurring in septic patients presenting to the ED. The secondary outcome is to identify a panel of biomarkers (including inflammatory and coagulation markers) with the routinely used laboratory tests and clinical scores of abnormal vital signs and organ dysfunction to aid in sepsis diagnosis.

Methods: SEPSIS-ED is an observational cohort study with a planned recruitment of 250 adult patients with the suspicion of sepsis from two EDs in Hamilton, Ontario. Samples were collected at two points: on their initial presentation to the ED (Timepoint 1) and 4 hrs after the initial sample collection (Timepoint 2). Cell-free DNA (cfDNA) levels was determined from plasma samples using a silica-membrane based DNA purification method and UV spectrophotometry. Procalcitonin, protein C (PC) and a Disintegrin and Metalloprotease with Thrombospondin type 1 motif, member 13 (ADAMTS13; an enzyme that cleaves Von Willebrand Factor) levels were measured using enzyme-linked immunosorbent assays. These markers will be compared with healthy controls (HC). Each case with suspected sepsis will be adjudicated using the Sepsis-3 definition to determine the septic or non-septic status.¹ Data is reported as mean \pm standard deviation or median (Interquartile range) depending on whether normally distributed.

Results: We report preliminary unadjudicated data on 174 patients presenting with the suspicion of sepsis to the ED, with a mean age of 69.2 ± 17.6 years, 51.7% of males, and mortality of 7.4% at 28 days. 71.8% of the patients had a SOFA score of more than 2. The leukocyte count was ($14.5 \pm 9.2 \times 10^9/L$) elevated compared to hospital standard, while platelet count ($238.1 \pm 117.4 \times 10^9/L$) was within the normal range. cfDNA and PC levels at both time points were not significantly different from the healthy controls. Procalcitonin levels were significantly higher in our cohort at both time points compared to the healthy controls (HC: 84.81 (44.06) pg/ml, T1: 146.2 (460.27) pg/ml, T2: 176.1 (523.08) pg/ml, $p < 0.0005$). We also observed that ADAMTS13 levels were significantly lower than healthy controls and declined further 4 hours after the initial presentation to the ED (HC: 897 (456.7) ng/ml, T1: 417.3 (340.3) ng/ml, T2: 363 (281.7) ng/ml, $p < 0.0001$). The multivariate receiver operating characteristic (ROC) curve analyses with the combination of biomarkers, vitals and laboratory parameters were performed. Amongst the various panels analyzed (table 1), a six-marker panel (including cfDNA, PC, procalcitonin, ADAMTS13, respiratory rate and heart rate) had the highest ROC area under the curve (T1: 0.757 and T2: 0.743).

Conclusion: Our preliminary data suggests that patients presenting to the ED with suspicion of sepsis have an associated coagulopathy as demonstrated primarily by a decrease in ADAMTS13, a marker linked to the initial inflammatory response. These results provide a rationale for exploring the impact of coagulation markers to facilitate

earlier, accurate diagnosis of sepsis in a larger multicentre study.

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Groups	Variables	R square	Adjusted R square	P value	Area under the ROC Curve ± Standard error
Group 1	HR, RR	0.116	0.106	0.000	0.704 ± 0.053
Group 2	Leuk, HR, RR	0.130	0.114	0.000	0.715 ± 0.054
Group 3	ADAMTS13 (T1), Protein C (T1), RR, HR	0.130	0.097	0.005	0.742 ± 0.053
Group 4	ADAMTS13 (T2), Protein C (T2), RR, HR	0.107	0.072	0.021	0.710 ± 0.053
Group 5	ADAMTS13 (T1), Protein C (T1), Leuk, RR, HR	0.129	0.086	0.015	0.750 ± 0.052
Group 6	ADAMTS13 (T2), Protein C (T2), Leuk, RR, HR	0.112	0.067	0.037	0.732 ± 0.052
Group 7	ADAMTS13 (T1), Protein C (T1), cfDNA (T1), PCT (T1), RR, HR	0.126	0.074	0.034	0.757 ± 0.052
Group 8	ADAMTS13 (T2), Protein C (T2), cfDNA (T2), PCT (T2), RR, HR	0.134	0.080	0.029	0.743 ± 0.054

Table 1: Multivariate receiver operating characteristic (ROC) curve analysis evaluating the ability of different panel of biomarkers to distinguish suspected sepsis patients from non-septic patients. ROC, receiver operating characteristic; HR, heart rate; RR, respiratory rate; Leuk, leukocyte count; ADAMTS13, a Disintegrin and Metalloprotease with Thrombospondin type 1 motif, member 13; cfDNA, cell-free DNA; PCT, Procalcitonin; T1, Time point 1 (on initial presentation to the emergency department, usually before antibiotic administration); T2, Time point 2 (4 hrs after the initial sample collection).

An Unexpected Airway Foreign Body

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Introduction: The National Health Service (NHS) in the United Kingdom has published patient safety alert " Risk of inadvertently cutting in-line (or closed) suction catheters" reporting nine incidents describing retained suction catheter tips in neonates and adults airway between January 2012 and August 2014 that appear to have resulted in moderate harm. Local investigations have identified the following: (1) In closed suction systems for neonates, the suction catheter is not easily visible if left inside the ET tube; (2) It was not always documented when and by whom the ET tube was cut; (3) Some patients were suctioned regularly and staff failed to fully withdraw the catheter following suction.

Objective: We report a case of inadvertently cutting closed loop suction catheter and implement strategies in order to prevent this human error.

Method: A 46-year-old male was intubated with an uncut Endotracheal Tube (ET) and ventilated in the Intensive Care Unit (ITU) due to respiratory failure as a result of community-acquired pneumonia. The ET needed to be cut while in situ in order to reduce dead space and facilitate lung suctioning; this was performed by senior ITU doctor and documented as straightforward procedure. Following this procedure, the patient oxygen requirement started going up with the ventilator started alarming air trapping and increasing end tidal carbon dioxide. A chest x-ray was performed and reported by the radiologist as left lower lobe volume loss and pleural effusion with no intrapulmonary abnormality demonstrated on the right side, multiple bilateral rib fractures noted.

Results: The tip of closed loop suction catheter was left inside the ET and was accidentally cut and fell into patient airway. This was only noticed twenty-four hours after when the catheter tip was identified lying inside the bronchus intermedius and occluding the right middle lobe bronchus and subsequently removed by bronchoscopy (image1).

Conclusion: Cutting of ET while in situ is an invasive procedure that could result in serious complications; this could be related to loss of airway or accidental cutting of closed loop suction catheter which can result in airway obstruction, infection and the need of undertaking invasive procedure to retrieve the foreign object. Introducing a step-by-step checklist for ET cutting while in situ (Image 2) could help to standardize practice and eliminate complications.

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Image 1 - Catheter Tip Removed by Bronchoscopy



Image 2 – Invasive Procedure Checklist: In situ endotracheal tube (ETT) cutting

BEFORE THE PROCEDURE	TIME OUT	Sign Out
Intubation grade checked? Yes No Back up plan for re-intubation discussed? Yes No Cutting length marked? Yes No Are there any concerns about this procedure for the patient? Yes No	Verbal confirmation between team members before start of procedure Is patient position optimised? Yes No Is the closed loop suction catheter pulled out of the ETT? Yes No Pre-oxygenate: 100% FIO2 for 3 mins Yes No Is the catheter mount-ETT male connector connection loosened? Yes No Is the ETT male connector disconnected from ETT before cutting the tube? Yes No	ETT position confirmed (ETCO2 trace) Yes No Any equipment issues? Yes No
	Procedure date: <input type="text"/> Time: <input type="text"/> Operator: <input type="text"/> Observer: <input type="text"/> Assistant: <input type="text"/> Level of supervision: SpR <input type="checkbox"/> Consultant <input type="checkbox"/> Equipment & trolley prepared: <input type="text"/>	Signature of responsible clinician completing the form: <input type="text"/> Patient Identity Sticker: <input type="text"/>

Analysis of Canadian Public Survey Responses Related to Consent in Deceased Organ

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Introduction: The need for donated organs vastly outweighs the number available for transplant in Canada. The disparity among availability of organs and identified need highlights that exploring factors affecting donation and transplantation should be a research priority. To explore these issues, Canadian Blood Service (CBS), a national not-for-profit charitable organization that manages organ and tissue donation and transplantation in Canada, commissioned Ipsos Reid to conduct a series of Canadian public surveys exploring awareness, knowledge, behaviours, and attitudes to organ and tissue donation. Thus, the purpose of this study was to explore and analyze this data in order to identify factors predictive of the intent to consent to organ donation, factors predictive of overriding another individual's pre-declared intent to donate their organs, and factors predictive of support for an opt-out consent model to organ donation legislation in Canada. Changes over time related to these factors were also explored.

Methods: We conducted a secondary analysis of four years of Canadian survey data, using univariate and multivariate regression analyses of various demographic variables against respondents' intent to donate their organs upon their death, support for an opt-out model of consent for organ donation, and willingness to override another's decision to donate their organs upon their death.

Results: Between 44%-46% of respondents remain undecided about their intent to donate organs for all years of study. Those with more knowledge of organ donation and who had higher approval ratings of organ donation were also more likely to declare their intent to donate. Intent to donate was found to be predictive of support for the opt-out model of consent for organ donation. And individuals that did not support organ donation or who were not intending to donate were more willing to override another's decision to donate. The year of study was not significantly associated with any of the outcomes of interest.

Conclusions: This is the first detailed analysis of previously unpublished Canadian Blood Services survey data. Our results suggest there is a need to explore qualitative and social factors that influence the personal decision to consent to organ donation as well as how these factors affect attitudes to opt-out consent and overriding another's decision to donate. Greater understanding in these areas will assist in creating initiatives targeted at potential gaps in education or service that would also affect the success of implementing legislative changes in other jurisdictions.

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Antimicrobial Stewardship, Procalcitonin Testing and Rapid Blood Culture Identification to Optimize Sepsis Care in Critically Ill Adult Patients

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Objectives: To examine outcomes associated with the implementation of a prospective antimicrobial stewardship program (ASP), procalcitonin (PCT) testing, and rapid blood culture identification (BCID) in adult intensive care unit (ICU) patients with suspected or confirmed sepsis.

Methods: We conducted a prospective, adaptive, time series evaluation of ASP using prospective audit and feedback, PCT and BCID in all adult ICU patients with suspected or confirmed sepsis (Sepsis-3 definitions) in two large academic mixed medical/surgical ICUs in Alberta in 2018. The study included 12-week baseline data (Phase 1) and implementation (Phase 2) phases. During implementation, ASP audits were conducted on admission and in follow-up 2-5 days post-admission. PCT was measured daily to a maximum of 7 days or until ICU discharge and BCID was performed on all positive blood cultures. The primary outcome was in-hospital mortality. Secondary outcomes included initial antimicrobial concordance with clinical practice guidelines, number and acceptance of ASP interventions, antimicrobial and health resource utilization, ICU and hospital lengths of stay and re-admissions, and costs and quality-adjusted life years (QALYs). Segmented logistic and linear regression analyses were performed to estimate associations.

Results: A total of 727 patients were included, 342 in Phase 1 and 385 in Phase 2. Patients were similar in phase 1 vs. 2, with mean (\pm SD) ages 59 (\pm 15) and 57 (\pm 15),

59% and 56% male sex, and APACHE II scores 24 (± 7) and 24 (± 9), respectively. There was no difference in hospital mortality between phases (25 vs 26%; $p=0.75$). The ASP team conducted 1023 assessments (692 initial; 331 follow-up) and reviewed 1247 prescriptions. 808/1247 (65%) of prescriptions were judged as appropriate while 122/1247 (10%) were considered not indicated by the ASP team. Empiric antimicrobials were guideline concordant in 861/998 (86.3%) of prescriptions. Full compliance with ASP recommendations was high (93%). Substantial changes in antimicrobial utilization (DDD/100 patient-days) included a 12% increase for third-generation cephalosporins, 11% increase for vancomycin utilization and a 19% reduction in piperacillin/tazobactam utilization.

PCT was measured at least once in 383 (99.5%) intervention patients (median 5.0 tests per patient). 277 (15%) PCT values were <0.25 ng/mL (stopping rule) while 1188 (66%) were >1 ng/mL (continuation rule). There were 44 positive blood cultures; most common isolates identified were *Staphylococcus aureus* and *Escherichia coli*.

There were no differences in change in daily SOFA score, incidence of delirium, or use and duration of mechanical ventilation, vasopressors or renal replacement therapy.

Mean ICU stay was shorter in the intervention phase (-2.15 days; 95%CI -3.85, -0.45, $p=0.013$); however, there were no differences in hospital stay or ICU or hospital readmission rates. Costs were decreased (-\$12,834 per patient) and QALYs were increased (0.16 vs 0.13) in the intervention phase compared with baseline.

Conclusions: ASP, PCT and BCID testing were effectively implemented and can aid in guiding antimicrobial prescriptions in adult critically ill patients with sepsis. Empiric antimicrobial prescriptions were highly guideline-concordant and ASP was well accepted. There were no differences in mortality or health resource utilization post-implementation but shorter ICU stays and associated cost-savings were observed.

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Care of Patients with Traumatic Brain Injury at Kingston Health Sciences Centre (KHSC): A Retrospective Review of Clinical Practice

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Introduction/Background: Traumatic Brain Injury (TBI) is among the most common neurological causes of admission to the intensive care unit (ICU) and is a common cause of death and disability.(1–3) In 2016, the Brain Trauma Foundation (BTF) published updated clinical practice guidelines (CPG) for the management of TBI.(4) Optimal rates of adherence to clinical practice guidelines are unknown.

Objectives: Our primary objective is to retrospectively characterize the degree of adherence between care received and CPG for patients admitted to the ICU with TBI. Our secondary objective is to evaluate mortality and functional outcomes.

Methods: This study is a retrospective analysis of all patients aged 18 years or older admitted to our level 3 ICU with a TBI between January 1, 2012 and December 31, 2017. Ethics approval was granted by the Queen's University Health Sciences & Affiliated Teaching Hospitals Research Ethics Board (HSREB). Eligible participants were identified through the patient discharge database using ICD 10 codes. Data was retrieved manually from patients' electronic charts and entered into a de-identified standardized data extraction excel spreadsheet. Descriptive statistics including median and interquartile ranges (IQR) were used to analyze the data. Outcomes of interest include patient demographic data, interventions used in case management, morbidity and mortality. Missing data was quantified as a proportion of the total data available.

Results: A total of 326 patients were identified, of these, 311 were eligible for inclusion. The most common reason for exclusion from the study was patients who did not experience a TBI. Key baseline characteristics are reported in Table 1.

A CT head was completed in 307 patients (99%), of which 283 (92%) had an abnormal finding. The median Marshall score was 3 (IQR: 2 to 5). Neurosurgical interventions were performed in 127 patients (41%), the most common being a craniotomy (n=44). Interventions to lower ICP were used in 117 patients and 48 patients had an ICP monitor placed. Details of ICP lowering therapy are outlined in table 2.

A total of 46 patients experienced a seizure prior to arrival at KHSC. Of the 262 patients who did not experience a seizure prior to presenting to hospital, 72 (27%) received seizure prophylaxis. Anti-seizure medications received are described in figure 1. Median duration of seizure prophylaxis was 7 days (IQR: 7 to 14 days). Despite prophylaxis, 20 patients experienced a seizure, of which 7 were diagnosed clinically and 13 on EEG.

The median mRS at time of discharge or transfer was 4 (IQR: 3 to 6). The median length of ICU stay was 6 days (IQR: 2 to 11) and total hospital stay was 11 days (IQR: 3 to 26). When available, the most common discharge destination was a rehabilitation facility (25%) followed by home (with or without supports) in 21%. Goals of care were documented on the official KHSC form in 13 (4%) of cases. A total of 102 (33%) of patients died before hospital discharge. The majority of deaths (n=101 [99%]) occurred in the ICU.

Conclusion: Our study confirms that TBI is associated with clinically important functional morbidity and mortality. Few patients received seizure prophylaxis or had an ICP monitor placed. These management strategies represent a potential opportunity for improved guideline adherence and will be the focus of a subsequent quality improvement initiative.

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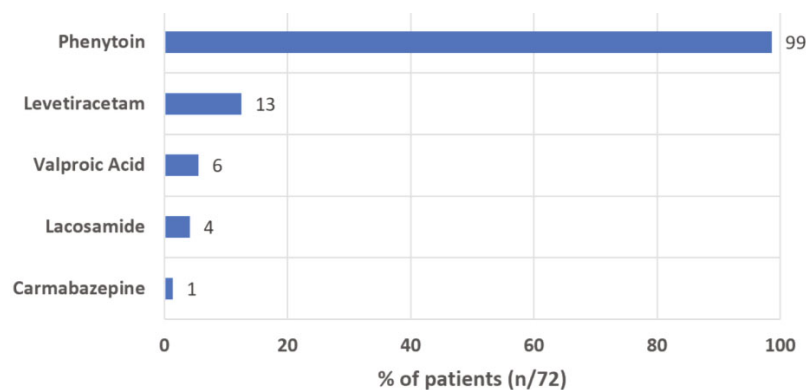
Table 1 – Key Baseline Characteristics N=311

Parameter	Finding	Missing data (n, %)
Age, median (IQR)	60 (37 to 73)	0
Male Sex, n (%)	223 (72%)	0
Patient residence prior to admission home, n (%)	294 (95%)	4 (1%)
Transferred from a peripheral hospital, n (%)	202 (65%)	1 (0.3%)
First documented GCS, median (IQR)	8 (5 to 14)	13 (4%)
GCS <9, n (%)	151 (49%)	
Intubated, n (%)		
pre-hospital	15 (5%)	1 (0.3%)
in-hospital	289 (93%)	
arrived at KHSC intubated	156 (50%)	2 (0.6%)
pre-intubation GCS, median (IQR)	6 (3 to 11)	50 (16%)
First documented PaO ₂ , median (IQR)	113 (83 to 164)	77 (25%)
First documented SBP, median (IQR)	140 (123 to 162)	13 (4%)
First documented DBP, median (IQR)	83 (71 to 94)	16 (5%)

Table 2 – ICP Therapy Received N=117

Intervention	n (%)
Sedation	113 (97)
Mannitol	81 (69)
Hypertonic Saline	47 (40)
Neuromuscular Blockade	33 (28)
CSF Removal	31 (26)
Hyperventilation	8 (7)

Figure 1 – Anti-Seizure Prophylaxis Received



Note: Multiple medications (>1) were used in 10 patients.

Comparison of Balanced Crystalloid Solutions: A Systematic Review and Meta-Analysis

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Introduction: The administration of intravenous fluids is nearly ubiquitous in hospital-based care, especially in the intensive care unit (ICU). The most widely used intravenous fluid, normal saline (NS), contains a supraphysiologic concentration of chloride, can lead to metabolic acidosis and has been associated with an increased risk of acute kidney injury when given in large volumes.^{1,2} Balanced fluids have a lower chloride concentration that more closely matches that of human plasma and there is emerging evidence that their use may be associated with improved outcomes compared to NS.³ Although there are a number of different balanced crystalloids, all with different electrolyte compositions, studies examining comparative effectiveness amongst these fluids are limited.

Objectives: The objective of this systematic review and meta-analysis is to summarize the randomized controlled trials (RCTs) comparing two or more balanced crystalloids. We examined metabolic outcomes (change in serum chloride, potassium, lactate, pH, and base excess) and patient-important outcomes (acute kidney injury, organ failure, need for life support, length of ICU or hospital stay, and hospital mortality).

Methods: We performed a comprehensive search of MEDLINE, EMBASE, PUBMED, and CENTRAL. For comparisons with sufficient data, we conducted meta-analysis using inverse variance method and random effects model. We present results as mean difference (MD) with associated 95% confidence intervals (CIs). For comparisons or outcomes with insufficient data to allow pooling, we describe narratively.

Results: Of 22669 initial citations, we included 18 RCTs which studied Plasmalyte, Ringer's Lactate, Ringer's Acetate, Ringerfundin, Hartmann's solution, Ringer's Bicarbonate and Sterofundin. Of the included studies, 11 were performed in the perioperative setting, 5 in the ICU, one in the emergency department, and one with healthy volunteers. Volumes of study fluid received ranged from 380 to 19626 mLs. Administration of Plasmalyte resulted in a lower post-infusion serum chloride concentration (MD 1.25 mmol/L lower, 95% CI 0.62 to 1.88 mmol/L lower), and higher post-infusion base excess (MD 0.70 mmol/L higher, 95% CI 0.11 to 1.30 mmol/L higher) compared to any other balanced crystalloid comparator. There were no important differences in post-infusion serum pH, lactate or potassium comparing Plasmalyte to other balanced crystalloids. Data on patient-important outcomes was sparsely reported and heterogenous which did not allow for pooling.

Conclusion: This systematic review and meta-analysis demonstrates that administration of Plasmalyte results in lower serum concentrations of chloride and higher base excess as compared to other balanced crystalloids. The certainty of these results are low as studies included heterogeneous populations, there were issues related to risk of bias as well as important imprecision for most outcomes. If balanced crystalloids are found to be beneficial compared to NS, future data examining comparative effectiveness amongst these fluids will be crucial.

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Figure 1 – Forest plot of mean difference of chloride concentration post infusion of Plasmalyte vs Comparator (Hartmann’s solution 1.1.1, Ringer’s Lactate 1.1.2 and Sterofundin 1.1.3

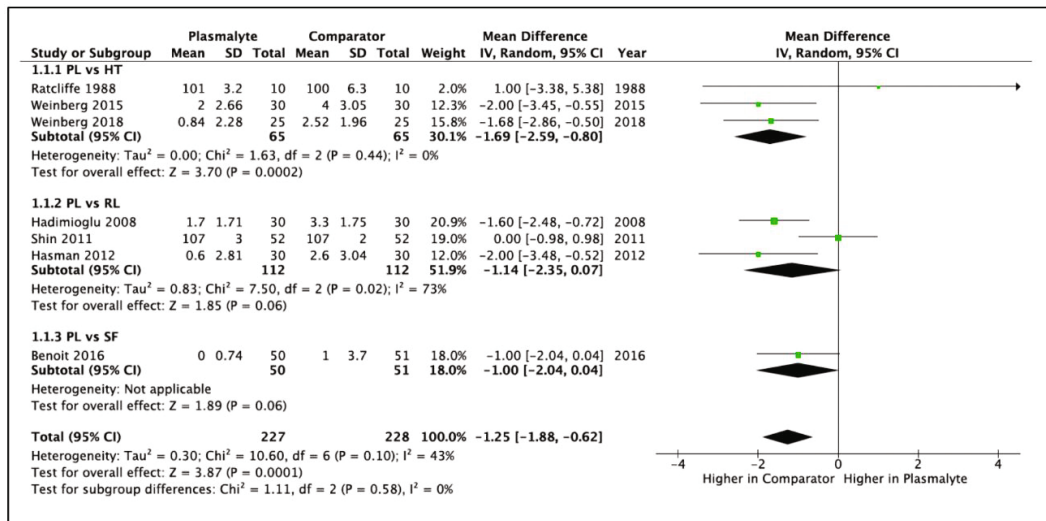
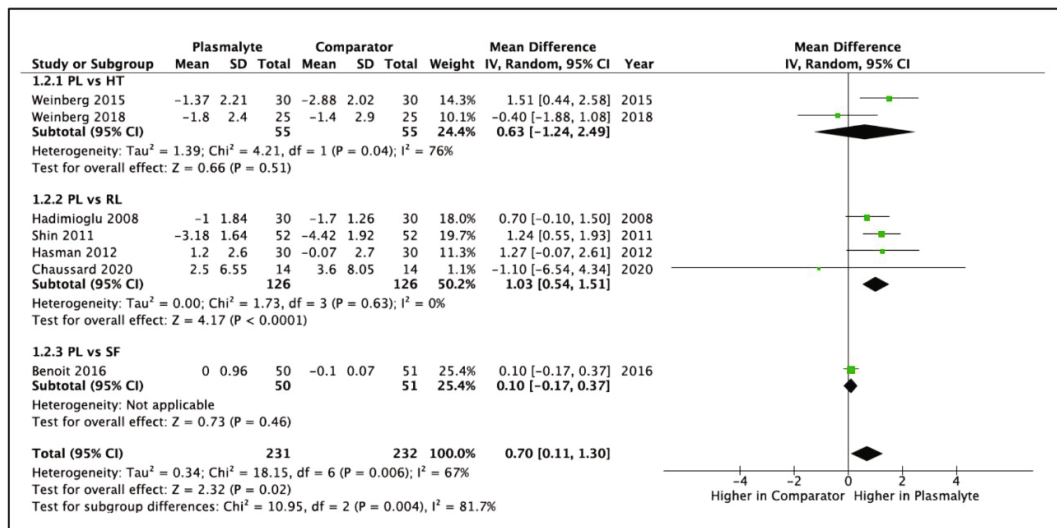


Figure 2 – Forest plot of mean difference of base excess post infusion of Plasmalyte vs Comparator (Hartmann’s solution 1.2.1, Ringer’s Lactate 1.2.2 and Sterofundin 1.2.3)



COVID-19 and the Creation of an Ontario Pediatric Pandemic Triage Plan

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Introduction: As the COVID-19 pandemic unfolded, the need for a pediatric triage framework for the whole of Ontario became evident. Early data pointed to an adult burden of COVID-19; two factors made a pediatric pandemic triage framework critical: 1) pediatric resources may need to be repurposed for adult care, 2) rapid evolution of resource scarcity highlights a need for a framework when a pediatric focused pathogen might occur.

Objective: To establish a pediatric pandemic triage framework that invokes anticipated mortality, baseline morbidity, and anticipated resource utilization in order to identify those patients who would be excluded or removed from intensive care support.

Methods: A literature review of adult and pediatric triage plans and consultations with PICU, NICU and bioethics colleagues were undertaken. A utilitarian view (saving the most lives, when not all lives can be saved) was prioritized based on consensus and broad support within the literature, and we initiated an iterative process of expert pediatric critical care consideration for broad categories. Legal and hospital administration provided input. We achieved consensus for reasonableness of the framework from the 4 PICU and 8 NICU stakeholder groups in Ontario. Each group had additional discretionary input from local bioethics, legal, and hospital administrative expertise.

Results: Two tiers were chosen to reflect any escalation in resource scarcity (Figure 1). Projected use of scarce resources (ventilators, extracorporeal life support) and mortality were major triage factors, since prolonged single-patient use of such resources – even with almost certain survival – could exclude multiple other patients from life-saving therapies. With high survival rates in general PICU/NICU populations, and relatively short anticipated length of stay, most patients would meet inclusion rather than exclusion criteria for ICU services. Thus, we also mapped out a triage algorithm (Figure 2); we established a first-come, first-served allocation to be used in such cases. No PICU/NICU patient subgroups were excluded, including patients with chronic comorbidities. While scoring tools are elusive in pediatric patients, mortality risk (with and without invasive support) is increasingly well understood by pediatric and neonatal critical care experts and allows anticipated survival to be incorporated in the framework. Additionally, we ensured that exclusion would not be predicated upon disability per se, or perceived quality of life, given the wide range of quality of life outcomes enjoyed by children and their families. Importantly, latitude would be required for decisions specific to unique disease processes. Our framework includes a model for triage team composition, including clinical, administrative and Bioethics expertise to reach rapid and transparent consensus decisions, with an appeal process where appropriate.

Conclusion: Ultimately, pediatric triage during a pandemic is an inherently fraught

process; our transparent and accountable framework for such decisions may help mitigate moral distress, and will allow a fair process in the worst-case scenario.

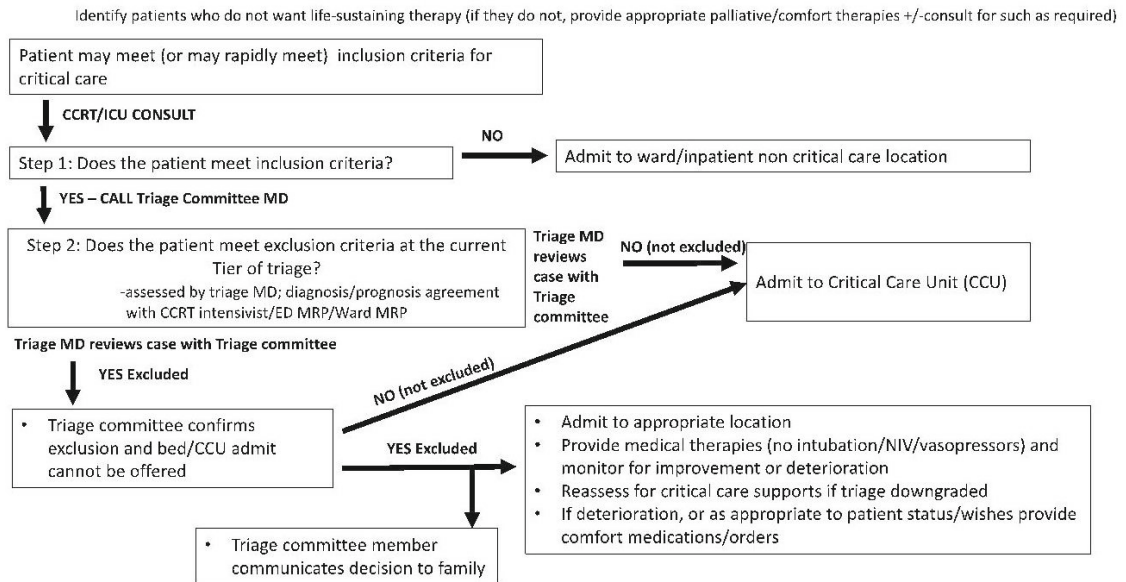
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Figure 1 – Pediatric Triage Tier System

Tier 1	Tier 2*
MORTALITY CRITERIA	
Anticipate mortality >70% within 7 days	Anticipate mortality >50% within 7 days
If newborn, anticipate mortality >70% within one year despite intervention	If newborn, anticipate mortality >50% within one year despite intervention
Life-limiting illness anticipate 70% mortality within 3 years despite intervention (<30% 3 year survival)	Life-limiting illness anticipate 60% mortality within 3 years with intervention (<40% 3 year survival)
MODS requiring >2 device** supports	MODS requiring >1 device supports
Requirement for ECMO with no identified reversible etiology or anticipate >5 day ECMO course	Requirement for ECMO (no ECMO provided)
RESUSCITATION CRITERIA	
Requirement for E-CPR (no E-CPR provided)	
VSA on arrival to hospital	
ROSC after CPR out of hospital >10 minutes	ROSC after CPR in hospital out of ICU >5 minutes
CPR in hospital without ROSC >10 minutes	
Requirement for repeat ECMO (previous run this hospitalization)	Requirement for ECMO (no ECMO provided)
RESPIRATORY SUPPORT NEEDS	
Oxygenation Index >16 (if newborn, then refer to mortality/resuscitation criteria, not OI)	Oxygenation Index >12 (if newborn, then refer to mortality/resuscitation criteria, not OI)
Anticipate prolonged ventilation >14 days in acute illness that is confounded by underlying comorbidity that impacts recovery	
NEUROLOGIC INJURY	
Acute GCS 3-8 on more than one measurement (acute not previous baseline)	Acute GCS <8 more than 12 hours (acute not previous baseline)
Persistent coma >24h beyond neurological insult (ex cardiac arrest, traumatic brain injury); if newborn then severe encephalopathy >72h	Encephalopathy >12hrs beyond neurological insult; if newborn then severe encephalopathy >48 hr
ONCOLOGIC	
>70% 5 year mortality anticipated despite treatment	>50% 5 year mortality anticipated with treatment
>70% mortality despite tumour resection	>50% survival despite tumour resection
>1 BMT	Unengrafted BMT
BURNS	
>80% TSA burn	>60% TSA burns
Inhalational injury - extensive	

Figure 2 - Triage algorithm - Pediatrics



Creation of a Public-Private-Civilian Partnership for Local Manufacturing of Personal Protective Equipment During the COVID-19 Pandemic

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Introduction: On March 11, 2019 SARS-CoV-2 was declared a global pandemic by the World Health Organization. Disruption to manufacturing and global supply chains rapidly led to worldwide shortages of personal protective equipment. To solve this problem, the Canadian government issued a call to action from manufacturers to help with the production of PPE.

Objectives: To describe the creation of a distributed manufacturing network to address shortages of face shields in long term care facilities, shelters and health centers in the province of Alberta.

Methods: Between March 16 and June 21 2020, Alberta 3D PPE operated with the goal of manufacturing and donating reusable face shields to long term care facilities, shelters and health centers in the province. The organization is a public-private-civilian partnership between healthcare providers, industrial designers, engineers, local business with expertise in medical device manufacturing, and the local 3D printing community. Production of face shields began after a 4-week period of team building, design selection, feedback from frontline healthcare providers and Infection Prevention and Control specialists, approval of decontamination protocols, Health Canada licensing and establishment of quality control procedures. Face shields were assembled from a 3D printed headband, a clear plastic visor, closed cell foam padding and an elastic head strap. Delivery was by pickup, courier or shipping. Public and media relations were managed by a University intern. Data on the organization's activities were collected for the period April 13 - June 21. Orders and production were tracked through Google Forms and Google Sheets (Google, CA). Membership was tracked using Slack analytics (Slack Technologies, CA) and active membership was defined as posting or reading in one of the organization's channels. Data on COVID-19 infections were obtained from the Alberta provincial website.

Results: During the 10 week data collection period, 2321 face shields were produced with 28 volunteers contributing to the 3D printing efforts. Peak production was achieved by week 4, with 778 face shields produced (Fig 1). Production mirrored infections in Alberta with a lag time of 2 weeks, as weekly COVID-19 cases peaked in the week of April 20. Production kept up with demand throughout the project. A total of 2177 face shields were ordered and 2071 were delivered based on predetermined criteria, with the highest number (515) in the week of May 25. The majority were from the Edmonton zone (1782, 88%) with less from Calgary (150, 7%), North (61, 3%) and Central (38, 2%) zones (Fig 2). 1380 face shields (68%) were ordered for assisted living and emergency lodging facilities including long term care, shelters, and seniors' residences. 341 (17%) were for community outreach organizations. 306(15%) were for outpatient medical care, including pharmacies, dental care, and optometry. 44 (2%) were for

inpatient settings including emergency departments, diagnostic imaging, and hospital laboratory settings. 157 volunteers participated over the 10-week period. Active membership peaked at 110 members in the week of April 20.

Conclusion: A public-private-civilian partnership model of distributed manufacturing through 3D printing was able to nimbly ramp up and ramp down production in response to demand that mirrored rising and falling COVID-19 cases in Alberta. The model represents a viable template for the efficient production of personal protective equipment at a regional level.

Figure 1 – Weekly activity metrics in relation on reported COVID-19 cases

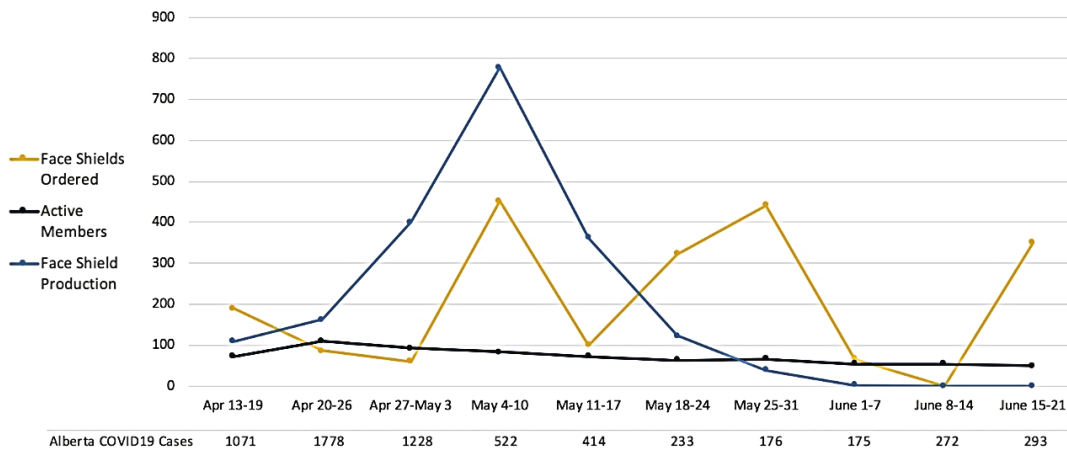
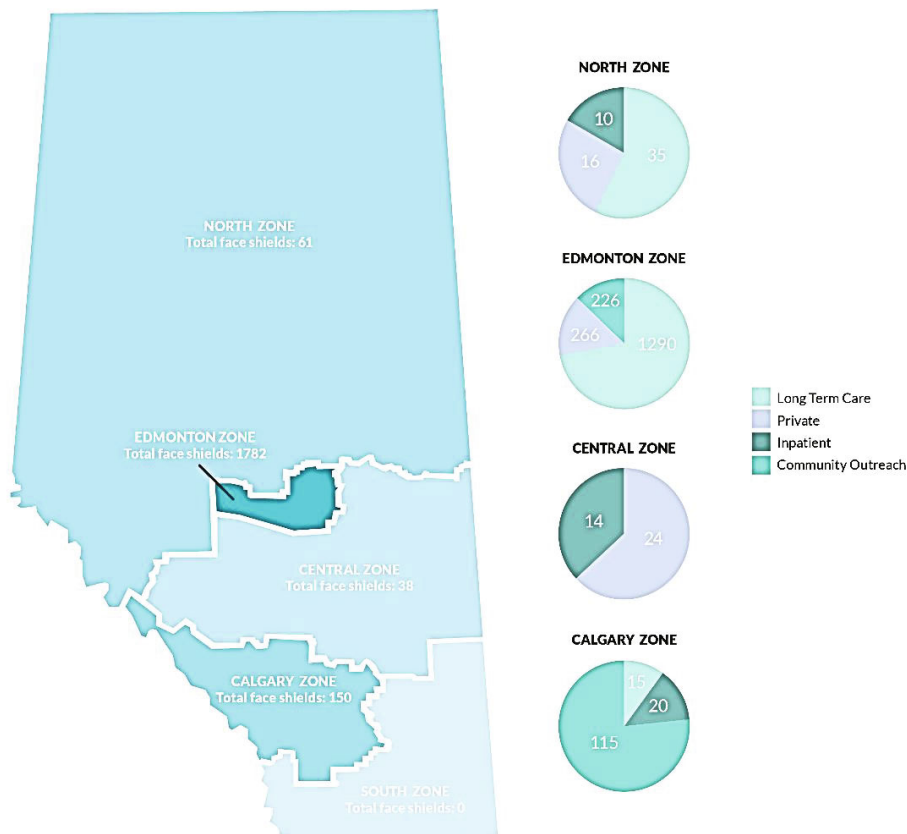


Figure 2 – Face shields orders by zone and order category



Description of the Validity of the Analgesia Nociception Index (ANI) and Nociception Level Index (NOL) for Nociception Assessment in Anesthetized and Sedated Surgical Patients: A Systematized Review

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Introduction: Maintaining optimum analgesia in anesthetized or sedated patients is challenging due to inability to self-report pain or to exhibit pain-related behaviours. Inadequate analgesia is associated with complications such as persistent postoperative pain and risk of developing chronic pain (1, 2). When only physiologic parameters are available, the measurement of nociception, the physiological process of encoding noxious stimuli (3), is indicated. The Analgesia Nociception Index (ANI) and the Nociception Level Index (NOL) are innovative technologies for nociception assessment and were selected for this review. The NOL is based on the simultaneous analysis of multiple parameters and their time derivatives, i.e., heart rate (HR), heart rate variability (HRV), photoplethysmography pulse wave amplitude, skin conductance level, its fluctuations, skin temperature. The ANI analyzes the high frequency spectrum of a single parameter, the HRV. These technologies were largely validated in perioperative care; however, the evidence is scarce in the ICU context where the prevalence of sedated critically ill adults is high (4-6).

Objectives: This review addressed the following research question: “What are the validation strategies used for the ANI and NOL for nociception assessment in anesthetized and sedated surgical patients?” The objectives were to describe the validation strategies and findings from studies for intraoperative nociception measurement with the ANI or NOL in this patient group.

Methods: A systematized review was conducted using a comprehensive search in four databases (MEDLINE, Embase, CINAHL, and PsycINFO) from their date of inception to January 28, 2020. The main search terms were nociception measurement, ANI, NOL, validation studies, and reproducibility. A quality assessment using an adapted GRADE approach for measurement tools (7), and a risk of bias assessment using QUADAS-2 tool (8) for diagnostic accuracy were performed by two reviewers. Discrepancies were discussed with a third reviewer to reach consensus.

Results: Out of 525 results, a total of 14 validation studies from 9 countries in 4 continents were included. Strategies included hypothesis testing, discriminative validation, and criterion validation (9). According to hypothesis testing, significant changes in ANI/NOL values were found in response to nociceptive stimuli at different opioid concentrations. Discriminative validation was supported with significant changes in ANI/NOL values between their responses to nociceptive stimuli (e.g., intubation, skin incision, tetanic stimulation) and a non-nociceptive period. Criterion validation was examined to detect nociceptive stimuli (used as the reference criterion) for the ANI and NOL with areas under the curve ranging from 0.83-0.99. Both technologies performed superiorly to traditional HR and blood pressure monitoring in detecting the nociceptive stimuli.

Conclusion: Hypothesis testing, discriminative, and criterion validation strategies are deemed appropriate for the testing of the ANI and NOL technologies. Nonetheless, in the absence of a gold standard, the criterion validation should be interpreted with caution. Moreover, reliability could be examined using the test-retest approach, as to expecting consistent values during a stable time interval (9). Future validation testing of these technologies in sedated/mechanically ventilated patients may support their use in the ICU context.

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Detection of Potential Organ Donors; An Automatic Approach on Temporal Data

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Introduction: Despite a slow improvement in total organ donors over the last 20 years¹, organ donation is still not meeting the demand. Organ transplantation depends on potential organ donor identification which is still a major challenge. Retrospective studies show that we may miss between 30% and 50 % of potential organ donors²⁻⁵. By increasing the total number of potential donors referred to an Organ Donation Organization (ODO), the number of organ donors could substantially increase.

Objectives: We aimed to develop a deep learning⁶ model using only routinely collected data that could help with the screening of potential organ donors. We present the development and validation of that model.

Methods: The model was derived using the electronic health record data from intensive care unit (ICU) stays from Jan 1st 2012, until Dec 31th 2019, in the CHUM (Montreal University Hospital Center, Montreal). We defined our organ donor population as (1) organ donors that were identified in the study institution (2) potential organ donors referred to the ODO but deemed ineligible for transplantation and (3) non-referred potential organ donors identified from manual chart review death audit. We included all laboratory analyses as well as the presence/absence of head scan. We developed a two-step model. First, we trained a deep convolutional neural network⁷ autoencoder (CNN-AE)⁸. This model was a non-supervised model that served as an embedding and a dimensionality reduction tool, to reduce noise⁹ and for transfer learning and pretraining¹⁰. The second step was to add a deep classifier to categorize each patient as donor/non-donor. We also implemented a one-layer logistical model (LM), based on the last available value, as a comparator to our neural network (NN) model. The CNN-AE was trained on 85% randomly selected non-donors. The NN model and LM were trained on the rest of the patients, randomly separated in a train (60%), validation (20%) and test (20%) sets.

We compared our NN model to our LM using a ROC curve, scaled Brier score and calibration curves¹¹ with bootstrap for confidence intervals. We manually reviewed the files of patients that were wrongly predicted as donor but who predicted a degree of confidence over 95% in the validation set.

Results: Our complete dataset used 19717 patients with 392 donors. After excluding rare laboratory analysis, the NN model and LM were trained on 105 distinct laboratory analyses. On the test set, NN model and LM performed similarly with a ROC-AUC of respectively of 0.950 (95%CI 0.923-0.974) and 0.947 (95%CI 0.9169-0.9730) and scaled Brier score of 0.313 (0.134-0.472) and 0.432 (0.270-0.580). At best accuracy, sensitivity and specificity were 82% (95%CI 73-90) and 92% (95%CI 89-94) for the NN model and 82% (95%CI 73-90) and 94% (95%CI 91-95) for the LM. The NN model accuracy was more consistent across subgroups compared to the LM (fig 1).

Conclusion: We present preliminary evidence that routinely collected medical data can be used to screen for potential organ donors. When comparing our more complex temporal model (NN) with its non-temporal simpler version (LM) both performed as well globally. However, the NN keeps a good accuracy in the more complex clinical patterns. Prospective and external validation of these models are required for further calibration before any potential clinical application.

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Figure 1 – ROC for donor subtypes vs rest (NN)

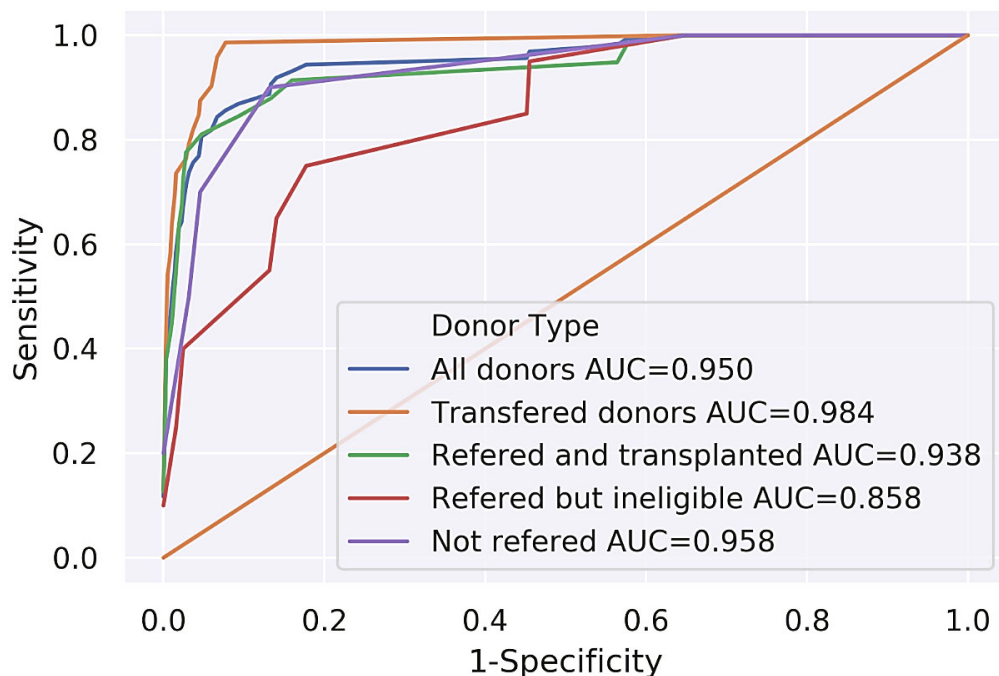
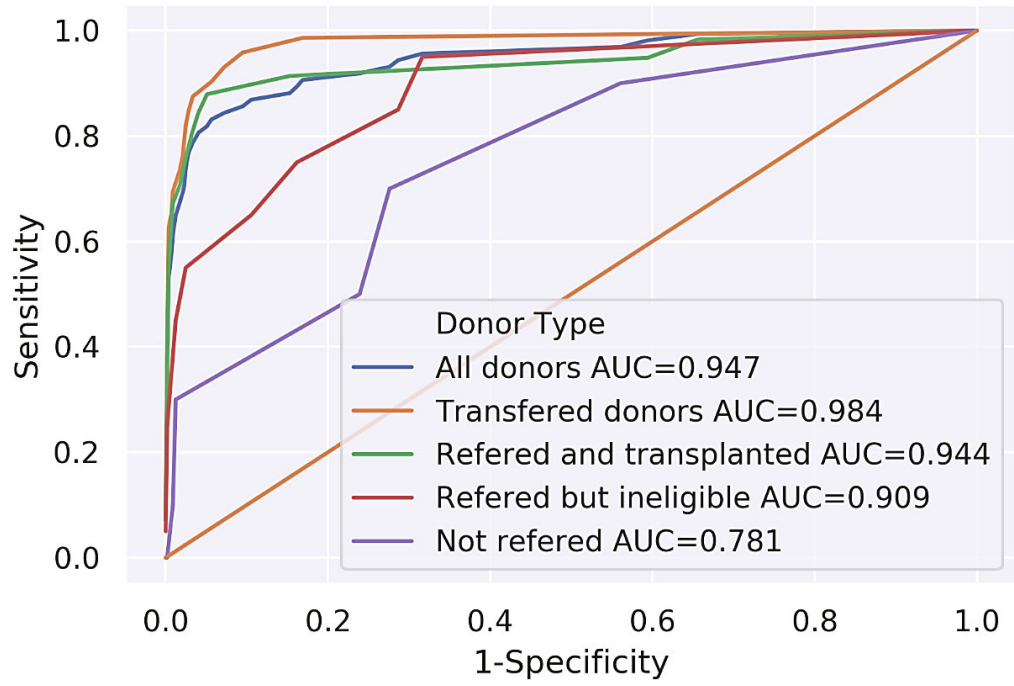


Figure 2 – ROC for donor subtype vs rest (LM)



Effect of Therapeutic Interventions on Long Term Mortality of Patients with ARDS: A Systematic Review and Network Meta-Analysis

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Introduction: Most clinical trials of interventions in patients with acute respiratory distress syndrome (ARDS) have focused on improvements in short-term mortality through a reduction in ventilator-induced lung injury (VILI). However, little is known about the impact of these interventions on longer term survival.

Objectives: We performed a network meta-analysis to explore the comparative efficacy of commonly used interventions on 180-day mortality by synthesizing the available evidence among patients with ARDS.

Methods:

Data sources: An electronic search of MEDLINE, MEDLINE In-Process/ePubs Ahead of Print, Embase, Cochrane Controlled Clinical Trial Register (Central), PubMed, and CINAHL was conducted, from database inception to March 6th, 2019.

Study selection: Randomized clinical trials comparing prespecified interventions for adult ARDS patients with lung protective ventilation (LPV). No language restrictions were applied.

Data extraction and synthesis: Data were independently extracted by 2 reviewers and synthesized with Bayesian random-effects network meta-analyses of fractional polynomials model.

Main outcomes and measures: The primary outcome was 180-day mortality.

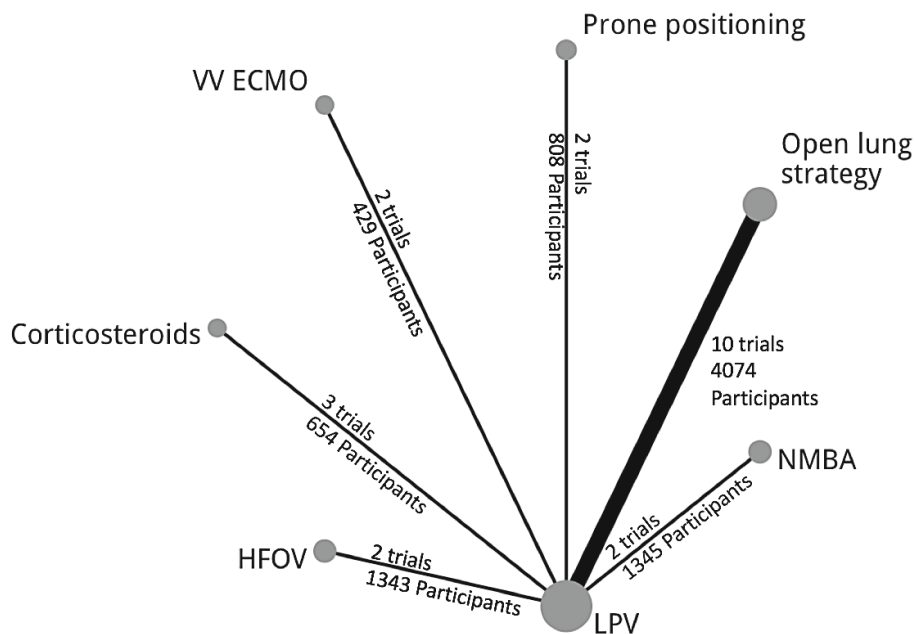
Results: Mortality data were extracted for 8653 participants from identified 21 eligible studies that assessed 6 different interventions (venovenous extracorporeal membrane oxygenation [VV ECMO], high-frequency oscillatory ventilation, open lung strategies, prone positioning, neuromuscular blockade [NMBA], and corticosteroids) and lung protective ventilation (LPV). Survival probability of LPV at 180-days was 0.50 (95% credible interval [CrI] 0.47 – 0.54). Interventions with higher or equal survival probability than LPV at 180 days were prone positioning (0.64, 95% CrI 0.49 – 0.74), corticosteroids (0.61, 95% CrI 0.47 – 0.71), VV ECMO (0.58, 0.37 – 0.73), NMBA (0.53, 0.36 – 0.66), and open lung strategies (0.51, 0.43 – 0.58). Pooled hazard ratios (HRs) for 180-day mortality for individual intervention compared with LPV derived from the primary network meta-analysis showed an advantage for prone positioning and corticosteroids (HR 0.57, 95% CrI 0.25 – 1.33 and HR 0.61, 95% CrI 0.21 – 1.76, respectively); however, these were not statistically significant. Indirect comparisons among those 6 interventions showed no statistical significance. In post-hoc sensitivity analyses, there was no difference in results by limiting to trials that included only patients with PaO₂/FiO₂ ratio less than 150 mmHg and no evidence of effect modification based on PaO₂/FiO₂ ratio using network meta-regression.

Conclusion:

This network meta-analysis found that none of 6 prespecified interventions were associated with improved 180-day mortality in patients with ARDS. Strategies to

improve longer term outcomes in patients with ARDS will need to employ interventions that are not focused on VILI.

Figure 1 – Network geometry of randomized clinical trials with 180-day mortality as an outcome



EHR-Based Sub-Phenotyping of Acute Respiratory Distress Syndrome Patients

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Introduction: Sub-phenotypes have been identified in Acute Respiratory Distress Syndrome (ARDS) using plasma biomarkers and clinical data¹⁻⁴. Preliminary research shows that these sub-phenotypes have the potential for differential prognosis and might predict treatment responses in patients with ARDS. But translation of these models is difficult as a number of the predictor variables employed in these models are not a part of the usual care of ARDS patients and are difficult to ascertain outside the controlled environs of research.

Objectives: Development of a model to identify ARDS sub-phenotypes using only routinely available clinical data.

Methods: Data available in the electronic health record as a part of routine ARDS care were queried from ARMA-KARMA-LARMA⁵⁻⁷ (n=473), ALVEOLI⁸ (n=537), and FACTT⁹⁻¹⁰ (n=1000) for algorithm training. Analysis was performed in python using the SciKitLearn toolkit¹¹. 20% of data was reserved as hold-out. Of the remaining data, 5-fold cross validation with 80/20 train/test ratio was performed. Data was z-scale transformed, and K-means clustering was applied to identify two clusters. Model performance was evaluated on a diverse population including the ART randomized control trial¹² (n=1,013), eICU Collaborative Research database¹³ (n=1757), and a consecutive series of adjudicated ARDS patients from the Cleveland Clinic (n=688). Only patients with all required data elements and in-hospital mortality data were included in final analysis.

Results: Based on our initial models we identified 2 distinct clusters of ARDS patients. The optimal K-means cluster model included 8 variables which are routinely available from routine care arterial blood gases, multiparametric monitors and serum blood tests. There was a significant difference in the severity of disease among the two clusters, and Cluster 1 patients tended to be sicker, with significantly higher APACHE and SAPS3 scores. Moreover, Cluster 1 patients had higher white blood cell counts, higher serum creatinine and bilirubin, lower platelets, bicarbonate and lower PaO₂/FiO₂ ratio compared to Cluster 2 patients. Both clusters had similar ARDS etiology rates (Table 1).

Significant in-hospital mortality differences between clusters were observed between Cluster 1 and Cluster 2 in the training (28.8% vs 17.4%, p <0.00001) and holdout (31.4% vs 16.7%, p=0.00076) datasets. These differences in outcomes were maintained between the two clusters in the validation (49.7% vs 25.4%, p<0.00001) cohort (Table 2).

Limited baseline biomarker data was available for a subpopulation of patients in the ARMA and ALVEOLI training datasets (Table 3). There was a clear distinction between circulating biomarkers among the two clusters identified in our cohort. Cluster 1 again exhibited a higher mortality and similar to Calfee *et al.*, with increased circulating levels of IL-6, IL-8, sTNFR1, PAI-1, ICAM1, and VWF. Additionally, Cluster 1 exhibited significantly increased IL-10 and sTNFR2.

Conclusion: These findings suggest the potential of an algorithm to sub-phenotype a diverse population of ARDS patients using only data available in the EHR as part of routine patient care. Comparison of mortality, clinical characteristics, and biomarker data with previously published work suggests these sub-phenotypes have similar

characteristics to previously published subphenotypes¹⁻⁴.

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Table 1

Clinical characteristics	Studies missing element*	Cluster 1 n=1488	Cluster 2 n=961	P
Age (years), median [IQR]		58.0 [46.0,69.0]	63.0 [51.0,73.0]	<0.001
Male, n (%)		837 (56.2)	579 (60.2)	0.055
Caucasian, n (%)	A	726 (73.3)	498 (70.0)	0.161
Etiology - SEPSIS (ART), n (%)	C, E	99 (19.9)	44 (17.6)	0.508
Etiology - PNEUMONIA (ART), n (%)	C, E	285 (57.3)	135 (54.0)	0.429
Etiology - ASPIRATION (ART), n (%)	C, E	25 (5.0)	17 (6.8)	0.411
Etiology - Other (ART), n (%)	C, E	88(17.7)	54 (21.6)	0.889
Etiology - SEPSIS (CLEVELAND), n (%)	A, E	420 (94.2)	80 (92.0)	0.588
APACHE III score, mean (SD)	A, C	85.9 (30.2)	66.7 (23.8)	<0.001
SAPS3 score, mean (SD)	C, E	64.9 (18.6)	58.7 (16.9)	<0.001
Charlson comorbidity index, mean (SD)	A, E	4.0 [2.0,6.0]	4.0[2.0,6.0]	0.632
BMI, median [IQR]		28.9 [24.2,34.8]	28.7 [24.2,35.3]	0.677
Maximum Temperature (°C), meand (SD)	A	36.5 (2.9)	36.2 (3.9)	0.124
Heart rate (beats per minute), mean (SD)		107.7 (25.1)	86.4 (19.1)	<0.001
Respiratory rate (breaths per minute), median [IQR]		28.0 [20.0,35.0]	20.0 [17.0,25.0]	<0.001
White blood cell count (thousands), median [IQR]	A	12.4 [6.3,17.9]	10.2 [5.7,15.2]	<0.001
Lowest platelet count (thousands), median [IQR]		169.0 [100.0,249.0]	189.0 [130.0,266.0]	<0.001
Creatinine (mg/dL), median [IQR]		1.6 [1.0,2.6]	1.0 [0.7,1.4]	<0.001
Highest total bilirubin (mg/dL), median [IQR]		0.8 [0.4,1.6]	0.6 [0.4,1.2]	<0.001
Lowest bicarbonate, mean (SD)		20.0 [16.6,23.0]	25.1 [22.0,29.3]	<0.001
Mean arterial pressure (mmHg), mean (SD)		70.0 [59.0,81.4]	80.0 [70.0,91.0]	<0.001
Arterial pH, median [IQR]		7.3 [7.2,7.3]	7.4 [7.3,7.4]	<0.001
PaCO2 (mmHg), median [IQR]		45.0 [37.0,56.0]	43.4 [37.5,52.0]	0.017
PaO2 (mmHg), median [IQR]		96.0 [73.0,139.0]	92.0 [71.0,127.0]	0.012
FIO2		0.9 [0.6,1.0]	0.6 [0.4,0.7]	<0.001
PaO2/FiO2 (Lowest), mean (SD)		121.0 [82.0,177.9]	157.1 [108.0,217.0]	<0.001
PEEP (cm H2O), median [IQR]		10.0 [8.0,14.0]	8.0 [5.0,10.0]	<0.001
Mean airway pressure (cm H2O), median [IQR]	A	16.0 [12.0,20.0]	11.0[10.0,15.0]	<0.001
Tidal volume (mL), median [IQR]		400.0 [345.0,500.0]	450.0 [360.0,500.0]	<0.001
Total minute ventilation (L/min), median [IQR]	E	9.9 [8.1,12.2]	9.0 [7.3,10.5]	<0.001

Datasets missing variables are denoted as A (ART study), E (eICU), and C (Cleveland Clinic). Data points were collected pre-randomization on ART trial and closest to the ARDS diagnosis for eICU and Cleveland Clinic datasets unless otherwise noted as highest and/or lowest. APACHE III= Acute Physiology and Chronic Health Evaluation III; SAPS 3 = Simplified Acute Physiology Score 3; SD= standard deviation; IQR = Interquartile range; BMI = Body mass index;

Table 2

	Train			Holdout			Validate			
	Cluster 1 n=556	Cluster 2 n=642	p-value	Cluster 1 n=153	Cluster 2 n=233	p-value	Study missing element*	Cluster 1 n=1488	Cluster 2 n=961	p-value
In hospital mortality, n (%)	160 (28.8)	112 (17.4)	<0.001	48 (31.4)	39 (16.7)	0.001	-	740 (49.7)	244 (25.4)	<0.001
ICU mortality, n (%)	-	-	-	-	-	-	E	550 (58.3)	133 (39.5)	<0.001
28d mortality, n (%)	173 (31.1)	104 (16.2)	<0.001	48 (31.4)	41 (17.6)	0.003	-	389 (47.4)	101 (32.0)	<0.001
90d mortality, n (%)	206 (37.1)	132 (20.6)	<0.001	53 (34.6)	54 (23.2)	0.019	-	461 (48.9)	135 (40.1)	0.006
Hospital LOS, median [IQR]	-	-	-	-	-	-	A	14.0 [7.7,24.0]	12.1 [7.3,19.4]	0.002
ICU LOS, median [IQR]	-	-	-	-	-	-	A	8.0 [3.7,15.0]	5.0 [2.4,10.8]	<0.001
Ventilator days, median [IQR]	-	-	-	-	-	-	-	8.0 [4.0,16.0]	5.5 [2.0,12.0]	<0.001

Datasets missing variables are denoted as A (ART study), E (eICU), and C (Cleveland Clinic). ICU = Intensive care unit, LOS = Length of stay; IQR=interquartile range;

Table 3

ALVEOLI trial	Cluster 1 n = 190	Cluster 2 n = 319	P-Value
In-hospital mortality, n (%)	51 (26.8)	49 (15.4)	0.002
ICAM-1 (ng/mL)	1046.8 [729.6,1546.7]	822.9 [563.7,1235.1]	<0.001
IL-6 (pg/mL)	528.0 [153.0,2333.0]	169.5 [72.8,410.2]	<0.001
ARMA trial	Cluster 1 n = 170	Cluster 2 n = 140	P-Value
In-hospital mortality, n (%)	63 (37.1)	34 (24.3)	0.022
PAI-1 (ng/mL)	246.0 (525.2)	95.3 (142.2)	0.001
IL-6 (pg/mL)	550.5 [194.8,1886.2]	160.5 [71.0,366.0]	<0.001
IL-8 (pg/mL)	76.8 [28.0,194.5]	34.0 [0.0,68.5]	<0.001
IL-10 (pg/mL)	29.0 [0.0,80.4]	0.0 [0.0,29.0]	<0.001
TNFR-I (pg/mL)	4310.0 [2744.8,9417.2]	2319.5 [1806.2,3521.8]	<0.001
TNFR-II (pg/mL)	13289.5 [7083.2,22530.2]	6034.0 [4695.5,8400.2]	<0.001
ICAM-1 (ng/mL)	813.0 [536.4,1343.9]	601.2 [342.3,856.5]	<0.001
VW (% control)	382.0 [216.8,547.2]	309.0 [192.5,416.5]	0.035

Bimarker data shown as median (interquartile range); ICAM-1 = intercellular adhesion molecule-1; IL-6 = interleukin-6; PAI-1=plasminogen activator inhibitor-1; IL-8 = interleukin-8; IL-10 = interleukin-10; TNFR-I = tumor necrosis factor receptor 1; TNFR-II = tumor necrosis factor II; VW = Von Willebrand factor

Electroencephalography in the Acute Care Environment: A Systematic Review of Educational Initiatives for Non-Experts

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Introduction and Objectives: Formal interpretation of electroencephalography (EEG) in acute-care units is often performed by trained experts, including neurophysiologists and epileptologists. Owing to the rapid expansion of EEG, delays in formal interpretation are often encountered, with possible implications for patient management. Numerous studies have investigated the role of educational programs to enable non-experts (e.g. nurses and residents) to recognize EEG patterns at the bedside. However, the overall content, structure, duration, and efficacy of these EEG training programs remains unknown. We therefore conducted a systematic review of EEG educational programs for non-experts in adult and pediatric/neonatal acute-care settings (emergency departments (ED) and intensive care units (ICU)). Our primary outcome was to describe important similarities, differences, and overarching themes among training programs.

Methods: We searched for studies published on MEDLINE, Embase, Cochrane central, CINAHL, and Web of science. To be considered for inclusion, studies were required to present sufficient details of their educational program, including (to the extent possible) content covered, program structure and duration, assessment methods, and trainee experience. Randomized control trials, cohort studies, and descriptive studies were all considered for inclusion. Data was presented in a qualitative manner and organized by theme.

Results: Our search yielded a total of 7,034 studies, of which 5,626 were screened. Twenty-six full-length studies met our predefined inclusion criteria. Studies were all published in English and included 23 cohort studies, two descriptive studies, and one RCT. The majority of studies were single center in design and originated in the USA. One study was performed in the ED, 15 in adult ICUs, four in pediatric ICUs, and six in neonatal ICUs. The majority of EEG training programs were geared towards ICU nurses (16 studies), followed by ICU physicians, and ICU fellows. Most training programs focused on quantitative or processed forms of EEG rather than short/intermittent EEG. By far the most common training program was for amplitude-integrated EEG (14 studies) followed by color density spectral array (6 studies). EEG education programs involved a mix of large group didactic lectures, small group sessions, and self-learning or one-on-one review with EEG experts. In 16 studies, the overall length of the training program was one day or shorter. Trainee response was positive in the subset of studies reporting this variable.

Conclusion: The majority of EEG training programs involve ICU nurses, quantitative EEG, and are relatively short in duration. Such data could inform future EEG curriculum design for non-experts in acute-care settings.

Examining Cerebral Neurophysiology at the End of Life: The DePPaRT-Neurologic Study

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Introduction/Background: Donation after circulatory death (DCD) has been practiced in Canada since 2006 in patients with poor prognosis without hope of meaningful recovery.¹ In DCD, death determination precedes organ recovery and occurs at 5 minutes following permanent cessation of circulation¹. This approach *assumes corresponding permanent cessation of brain activity*, but objective data to support this assumption is lacking. In the absence of objective data, current DCD approach risks unnecessary damage to donated organs, or unnecessary suffering of organ donors, if brain activity ceases earlier or later than expected.

Objectives: In patients who progress to death following withdrawal of life sustaining measures (WLSM), we aimed to 1) establish the feasibility of monitoring cerebral electrical activity, and 2) examine the temporal association between cessation of brain activity and cessation of cardio-circulatory function.

Methods: We enrolled adult patients from the local cohort of the Death Prediction and Physiology after Removal of Therapy (DePPaRT) study at Western University. In addition to DePPaRT physiological monitoring (electrocardiogram, arterial blood pressure [ABP], plethysmography), we recorded electroencephalographic (EEG) data using the 10-20 International System. Data were recorded from the start of the WLSM and until 30 minutes following circulatory arrest. For feasibility outcomes, we reported consent rate. Raw EEG signals were processed to calculate EEG amplitude, frequency, and power spectra over time, and examined by two certified electroencephalographers to determine the time of electrocerebral inactivity.

Results: We enrolled eight (5 male) participants with a mean age of 64.3 ± 19.9 years. The consent rate was >80%. Table 1 outlines basic demographic information. Figure 1 shows systemic and neurologic recordings during study procedures in a representative patient. EEG amplitude and frequencies decreased with time from the start of WLSM. Of interest, in five patients there was a surge in EEG power during the dying process. Median time of electrocerebral inactivity was 78.5 seconds (IQR=497.5s) prior to cardio-circulatory cessation.

Conclusion: Our study confirms that cerebral neurophysiologic monitoring during the dying process is both technically feasible and acceptable to patients' substitute decision makers. Future studies with larger sample sizes and video-EEG to reconcile potential artifacts are needed to provide more precise estimates. Additional neuromonitoring methods that assess brainstem and cortical function, such as event-

related potentials and evoked potentials, should also be considered. These objective neurophysiologic data will inform ongoing work regarding unified brain-based determination of death³ and inform future DCD practices.

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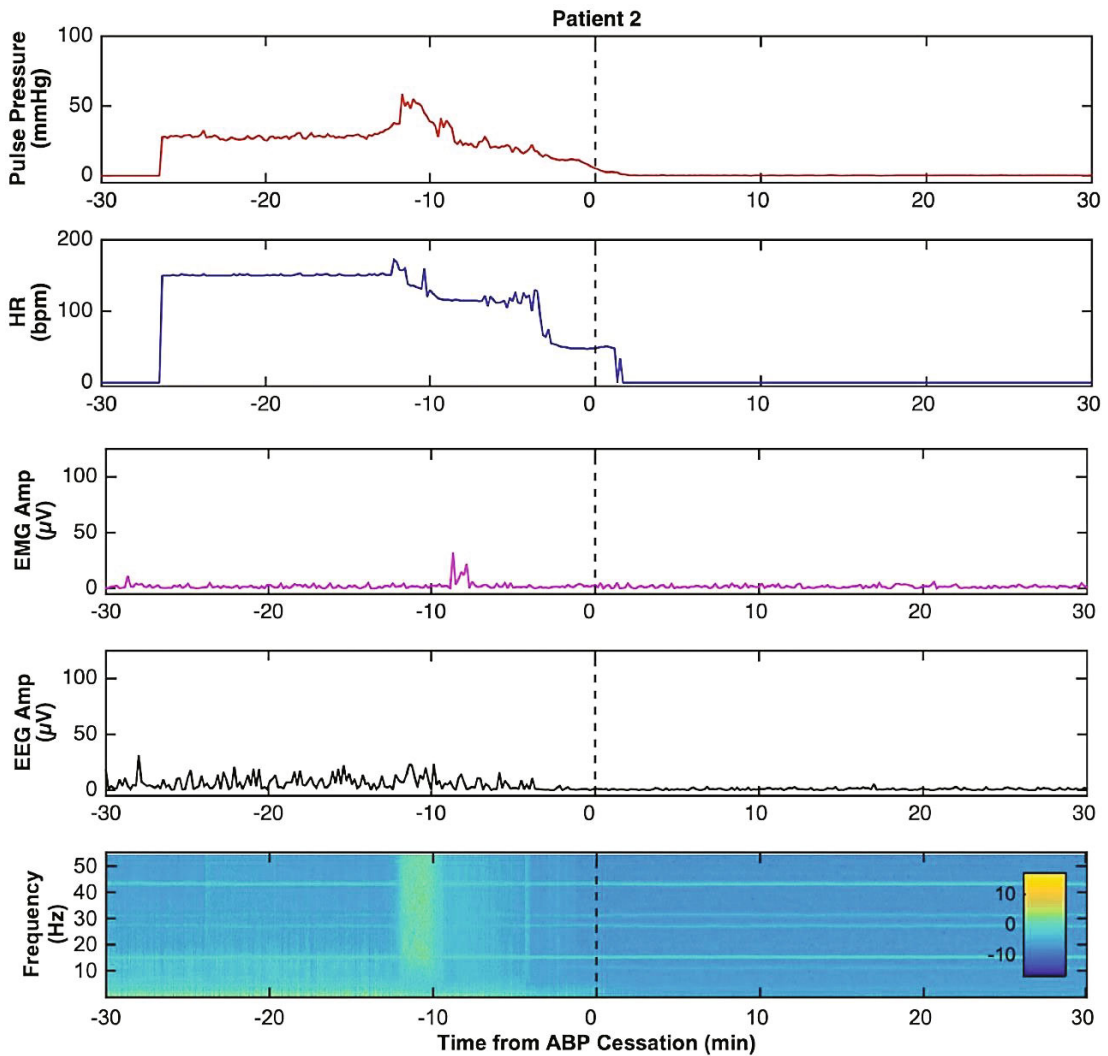
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Table 1 - Demographic information of participants. Abbreviations: ABP = arterial blood pressure, EEG = electroencephalogram, GCS = Glasgow Coma Scale, HR = heart rate, WLST = withdrawal of life sustaining therapies

Patient	Age	Gender	Admitting diagnosis	GCS at WLST	ABP at WLST	HR at WLST	EEG Classification at WLST
1	84	M	TBI	3T	110/55	105	suppression grade II generalised
2	26	F	septic shock	3T	80/40	150	delta II generalised, ++ beta
3	60	M	TBI	5T	100/50	78	suppression grade II gen
4	84	M	shortness of breath	6T	140/50	72	dysrhythmia grade IV status epilepticus
5	74	F	pulmonary edema	3T	105/45	62	suppression grade I generalised, delta grade II generalised
6	62	M	myocardial infarction	3T	145/55	78	Dysrhythmia grade IV status epilepticus
7	48	F	cardiac arrest	3T	130/65	105	burst-suppression
8	76	M	cardiac arrest (PEA)	3T	88/38	85	suppression grade II generalised

Figure 1. Physiologic recordings for 30 minutes before cessation of pulsatile arterial blood pressure, at the time of cessation of pulsatile arterial blood pressure and for 30 minutes afterwards in participant 2. From top to bottom the graphs represent pulse pressure, heart rate (HR), electromyography (EMG) amplitude, electroencephalography (EEG) amplitude and EEG spectrogram. EEG amplitude is <2 microvolts before cessation of pulsatile arterial blood pressure.



Extubation Failure in Intensive Care Units in Nova Scotia: A Descriptive Study

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Introduction: Extubation failure has been demonstrated to be independently associated with poor clinical outcomes such as increased pneumonia rates and mortality^{1,2}. Although the extubation failure rate is often considered a benchmark for quality assurance in the intensive care unit (ICU), the reported rates of extubation failure are varied, from 2% to greater than 30%^{3,4,5}. Extubation failure rates and the associated clinical outcomes within adult medical surgical ICUs across the province of Nova Scotia (NS) have not yet been described.

Objectives: This is a descriptive study of extubation failure in 12 medical surgical ICUs in NS.

Methods: All visits to 12 adult medical-surgical ICUs in NS between April 1, 2018 and March 31, 2020 that involved invasive ventilation were analyzed. Extubation failure was defined as requirement for invasive ventilation within 48 hours of extubation. For each visit, data on patient demographics, transfer status, APACHE IV score, ventilation, delirium, mortality, and length of stay was obtained from the NS Provincial ICU database. The NS Provincial ICU database has prospectively captured data since April 1, 2018 for all patients admitted to one of the 12 adult ICUs in the province. Characteristics examined include demographic variables, ventilation characteristics, clinical characteristics, and outcomes.

Results: A total of 10,028 ICU visits were recorded from April 1, 2018 to March 31, 2020. During this time, 3,049 ICU visits had at least one episode of invasive ventilation (30.4% of ICU visits in NS). A total of 3197 extubations occurred during the study period, with 236 extubation failures (7.4% extubation failure rate).

In the population of patients who failed extubation, median age was 65 yrs (min 21 yrs, max 92 yrs, IQR 17 yrs), 42% were female, average Acute Physiology and Chronic Health Evaluation (APACHE) IV predicted mortality was 36.31%, hospital mortality was 30.9%, and standardized mortality ratio (SMR) was 0.85. In patients requiring re-intubation, 70.1% were delirious at some point in their ICU stay. Median time on invasive ventilation was 7 days (IQR 8.88 days). Median time to reintubation from extubation was 12.6 hours (IQR 21.2 hours).

In the patients that were extubated and did not require reintubation, median age was 63.5 yrs, (min 16 yrs, max 98 yrs, IQR 20 yrs), 40.8% were female, APACHE IV predicted hospital mortality was 35.7%, hospital mortality was 32.6%, SMR 0.91. In patients who were extubated and did not require reintubation 36.2% were delirious at some point in their ICU stay. Median time on invasive ventilation was 1.45 days (IQR 2.9 days).

There were no significant differences in the demographic variables of patients who fail extubation and those that do not. Patients who fail extubation are more likely to be delirious (70.1% vs 36.2%) and have longer time on invasive ventilation.

Conclusions: This is the first descriptive study of extubation failure in NS ICU patients. Invasive ventilation occurred in 30.4% of ICU visits in NS, and 7.4% of all extubations result in the requirement for reintubation within 48 hours. Most extubation failures occur within 12 hours of extubation. The higher rate of delirium in patients who fail extubation indicates that extra caution should be taken to observe delirious patients who are extubated. Further analyses are required to help determine predictors of extubation failure in ICU patients in NS.

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Family Presence During the Pandemic: Clinician Experiences from the 3 Wishes Project

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Introduction: The COVID-19 (C19) pandemic has led hospitals to implement restricted visiting policies. While important to minimize viral transmission, limiting family presence for dying patients may have consequences for all stakeholders. The 3 Wishes Project (3WP) is a clinical program with the goal of personalizing the dying process for patients and their families which has been shown to foster meaningful connections among patients, relatives and clinicians and ease family grief.

Objectives: To evaluate whether the 3WP is *feasible* and *valuable* for patients during the pandemic in 3 units at St. Joseph's Healthcare in Hamilton, Ontario. In this analysis, we focus on findings related to visiting restrictions at the end-of-life (EOL) from the perspectives of clinicians.

Methods: In an embedded mixed-methods study, we enrolled patients who had $\geq 95\%$ probability of death or plans to withdraw life support. We recorded patient, wish and clinician characteristics. We interviewed clinicians who cared for ≥ 1 patient within 2-10 weeks of each death; transcripts were analyzed using a qualitative descriptive approach.

Results: From March 16-July 1, 2020, 45 medical patients were enrolled in the 3WP in the ICU (n=34); COVID ward (n=7) or medical step-down unit (n=4). Pre-hospital living arrangements were: home (27, 60%), assisted care (10, 22%), congregate setting (4, 9%) and other hospital (4, 9%).

Almost half the patients 20(44%) had family at the bedside at the time of death. Of families unable to visit, 13(52%) already said goodbye, 2(8%) were geographically distant, 3(12%) had personal comorbidities, 1(4%) were at high risk of contracting COVID-19, and 5(20%) did not arrive in time before their loved one died. Although terminal wishes were most commonly those of families (159, 67% wishes), most implemented wishes were facilitated by clinicians involvement (156, 89%).

We interviewed 45 clinicians with 13.7 (11.5) [mean (SD)] years of clinical experience conducted by Zoom (n=25) or phone (n=20). Analysis identified 3 themes related to the influence of family member presence on clinicians: a) **Clinicians 'filling the gap' for patients when their relatives were not at the bedside.** Strategies included increased clinician bedside presence when possible, more sensory stimulation to ensure connections (tactile, auditory and gustatory), and providing enhanced emotional,

spiritual and physical support. b) **Clinicians assuming the role of 'life line,' connecting families to patients.** Liaising with relatives on the phone, clinicians recounted being the voice to relay loving sentiments or express terminal goodbyes. Holding tablets during family videoconferences, clinicians were distressed bearing witness to the angst of separation. c) **Implications for future care.** Clinicians emphasized the importance of sharing EOL details if families were interested (e.g., patient comfort, clinician bedside presence), family gratitude for terminal wishes including keepsakes as tangible legacy items (e.g., fingerprint key chains, locks of hair), and concern for complicated grief in family members during the pandemic. **Conclusions:** During the pandemic, the restricted presence of family members at the EOL informed more intentional ways to support dying patients and their families, generating lessons that can inform care of future patients with distant relatives and in future pandemic waves.

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Feasibility of Lung and Diaphragm-Protective Ventilation with and without Extracorporeal CO₂ Removal in Acute Respiratory Failure: An *In Silico* Clinical Trial

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Introduction: Mechanical ventilation (MV) induces both lung and diaphragm injury^{1,2}. We propose a lung and diaphragm protective ventilation (LDPV) strategy targeting a dynamic transpulmonary pressure (DP_L) <15cmH₂O, an esophageal pressure swing (DPes) of -3 to -8 cmH₂O, and a pH>7.25. Meeting these targets at the bedside may be complex. We implemented a recently developed physiologically based mathematical model³ to simulate how patients respond to changes in ventilation, sedation, and extracorporeal CO₂ removal (ECCO₂R) to determine which patients could theoretically reach the goals of the LDPV strategy.

Objectives: To estimate the proportion of patients in whom the LDPV target values can be achieved, to determine whether the application of ECCO₂R substantially increases the probability of reaching the targets, and to identify which patients may require ECCO₂R to achieve the LDPV goals.

Methods: We simulated a population of 100 patients with randomly selected baseline physiological characteristics. The main inputs to the model were PaO₂, lung (C_L) and chest wall (C_{CW}) compliance, airway resistance, intrinsic PEEP, V_{CO_2} , alveolar dead space fraction (V_{Dalv}/V_T), respiratory rate, and the strong ion difference (SID). These patients were submitted to titration of ventilation and sedation to achieve targets according to a pre-defined algorithm. Patients who were unable to meet the LDPV targets were submitted to gradually increasing levels of ECCO₂R and then the algorithm was re-run. The characteristics of the patients succeeding LDPV with or without ECCO₂R were analyzed in a univariate analysis. Paired sampled t-tests and Wilcoxon rank sum test were performed to determine the effect of variables on the algorithm performance and on the algorithm performance after the use of ECCO₂R, respectively. p-value <0.05 are significant.

Results: Of 100 simulated patients (Table 1), 49 patients reached the targets of LDPV without requiring ECCO₂R (15 at baseline, 34 after applying the algorithm). In the 51 patients who failed, none could reach the DP_L target and 23/51 could not reach the DPes target. LDPV failure was associated with higher alveolar dead space (0.41 vs 0.27, p<0.001), lower lung compliance (44 vs 53 ml/cmH₂O, p=0.0013) and greater metabolic acidosis (strong ion difference 34 vs 37 mEq/l, p<0.049). Of the patients who failed, the application of ECCO₂R enabled 40/51 patients to meet the targets at a median CO₂ removal rate of 30% of V_{CO_2} (IQR 17.5-50) from baseline. Eleven patients could not reach LDPV targets even with ECCO₂R. The main determinants of failure after ECCO₂R were higher V_{Dalv}/V_T (0.59 vs 0.37, p<0.0001) and lower C_L (34 vs 45 ml/cmH₂O, p=0.011) (Figure 1).

Conclusion: In this *in silico* clinical trial, LDPV targets could be achieved in 49% of our simulated population. ECCO₂R increased the probability of reaching the targets of LDPV from 49% to 89%. The main determinants of failure of LDPV strategy are decreased lung compliance and an increased alveolar dead space to tidal volume ratio.

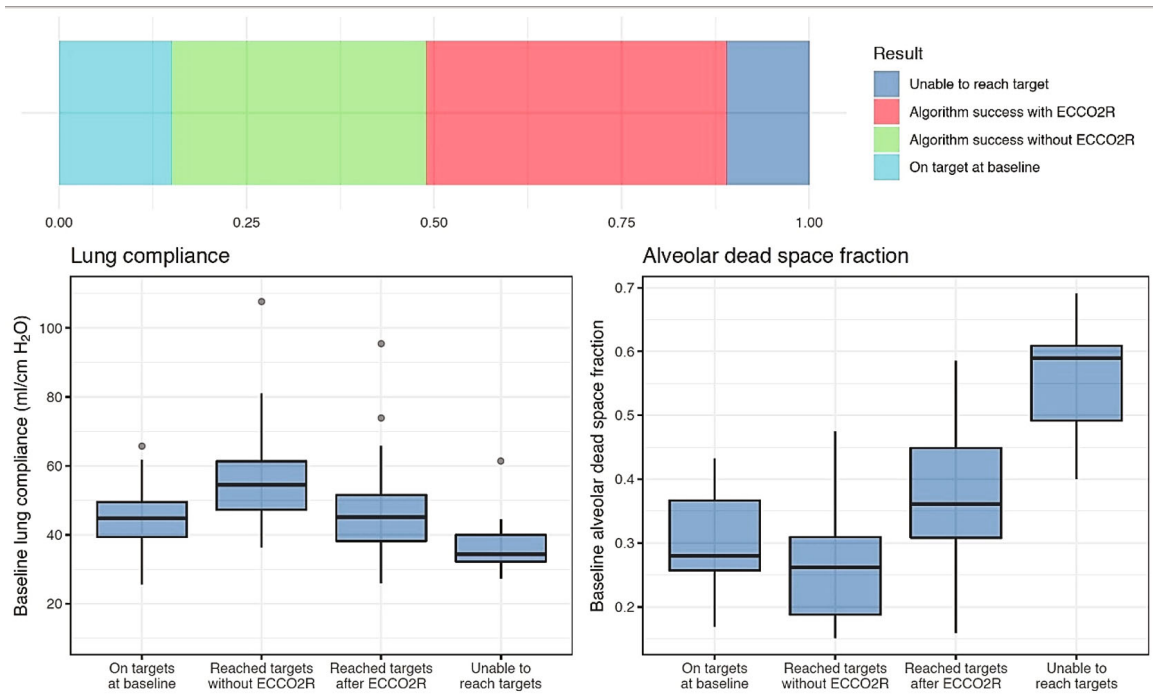
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Table 1 Baseline characteristics (n=100)	Mean (SD)
PaO ₂ [mmHg]	102 (21)
VCO ₂ [ml/min]	229 (39)
Airway resistance [cmH ₂ O/l/s]	11 (2)
Intrinsic PEEP [cmH ₂ O]	1.4 (1)
Respiratory rate [breath/min]	28 (4)
Strong ion difference [mEq/l]	35 (7)
Lung compliance[ml/cmH ₂ O]	49 (14)
Chest wall compliance[ml/cmH ₂ O]	128 (96)
Alveolar dead space fraction	0.34 (0.13)

Figure 1



Healthcare Professionals' Understandings of the Definition and Determination of Death: A Scoping Review

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Introduction: During the 1950s, the advances in technology within critical care medicine, particularly mechanical ventilation, cardiopulmonary resuscitation (CPR), and the innovations in the practice of organ transplantation together altered the relationship between organ failure and death. Since then, there has been a shift away from the traditional cardiopulmonary death criteria to a brain-based criteria. However, much of the academic literature has been dedicated to the controversy surrounding the definition and determination of brain death. Yet clinically, the determination of brain death in critically ill patients is practised worldwide and seemingly highly accepted by clinicians.

Objectives: To develop a comprehensive description of the current understandings of healthcare professionals regarding the meaning, definition and determination of death.

Methods: This scoping review was conducted in compliance with the PRISMA-ScR checklist¹. Online databases were used to identify papers published from 2003 to 2020. Additional sources were searched for conference proceedings and theses. Two reviewers (SS & KZ) screened the papers using predefined inclusion and exclusion criteria, extracted data for specific content variables and performed descriptive examination. Complementary searches and review of reference lists were used to complement the final study selection. A search strategy using vocabulary of the respective databases was created, and criteria for the inclusion and exclusion of the articles was established. A data extraction instrument was developed to iteratively chart the results of the review. A qualitative approach was conducted to thematically analyze the data.

Results: We screened a total of 4935 papers, of which 64 met the full inclusion criteria. Fifteen additional papers were added from complementary searches, totalling 79 papers overall. Identified themes included: 1) the historical evolution of brain death, 2) persistent controversies about brain death and death determination, 3) wide variability in healthcare professionals' knowledge and attitudes about death determination, 4) critical need for brain death determination revision.

Conclusion: We concluded that although brain death is widely accepted, there exists variation in healthcare providers' understanding of its conceptual basis. Death determination remains a divisive issue among scholars. This review found there is a need for increased opportunities for formal training on brain death among healthcare providers.

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High Flow Nasal Cannula Oxygen Therapy with The Mouth Open or Close: Comparison to CPAP

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Introduction: High flow nasal cannula oxygen therapy (HFNC) is a promising treatment for adults with respiratory failure. It provides washout of anatomic dead space and generates positive pressure in the nasopharynx and the alveoli as illustrated by increased end-expiratory lung volume.

Objective: Whether the effects of HFNC are similar to continuous positive airway pressure (CPAP) is unclear and changes in respiratory rate are not well explained. Last, the effects of mouth close vs. open are unclear. We performed a bench and a physiological study to address these questions.

Methods: 1) Bench study using a manikin's head and lungs connected to a breathing simulator generating steady inspiratory efforts with set lung compliance and airway resistance. Nasopharyngeal pressure was measured with a dedicated catheter and tidal volume was obtained from the simulator under different conditions with HFNC from 0 to 60L/min. 2) Physiological cross-over study on 10 healthy volunteers breathing mouth open or close under HFNC at 20, 40 and 60L/min and under CPAP 4cmH₂O. Nasopharyngeal pressure was measured using a dedicated 12 French catheter, as well as esophageal pressure (Cooper catheter). Tidal volume and flow were estimated using calibrated electrical impedance tomography (Pulmovista). We calculated the pressure-time product of the respiratory muscles, inspiratory and expiratory resistance. We used Friedman test and Nemenyi post hoc test, two-way ANOVA and Bonferroni post hoc test.

Results: The bench data simulating mouth closed showed that pressure increased with flow up to 4 cm H₂O while a progressive reduction in tidal volume was observed with increasing flow. The study in healthy subjects showed a nasopharyngeal pressure at 60L/min close to 7 cmH₂O with mouth closed, higher than CPAP; a decrement in respiratory rate (by lengthening expiration) and a relative worsening of mechanic, with no change in tidal volume. The decreased rate explained a reduced effort (pressure time product). With mouth closed we observed an increased resistance to breathing, both inspiratory and expiratory. Mouth open showed much less pressure and physiological effect of HFNC.

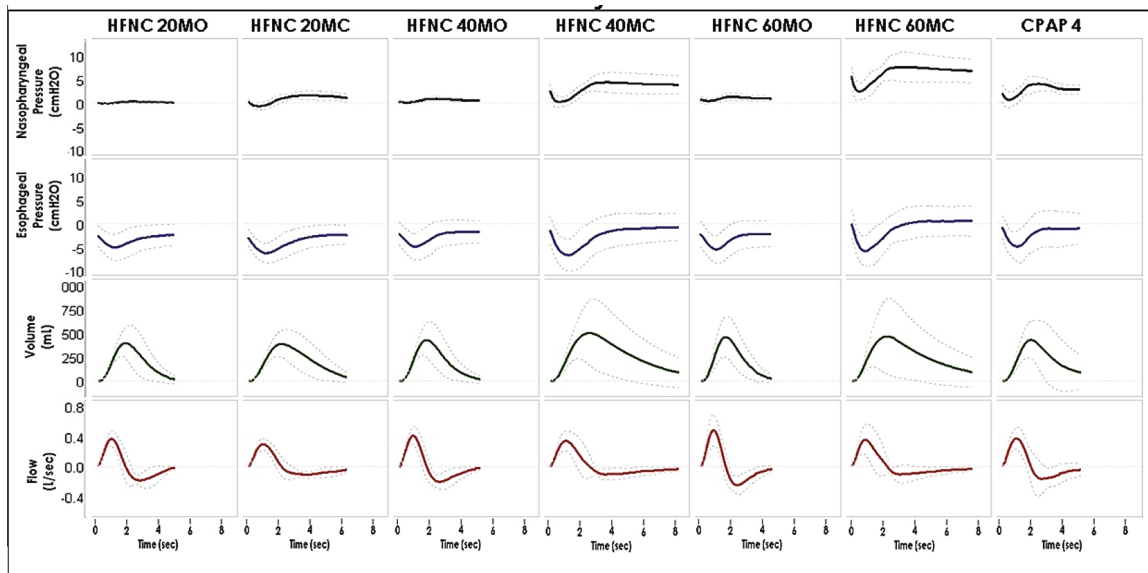
Conclusions: During HFNC, strictly closing the mouth can result in increased resistance to breathing both in a bench and in a healthy volunteer study. In healthy volunteers with mouth closed, HFNC at a flow of 40L/min delivers pressures comparable to CPAP 4cmH₂O, whereas at 60L/min it delivers pressures close to 7 cmH₂O. The increase in inspiratory and expiratory resistance might explain the decrease in respiratory rate and the prolonged expiration.

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Figure 1 – Mean Breath Summary



Intraoperative Predictors of Delirium Post Cardiac Surgery: Analysis of the B-Free Pilot

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Background: Delirium is defined as an acute state of confusion that affects 15-52% of adults after cardiac surgery.(1-4) Delirium is associated with prolonged hospital stay, long-term cognitive decline and death. (5-7) No studies have explored the association between intraoperative anesthetic medications and delirium after cardiac surgery.

Objective: We sought to determine whether the administration and dose of intraoperative benzodiazepines, dexmedetomidine, and opioids were associated with an increased risk of delirium after cardiac surgery.

Methods: The Benzodiazepine-Free Cardiac Anesthesia for the Reduction of Post-operative Delirium (B-Free) pilot study enrolled patients undergoing cardiac surgery in Hamilton, Ontario and Winnipeg, Manitoba. Patients were assessed for post-operative delirium in the cardiovascular intensive care unit using the Confusion Assessment Method Intensive Care Unit (CAM-ICU). We evaluated a base case mixed-effects multivariable logistic regression of 6 known risk factors against a novel model to determine if intraoperative medications are associated with an increased incidence of delirium.

Results: B-Free enrolled 1343 consecutive participants. Two hundred and forty-three (18.1%) participants developed delirium as assessed by at least 1 positive CAM-ICU score after cardiac surgery. The base model containing known predictors specified odds-ratio estimates of effect with bootstrapped estimates of the 95% confidence interval. The base model confirmed that age in years (1.02 [1.01-1.04], $p = 0.001$), past medical history of cerebrovascular disease (1.65 [1.01-2.70], $p = 0.047$), emergency surgery (1.97 [1.23-3.16], $p = 0.005$), and cardiopulmonary bypass time in minutes (1.00 [1.00-1.01], $p = 0.006$) were associated with increased incidence of delirium. In the novel model that added intraoperative medications, benzodiazepines (0.90 [0.67-1.21], $p = 0.488$), dexmedetomidine (1.00 [0.43-2.34], $p = 0.998$), and cumulative standardized opioids (1.00 [0.99-1.00], $p = 0.797$) were not significantly associated with post-operative delirium. There were no measurable, systematic differences between sites that predicted delirium. Adjusting for intraoperative medications did not improve model performance in predicting delirium after adjusting for known covariates ($\chi^2 = 0.551$, $p = 0.908$).

Conclusion: Intraoperative benzodiazepine, dexmedetomidine or opioid administration or dose were not associated with an increased risk for delirium after cardiac surgery.

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Table 1 – Multivariable Analysis for Predictors of Delirium after Cardiac Surgery

Risk Factor	Base Model		Novel Model	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age (years)	1.02 (1.01 – 1.04)	0.001	1.02 (1.01 – 1.04)	0.001
Sex (Male vs. Female ‘reference’)	0.80 (0.57 – 1.12)	0.191	0.80 (0.57 – 1.13)	0.205
Past medical history of Cerebrovascular disease (Yes vs. No ‘reference’)	1.65 (1.01 – 2.70)	0.047	1.67 (1.02 – 2.73)	0.043
Emergency Surgery Status (Yes vs. No ‘reference’)	1.97 (1.23 – 3.16)	0.005	2.01 (1.25 – 3.22)	0.004
Isolated CABG surgery (No vs. Yes ‘reference’)	0.98 (0.71 – 1.36)	0.918	0.98 (0.71 – 1.36)	0.906
Cardiopulmonary bypass ‘CPB’ time (minutes)	1.00 (1.00-1.01)	0.006	1.00 (1.00 – 1.01)	0.006
Total Standardized Intraoperative Opioids (mg)			1.00 (1.00 – 1.00)	0.797
Intraoperative Benzodiazepines (mg; Yes vs. No ‘reference’)			0.90 (0.67 – 1.21)	0.488
Intraoperative dexmedetomidine (mg; Yes vs. No ‘reference’)			1.00 (0.43 – 2.34)	0.998

Levetiracetam Versus (Fos)Phenytoin for Second-Line Treatment of Pediatric Status Epilepticus: Systematic Review and Meta-Analysis

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Background: Status epilepticus is a common neurologic emergency in children with potentially devastating outcomes. Approximately one third of patients do not respond to first-line treatment.¹ The most effective and safe second-line agent remains unclear.

Objective: To synthesize the available evidence examining the efficacy and safety of levetiracetam compared to phenytoin or fosphenytoin in benzodiazepine-refractory pediatric status epilepticus.

Methods: We searched (from inception until April 27, 2020) Ovid MEDLINE, EMBASE, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) for randomized controlled trials (RCTs). Two reviewers, independently and in duplicate, screened citations to identify eligible RCTs that compared levetiracetam to (fos)phenytoin for benzodiazepine-refractory status epilepticus in children, or had data from a subgroup of children. Independently and in duplicate, we performed data abstraction, risk of bias (RoB) assessment using the Cochrane RoB tool and certainty assessment using GRADE. We performed meta-analyses using random-effect models or presented findings narratively if there were insufficient data for quantitative analysis.

Results: We identified 7 RCTs ($n = 1,575$)²⁻⁸. Four RCTs used phenytoin and 3 used fosphenytoin as the comparator. Pooled analysis demonstrated low certainty evidence of no difference of levetiracetam on time to seizure cessation (mean difference -3.11 minutes, 95% confidence interval (CI) -6.67 to 0.45), early seizure cessation (relative risk (RR) 1.09, 95% CI 0.95 to 1.26) or late seizure cessation (RR 1.05, 95% CI 0.93 to 1.18) as compared to phenytoin or fosphenytoin. In general, adverse event outcomes were not consistently reported, and our conclusions are limited by imprecision due to low numbers of events. We found low certainty evidence for less respiratory depression with levetiracetam (RR 0.28, 95% CI 0.12 to 0.69).

Conclusions: The efficacy of levetiracetam is comparable to phenytoin or fosphenytoin in children with benzodiazepine-refractory status epilepticus (low certainty evidence). Levetiracetam may cause less respiratory depression. Clinicians and guideline developers should weigh safety profiles and practical considerations when choosing between these agents.

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Lung Protective Approach and Respiratory Mechanical Characteristics During Lung Donor Support: A Cohort Study

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Background: Lung protective ventilation (PV) using low tidal volumes (Vt) and high positive end-expiratory pressure (PEEP) has been advocated in organ donors (OD) to increase the rate of lung procurement. Although one randomized-control trial (1) and observational studies support this approach, PV was part of a larger bundle of short-term interventions, and its contribution to the observed benefits is not well understood. Furthermore, a recent large French cohort study showed that this approach, even if it increased procurements, is applied in less than in 30% of ODs at the time of lung proposal (2). A better understanding of the ventilatory settings and interventions in this population could inform future studies.

Objective: Our first aim was to determine the frequency and how PV was achieved for ODs in our center. Our second aim was to describe the overall characteristics of the respiratory mechanics at the beginning and at the end of the lung support process in our population.

Methods: We conducted a retrospective observational cohort study including all consecutive ODs with a neurological determination of death (NDD) between June 2013 and May 2018. ODs not eligible for potential lung donation based on local OPO criteria were excluded. Respiratory rate (RR), tidal volume (Vt), PEEP, Plateau Pressure (PPLAT), Driving Pressure, PaO₂/FiO₂ (P/F) ratio were collected at the time of NDD (T0) and at the time of refusal or at the closest time to lung retrieval (T1). Median values and proportions of the different measures at T0 and T1 are reported, and simple comparisons between non procured and procured lungs are presented without adjustment for baseline characteristics.

Results: Among 222 potential ODs after NDD, 184 gave organs, of which 145 were supported for potential lung procurement and 90 finally procured (62%). The majority were males (75%), with a mean age of 50 ± 18 years old and a BMI of 27.3 ± 5.5. The median duration of intubation was 3 days (IQR 2;4), the median duration of support after NDD was 25 hours (IQR 18;35) and the principal modes of ventilation were volume Control (56%) or pressure Control (40%). Recruitment maneuvers were done at least once in 67% and twice in 48% of the cases (no difference between lungs procured or not). As displayed in Table 1, median Vt was 8.3 (7.5;9.5) mL/kg and PEEP = 5 (5;8) cmH₂O at T0 vs 8.7 (10.7;10.2) mL/kg and PEEP = 8 (5;10) cmH₂O at T1. Vt was set at ≤ 8 mL/kg in 40.5% at T0, but decreased to 34.6% at T1 (p>0.5), which is driven by the group with lungs that were not procured; in contrast PEEP was set ≥ 8 cmH₂O in 32.6% at T0 and increased to 64.9% at T1 (p<0.001). In all groups the median PPLAT and Driving Pressure did not change significantly between T0 and T1 (Table 2). Comparing procured and non procured lungs, the proportion of PV (for Vt and PEEP) showed no differences (Table 1). However, the P/F ratio was higher both at T0 and at T1 for the procured lungs (Table 2), in addition to a significant improvement during support (Delta P/F= 92), which could suggest the effect of other interventions

Conclusion: In our cohort, a small proportion of ODs were exposed to the low Vt aspect of PV, and more frequently to the higher PEEP. According to Driving Pressure and PPLAT, the ventilation remained “protective”, which might be due to alveolar recruitment. The better Delta P/F ratio observed in the procured lung group deserves further analysis to determine the interventions responsible for P/F improvement.

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Table 1

TABLE 1	TOTAL (N=145)				Lung outcome								p-value*
	Median	P25	P75	Proportion	Not procured (N=55)				Procured (N=90)				
					Median	P25	P75	Proportion	Median	P25	P75	Proportion	
RR at T0	14	12	17		15	12	16		14	12	17		0.619
RR at T1	14	12	17		16	12	18		14	10	16		0.011
Vt (ml) at T0	550	500	600		550	500	600		550	500	600		0.703
ml/kg of IBW at T0	8.3	7.5	9.5		8.5	7.3	9.4		8.3	7.5	9.5		0.752
Vt ≤ 8ml/kg at T0				40.5%				38.8%				41.6%	0.680
Vt (ml) at T1	560	500	650		553	500	650		560	500	650		0.864
ml/kg IBW at T1	8.7	7.7	10.2		8.5	7.3	10.3		8.7	7.7	10.2		0.844
Vt ≤ 8ml/kg at T1				34.6%				41.8%				30.3%	0.180
Delta Vt (T1-T0)	0	0	55		0	0	50		0	-3	80		0.973
PEEP (cm H2O) at T0	5	5	8		5	5	10		5	5	8		0.245
PEEP ≥ 8 cmH2O at T0				32.6%				38.2%				29.1%	0.265
PEEP (cm H2O) at T1	8	5	10		8	5	10		8	7	10		0.874
PEEP ≥ 8 cmH2O at T1				64.9%				58.2%				69.0%	0.174

RR: Respiratory rate; Vt: Tidal volume; IBW: Ideal bodyweight. Data are reported as Median (25-75 percentile) or proportions (%)

* Procured vs not procured: Mann-Whitney U Test for continuous variables and Chi-square for categorical variables

Table 2

TABLE 2	TOTAL (N=145)			Lung outcome						p-value*
	Median	P25	P75	Not procured (N=55)			Procured (N=90)			
				Median	P25	P75	Median	P25	P75	
PIP (cm H2O) at T0	22	19	26	23	20	27	22	18	25	0.070
PIP (cm H2O) at T1	22	20	26	23	20	27	22	20	24	0.113
PPLAT (cm H2O) at T0	18	16	21	19	16	22	18	16	20	0.074
PPLAT (cm H2O) at T1	19	17	21	19	17	22	19	17	21	0.493
DrivingP (cm H2O) at T0	11	10	14	12	10	14	11	10	13	0.317
DrivingP (cm H2O) at T1	11	9	13	11	9	13	10.5	9	13	0.216
PaO2/FiO2 at T0	376	319	434	348	243	411	390	339	448	0.001
PaO2/FiO2 at T1	444	385	507	385	321	431	488	428	523	<0.001
Delta P/F (T1-T0)	65	-11	129	0	-35	107	92	26	141	0.003

PIP: Peak inspiratory pressure; PPLAT: Plateau Pressure; * Procured vs not procured: Mann-Whitney U Test

Normal Saline Compared to Balanced Crystalloid in Diabetic Ketoacidosis: A Systematic Review and Meta-Analysis

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Introduction: Preliminary data suggests use of balanced crystalloid solutions (BES) may be more beneficial compared to normal saline (NS) in critically ill patients^{1,2}, however large randomized controlled trials (RCTs) are ongoing^{3,4}. Even more uncertainty remains regarding optimal crystalloid in the setting of diabetic ketoacidosis (DKA), a condition in which often requires large volume resuscitation and challenging electrolyte management. This systematic review and meta-analysis summarize the effect of BES versus NS in DKA patients.

Methods: We performed a comprehensive search of MEDLINE, EMBASE and Cochrane library. We included RCTs that compared BES vs NS in DKA patients. We pooled estimates of effect using relative risk (RR) for dichotomous outcomes and mean differences (MD) for continuous outcomes with 95% confidence intervals (CIs). We assessed risk of bias for included RCTs using a modified Cochrane tool and certainty of evidence using GRADE methodology.

Results: We included 6 RCTs (n= 324 patients). There was no important difference in DKA resolution (RR 1.00, 95% CI 0.94 to 1.05, moderate certainty) or post resuscitation serum chloride (MD 1.44 mmol/L higher, 95% CI 1.74 lower to 4.63 higher, moderate certainty) and an uncertain effect on mortality (RR 0.66, 95% CI 0.14 to 3.13, low certainty) when using NS compared to BES. Time to DKA resolution was likely longer in the NS group (MD 3.12 hours longer, 95% CI 0.30 shorter to 6.53 longer, moderate certainty). NS use was associated with a lower post resuscitation serum bicarbonate (MD 1.77 mmol/L, 95% CI 0.27 lower to 3.27 lower, moderate certainty) and longer hospital stay (MD 0.87 days longer in NS group, 95% CI 0.30 days longer to 1.45 days longer, moderate certainty) compared to BES. Complications from IV fluids were rare and rates were similar between each type of fluid.

Conclusion: In patients with DKA, there was no difference between NS and BES in terms of DKA resolution or serum chloride, with an uncertain effect on mortality. NS may be associated with longer time to DKA resolution, lower post-resuscitation serum bicarbonate levels and longer hospital stay compared to BES.

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Table 1

Study or Subgroup	NS		BES		Total	Weight	Mean Difference IV, Random, 95% CI	
	Mean	SD	Mean	SD				
Tsui 2019	31	14.81	20	11.85	22	12.8%	13.00 [4.84, 21.16]	
Van Zyl 2012	14.1	10.1	19	14.5	15.17	20	13.1%	-0.40 [-8.45, 7.65]
Williams 2020	16	8.88	32	14.5	5.92	32	30.8%	1.50 [-2.20, 5.20]
Yung 2016	8.6	2.3	38	6.2	4.7	38	43.3%	2.40 [0.74, 4.06]
Total (95% CI)	109		112		100.0%		3.12 [-0.30, 6.53]	

Heterogeneity: Tau² = 6.29; Chi² = 7.15, df = 3 (P = 0.07); I² = 58%
Test for overall effect: Z = 1.79 (P = 0.07)

Table 2

Author(s): Naif Alghamdi, Paityn Major, Dipayan Chaudhuri, Janice Tsui, Brent Brown, Bram Rochweg
Question: Balanced electrolyte solutions compared to normal saline for DKA resuscitation.
Setting: S R of RCTs.
Bibliography:

Certainty assessment							N ₁ of patients		Effect		Certainty	Importance
N ₁ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Balanced electrolyte solutions	normal saline	Relative (95% CI)	Absolute (95% CI)		
DKA resolution.												
4	randomised trials	not serious	not serious	not serious	serious ^a	none	106/118 (89.8%)	110/121 (90.9%)	RR 1.00 (0.94 to 1.05)	0 fewer per 1,000 (from 55 fewer to 45 more)	⊕⊕⊕○ MODERATE	CRITICAL
Time to DKA resolution. (assessed with: Hours.)												
4	randomised trials	not serious	not serious	not serious	serious ^b	none	109	112	-	MD 3.12 Hours higher (0.3 lower to 6.53 higher)	⊕⊕⊕○ MODERATE	CRITICAL
Post treat HCO₃ (assessed with: mmol/L)												
3	randomised trials	not serious	not serious	not serious	serious ^c	none	82	83	-	MD 1.77 meq/L lower (3.27 lower to 0.27 lower)	⊕⊕⊕○ MODERATE	CRITICAL
Duration of hospital days. (assessed with: days.)												
3	randomised trials	not serious	not serious	not serious	serious ^d	none	79	83	-	MD 0.87 days higher (0.3 higher to 1.45 higher)	⊕⊕⊕○ MODERATE	CRITICAL
Post treat Cl (assessed with: mmol/L)												
4	randomised trials	not serious	serious ^e	not serious	serious ^f	none	120	121	-	MD 1.44 mmol/L higher (1.74 lower to 4.63 higher)	⊕⊕○○ LOW	CRITICAL
Mortality.												

Table 3

4	randomised trials	not serious	not serious	not serious	very serious ^f	none	2/94 (2.1%)	4/98 (4.1%)	RR 0.66 (0.14 to 3.13)	14 fewer per 1,000 (from 35 fewer to 87 more)	⊕⊕○○ LOW	CRITICAL
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CI: Confidence interval; RR: Risk ratio; MD: Mean difference

Explanations

- Despite point estimate that suggests no effect, 95% confidence intervals do not rule out important benefit or harm. Also, low event number contributes to imprecision.
- Point estimate suggests longer time to DKA resolution with NS, however lower end of the 95% CI suggests no effect thereby contributing to imprecision.
- Point estimate suggests lower bicarbonate level with NS, however low patients number contributes to imprecision.
- Point estimate demonstrates higher length of stay in NS, however low number of patients contributes to imprecision.
- Important statistical heterogeneity given high I squared and significant Chi-squared test.
- Very wide confidence intervals which do not exclude significant benefit or significant harm.

Outcomes in Critically Ill Adults with Influenza Infection

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Introduction: Influenza is responsible for hundreds of ICU admissions and many ICU deaths in Canada annually. Few studies have described the course of influenza infections in the critically ill in Canada in terms of ICU specific outcomes and resource utilization.

Objectives: To describe the epidemiology of influenza infection in critically ill patients and identify independent associations with 30-day mortality. In addition, measures of resource utilization including mechanical ventilation, vasopressor use, continuous renal replacement therapy (CRRT) and extracorporeal membrane oxygenation (ECMO) support, as well as ICU and hospital lengths of stay, will be analyzed.

Methods: Local microbiology and critical care datasets were used to identify patients with influenza infection admitted to any one of three adult critical care units from 2014-2019 at a large Canadian academic center. Patient characteristics (demographics, comorbidities), influenza type/subtype, severity indicators, antiviral treatment, critical care resource utilization, and 30-day mortality from time of ICU admission were collected. Independent predictors of mortality were identified using multivariable Cox regression modeling.

Results: 130 patients with PCR-confirmed influenza infection were identified. Mean (\pm SD) patient age was 56 years (\pm 16), 72 (55%) were male. Admission diagnoses were medical in 112 (86%) patients and surgical in 18 (14%). Mean APACHE II score was 22 (\pm 9), SOFA score 8 (\pm 4), and Charlson Comorbidity Index (CCI) score 3.4 (\pm 2.5). 107 (82%) patients were positive for influenza A [60 (46%) H1N1pdm09, 43 (33%) H3N2, 4 (3%) untyped], and 22 (17%) had influenza B infection; 1 patient was co-infected with both influenza A and B. 77 (44%) of patients had microbiologically confirmed lower respiratory tract disease (positive from endotracheal aspirate or bronchoscopic sample). 62 (48%) patients had evidence of bacterial co-infection and 8 (6%) had fungal co-infection during ICU admission. Only 12 patients (10%) had a documented history of seasonal influenza vaccination. 15 (12%) cases were hospital-acquired (diagnosed \geq 48h after hospital admission).

108 (83%) of patients required mechanical ventilation, 94 (72%) vasopressor support, 26 (20%) CRRT and 11 (9%) ECMO. 121 (93%) patients received antiviral therapy (all with oseltamivir) for a median duration of 5 days (IQR 5-9). Only 33 (25%) received antiviral treatment within 5 days of symptom onset. 30-day mortality was 23%. ICU and hospital mortality rates were 22% and 28%, respectively. Median lengths of stay were 10 days (IQR 5-22) in ICU and 15 days (IQR 9-32) in hospital. Patients who received antiviral treatment were more likely to survive to 30 days (log rank test $p=0.009$) with an adjusted hazard ratio (aHR) 0.15, 95%CI 0.04-0.51, $p=0.003$. Independent predictors of 30-day mortality also included the need for continuous renal replacement therapy (aHR 2.48, 95%CI 1.14-5.43, $p=0.023$), higher APACHE II score (aHR 1.08, 95%CI 1.02-1.14, $p=0.011$), and influenza A (aHR 7.10, 95%CI 1.37-36.8, $p=0.020$) compared to influenza B infection.

Conclusion: Thirty-day mortality in critically ill patients with influenza infection is high; 23% in this retrospective cohort. Most patients were infected with influenza A H1N1pdm09 strain and just under half had concomitant bacterial pneumonia. Antiviral therapy was independently associated with 30-day survival while the need for CRRT, higher severity of illness and influenza A infection were independently associated with mortality.

Patterns of Anxiety and Depression Symptoms Among Family Caregivers of Critically Ill Patients with Delirium: A Latent Profile Analysis

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Introduction: Critically ill patients admitted to intensive care units (ICUs) frequently rely on family caregivers (e.g., partners, friends) to act as surrogate-decision makers and important emotional supports.^{1,2} Apart from dealing with emotional burden of the patient's critical illness, having to make difficult decisions on behalf of the patient is an additional stress for a family caregiver.³ Delirium is frequently experienced by patients in the ICU⁴ and is distressing to patients and family caregivers. Family caregivers of critically ill patients are reported to have long-lasting negative psychological sequelae, including anxiety and depression. We aimed to examine patterns of co-occurrence between anxiety and depression symptoms among family caregivers of critically ill patients with delirium.

Methods: Latent class analysis was used to examine patterns of self-reported anxiety and depression symptoms among family caregivers for critically ill patients enrolled in a single-centre validation study conducted at a large academic hospital (Calgary, Canada) in a single-payer healthcare system. Patient-family dyads were included if family member anxiety and depression were assessed at the same time as the first patient delirium assessment. The seven-item Generalized Anxiety Disorder-7 (GAD-7) scale was used to assess self-reported symptoms of anxiety; symptom severity was classified as none, mild, moderate or severe. Patient Health Questionnaire-9 (PHQ-9) was used to assess symptoms of depression; symptom severity was classified as none, mild, moderate, moderately severe or severe. Patient delirium was assessed by the Confusion Assessment Method for ICU (CAM-ICU), a four-item ICU delirium detection tool with high sensitivity (93-100%) and specificity (98-100%). Latent class membership was estimated based on the latent class posterior distribution. Family caregiver age (dichotomized at 65 years) and family caregiver sex were treated as independent variables to predict latent class membership. Two- to five-class models were calculated and compared on Bayesian information criterion values.

Results: Three distinct classes for patterns of co-occurrence between anxiety and depression symptoms were identified. Class membership differed by anxiety and depression symptom severity. Among 40 family caregivers (median age 53 years [IQR 44-63 yr]; 80% female), the classes identified were (1) no anxiety/no depression; (2) mild-moderate anxiety/mild depression; and (3) severe anxiety/moderate-severe depression. Among 92 family caregivers for critically ill patients without delirium (median age 57 years [IQR 46-67 yr]; 72.8% female), the classes identified were (1) no-mild anxiety/no-mild depression; (2) moderate anxiety/moderate depression; and (3) moderate-severe anxiety/moderate-severe depression. Class membership for all caregivers (N=132) was significantly predicted ($p<0.05$) by family caregiver age (class 1 versus class 3) and family caregiver sex (class 2 versus class 3).

Conclusion: Our findings contribute to knowledge on co-occurrence patterns of anxiety and depression among family caregivers of critically ill patients. The mental health of family caregivers of critically ill patients with delirium may require different targets in mental health interventions. These findings lay the foundation to assess overlapping trajectories for anxiety and depression symptoms and may inform future mental health treatments.

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Perceptions of the Multidisciplinary Health Care Team on In-Situ Simulation

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Introduction: In-situ simulation shows promise as an effective multidisciplinary team training tool to identify latent safety errors, optimize communication and system processes. The COVID pandemic has required the rapid adoption of new system processes in the ICU that are ideally evaluated and practiced in the actual care environment. In-situ simulation is an ideal tool for this, however, its disruptive nature is a major downside. Although the benefits of in-situ simulation in the ICU setting have been described, the potential perceived harm to patient care of running an unscheduled simulation using actual working staff are unknown. The aim of this study is to assess the multidisciplinary team member's perceptions regarding the value of in-situ simulation relative to its perceived impact on patient care, practicing the transfer of a COVID positive trauma patient from the trauma bay to the ICU.

Methods: We conducted a longitudinal survey study including all members of the multidisciplinary ICU team and trauma team at the QEII Health Sciences Centre, a level 1 trauma centre in Nova Scotia. Following an in-situ simulation involving the transfer of a COVID positive trauma patient from the trauma bay to the ICU, participants were given a 10-question survey with answers on a 5 point Likert scale exploring the perceived harms and benefits of the experience.

Results: Response rate was 100%, for a total of 43 surveys administered after 4 in-situ simulations that took place at the start of the COVID pandemic. The survey respondents were, attending staff (21%), nurses (21%), paramedics (7%), respiratory therapist (9%) and residents (42%). Respondents felt that participating in the in-situ simulation delayed (28%) or compromised patient care (5%) infrequently. No respondents felt that patients were harmed on account of running the simulation. In-situ simulation was felt to identify important safety issues (70%), improve team communication (89%) and improve patient care (89%). The in-situ simulation was considered enjoyable (92%) and identified as a good educational experience (93%).

Conclusions: In-situ simulation is not felt to cause delays or compromise patient care. It is considered to be a good learning opportunity that identifies safety issues and improves patient care. This study can help inform other trauma programs who are contemplating starting in-situ simulations, but are concerned about its possible impact on patient care and team buy in.

Reliability of Inspiratory Holds During Pressure Support Ventilation by Independent Raters Evaluation

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Introduction: Evidence has emerged that driving pressure during pressure support ventilation (PSV) is associated with outcome, as in controlled mechanical ventilation[1]. This measurement, however, is not routinely performed, as it requires a reliable assessment of Plateau Pressure (Pplat) during an inspiratory hold. In fact, not all ventilators allow to perform an inspiratory hold during assisted ventilation modes and the interpretation of the result might not be straightforward because of ongoing patient's muscular activity. Nevertheless, the Pplat value can be of invaluable help in clinical practice, both to compute driving pressure under PSV[1] and to monitor patient's inspiratory effort[2].

Objectives: To evaluate the reliability in assessing inspiratory holds performed during PSV as general "readability" (determining if the hold reveals a stable airway Pplat) and as the value and duration of the plateau.

Methods: This is an ancillary analysis of pressure and flow curves obtained during a multicenter observational study aimed to describe the incidence of patient-ventilator asynchronies in ARDS patients (BEARDS, NCT03447288). Tracings were evaluated by six independent raters, experienced with ventilator waveforms assessment. We selected tracings with an inspiratory hold and a reliable Pes tracing acquired simultaneously. The raters evaluated the same tracing twice, with and without a Pes tracing available, and in random order (Fig1-2). For each tracing, raters were asked to determine the readability of the plateau (readable yes/no) based on the following criteria: 1) flat plateau 2) zero flow 3) in presence of inspiratory efforts, flat plateau before and after the efforts. For the holds considered readable, the value of the plateau and its duration were measured.

Krippendorff's alpha (α) test was used to estimate the interobserver agreement on the general readability of the hold. Intraclass correlation coefficient (ICC) was used to estimate the agreement on continuous variables. α and ICC values >0.75 were considered as good agreement.

Results: 91 tracings (35patients from 11centers) were selected for analysis. The interobserver agreement on the general readability of the hold when evaluating ventilator tracings without Pes available was relatively low ($\alpha=0.466$ [0.418-0.513]) and increased slightly when Pes tracing was added ($\alpha=0.502$ [0.458-0.555]). Considering the tracings without Pes, the raters reached a 100% agreement on 37 plateaus (15 of which were considered non readable and 22 readable). When the Pes tracing was added, 100% agreement was reached in 43 out of 91 holds, 13 considered not readable and 30 readable. There was perfect agreement on the Pplat value for the 30 holds which reached universal agreement on readability (0.999 [0.998-1.000] for the tracings with Pes). On average, intra-rater agreement for the 22 Pplat values as scored with and without Pes tracings visible was 0.919. In regards of the duration of the Pplat, the ICC was 0.770 [0.571-0.898] for the tracings without Pes and 0.810 [0.661-0.905] for the tracings with Pes.

Conclusion: The interobserver agreement in evaluating inspiratory holds during PSV was relatively low, but when an agreement was reached the interpretation of the value and duration of the plateau were very consistent among raters, as well as the intra-rater agreement in evaluating the same hold with and without Pes. Further analyses are ongoing to evaluate 1) the main reasons for which holds were not uniformly interpreted 2) the features of readable holds.

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Figure 1 – Two examples of ventilator tracing with esophageal pressure tracing acquired simultaneously. The right panel shows a plateau considered readable, the left panel shows a plateau considered non readable.

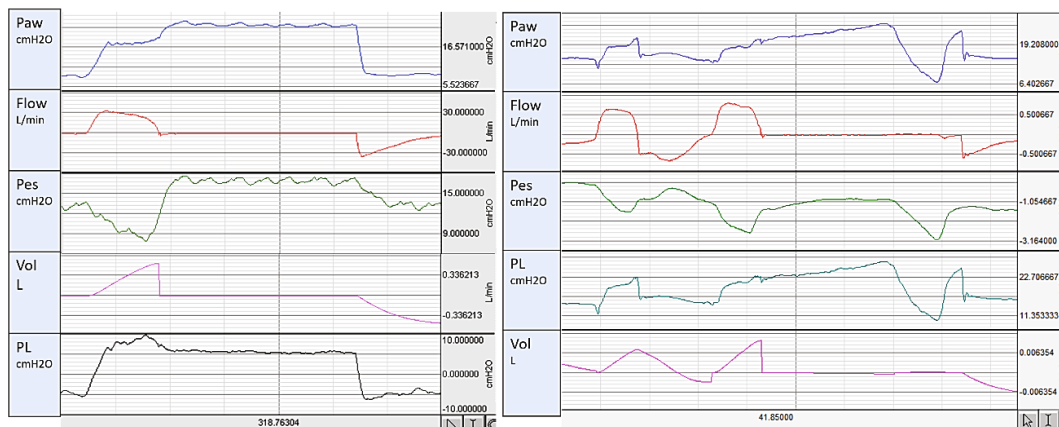
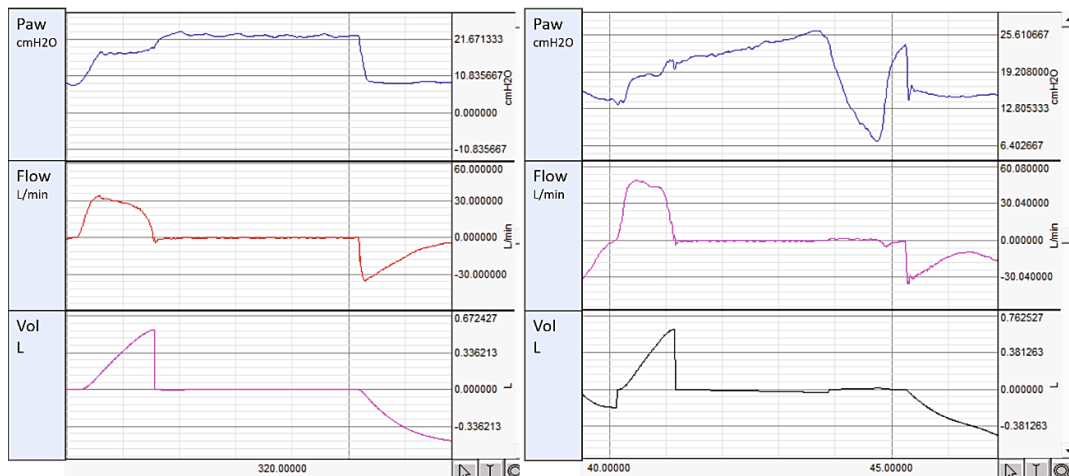


Figure 2 – The same 2 plateau without esophageal pressure tracing



Risk Factors for Unplanned Extubation in Pediatric Critical Care: A Matched Case-Control Study

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Introduction: An unplanned extubation (UE) is the uncontrolled and accidental removal of an endotracheal tube, which is a potentially life threatening and traumatic event.¹ UEs are one of the standardized quality indicators within pediatric critical care,² and have been found to be associated with a number of variables including age, sedation level, tube fixation strategies, nurse-to-patient ratios and patient procedures.^{13,15,16} To our knowledge, a matched case-control study design has not been used to explore the variables associated with increased risk of UE in critically-ill children.

Objective: Our aim was to investigate the association between UE and patient, environmental, and care-related characteristics.

Methods: We performed a retrospective case-control study in a Canadian Pediatric ICU (PICU), including children who were admitted between January 2004 - December 2014. Cases included children who experienced a UE during their admission; cases were matched with controls (4:1) who did not experience a UE. Cases and controls were matched by age, sex, and the length of stay in the critical care unit at the time of event; data was obtained using manual review of electronic health records. Univariate and multivariate conditional logistic regression was used to evaluate associations between the exposures (patient, environmental, and care-related characteristics) and the outcome (UE), taking into account the matched study design. Odds Ratios (OR) with 95% confidence intervals (95% CI) were used to represent magnitude of effect.

Results: There was a total of 458 cases, and 1601 controls. Children who were nasally intubated had 0.37 (95% CI: 0.29 – 0.48) the odds of having a UE, compared to children who were orally intubated. When adjusted for confounding variables such as endotracheal tube sections, restraints, sedation level, muscle relaxation, room set-up and number of previous intubations, the odds ratio remained significant at 0.41 (95% CI: 0.29-0.58). Children who were in a shared room had lower odds of UE compared to children in a single room (OR 0.66, 95% CI: 0.46-0.95). The number of previous intubations in the past two years also significantly increased the estimated odds of UE, even after adjusting for confounders.

Discussion: The results suggest that nasotracheal intubations are associated with lower odds of UE when compared to orotracheal intubations, which is consistent with a recent multi-site retrospective review using a large PICU database.⁸ Our study provides further evidence by controlling for clinical confounders such as endotracheal tube secretions, restraints and sedation level. Clinicians should weigh this evidence against the possible complications from nasotracheal intubation, such as tissue injury and ventilator associated pneumonia.⁸ Our results also suggest that patients in shared rooms had lower odds of UE, which is likely related to the number of clinicians within

direct eyesight of the intubated patient.⁹ We found that patients who have previously experienced a UE had increased odds of experiencing another UE, which is consistent with adult critical care literature.¹⁰ This study, to our knowledge, is the first matched case-control study assessing risk factors for UE in critically ill children. These findings can help clinicians identify the patients who are at higher risk of UE, increasing patient safety in pediatric critical care.

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Table 1 – Demographic and Clinical Variable for Cases and Controls, N (%) or Mean (95% CI)

		Cases	Controls
Age Categories	< 3 months	167 (36.5%)	572 (35.7%)
	3-12 months	109 (23.8%)	379 (23.7%)
	1-5 years	109 (23.8%)	385 (24.0%)
	5-12 years	45 (9.8%)	162 (10.1%)
	>12 years	28 (6.1%)	103 (6.4%)
Sex	Male	256 (55.9%)	904 (56.5%)
	Female	202 (44.1%)	697 (43.5%)
When Unplanned Extubation Occurred (Day/ Night Shift)	Day	241 (52.6%)	818 (51.1%)
	Night	217 (47.4%)	783 (48.9%)
When Unplanned Extubation Occurred (Weekday/ Weekend)	Weekday	338 (73.8%)	1,228 (76.7%)
	Weekend	120 (26.2%)	373 (23.3%)
Number of Patients in ICU		31.8 (31.3-32.3)	31.8 (31.5-32.0)
Number of Ventilated Patients in ICU		19.8 (19.4-20.1)	20.0 (19.8-20.2)
Number of Admissions in Past 2 Years (Including Current Admission)	1	313 (69.6%)	1,249 (78.3%)
	2	77 (17.1%)	222 (13.9%)
	≥3	60 (13.3%)	125 (7.8%)
Number of ICU Days in the Past 2 Years (Including Current Admission)		17.6 (14.8-20.4)	9.6 (8.8-10.3)
Number of Intubations in Past 2 Years (Including Current Intubation)	1	300 (66.7%)	1,442 (90.1%)
	2	85 (18.9%)	135 (8.4%)
	≥3	65 (14.4%)	24 (1.5%)
Type of Intubation	Nasal	231 (51.3%)	1,042 (65.1%)
	Oral	213 (47.3%)	486 (20.4%)
	Unknown	6 (1.3%)	73 (4.6%)
Type of Endotracheal Tube	Cuffed	104 (23.1%)	469 (29.3%)
	Uncuffed	339 (75.3%)	0 (0%)
	Unknown	7 (1.6%)	1,132 (70.7)
Mechanical Ventilation Mode	Conventional (CMV)	445 (98.9%)	1,549 (96.8%)
	High-Frequency Oscillation (HFO)	4 (0.9%)	0 (0%)
	Jet Ventilation	1 (0.2%)	0 (0%)
	Unknown	0 (0%)	52 (3.3%)
ETT Securement Method	Tape	409 (90.9%)	1,113 (69.5%)
	Suture/ Wire	6 (1.3%)	13 (0.8%)
	Device	1 (0.2%)	0 (0%)
	Unknown	34 (7.6%)	475 (29.7%)
Oral/ Nasal Secretions	Small	100 (22.2%)	69 (4.3%)
	Moderate	94 (20.9%)	146 (9.1%)
	Copious	48 (10.7%)	65 (4.1%)
	Unknown	208 (46.2%)	1,321 (82.5%)
ETT Secretions	Small	66 (14.7%)	335 (20.9%)
	Moderate	234 (52.0%)	703 (43.9%)
	Copious	94 (20.9%)	282 (17.6%)
	Unknown	56 (12.4%)	281 (17.6%)
Sedated	Yes	345 (76.7%)	1,389 (86.8%)
	No	105 (23.3%)	212 (13.2%)
Muscle Relaxed	Yes	28 (6.2%)	300 (18.7%)
	No	422 (93.8%)	989 (61.8%)
	Unknown	0 (0%)	312 (19.5%)
Restraints Used	Yes	238 (52.9%)	656 (41.0%)
	No	212 (47.1%)	945 (59.0%)
Died in the ICU (During this Admission)	Yes	26 (5.8%)	143 (8.9%)
	No	424 (94.2%)	1,458 (91.1%)
ICU Length of Stay		26.5 (22.0-31.0)	13.0 (12.1-13.8)
ICU Room Type	Single-Patient	145 (31.7%)	348 (21.8%)
	Multiple-Patient	313 (68.3%)	1,252 (78.3%)

Table 2 – Estimated Odds of Unplanned Extubation (Univariate Analyses)

Variable	Odds Ratio (OR)	P-Value	95% CI
Nasal Intubation	0.37	<0.001	(0.29 – 0.48)
ECMO	0.32	0.017	(0.13 – 0.82)
Oral/Nasal Secretions (Baseline = small)			
Moderate	0.83	0.551	(0.46 – 1.51)
Copious	1.45	0.349	(0.67 – 3.16)
ETT Secretions (Baseline = Small)			
Moderate	1.64	0.002	(1.20 – 2.24)
Copious	1.71	0.004	(1.18 – 2.48)
Muscle Relaxed	0.24	<0.001	(0.16 – 0.37)
Narcotic (Continuous Infusion)	0.38	<0.001	(0.30 – 0.48)
Narcotic (Intermittent)	0.69	0.005	(0.54 – 0.89)
Benzo (Continuous Infusion)	1.00	0.978	(0.53 – 1.91)
Benzo (Intermittent)	0.68	0.003	(0.52 – 0.88)
Muscle Relaxant (Intermittent)	0.86	0.311	(0.64 – 1.15)
Other medication (continuous)	0.74	0.217	(0.46 – 1.19)
Other medication (intermittent)	1.94	<0.001	(1.49 – 2.54)
Restraints	1.73	<0.001	(1.39 – 2.16)
Sedated	0.50	<0.001	(0.38 – 0.65)
Shared Room	0.57	<0.001	(0.44 – 0.73)
Day (vs Night)	1.05	0.670	(0.85 – 1.29)
Weekday (vs Weekend)	0.86	0.208	(0.67 – 1.09)
ICU Census	1.01	0.676	(0.98 – 1.03)
ICU Vent Census	0.99	0.340	(0.96 – 1.02)
Number of ICU Admissions in Past 2y (including this admission)	1.25	<0.001	(1.11 – 1.40)
Number of ICU Days in Past 2y	1.02	<0.001	(1.01 – 1.03)
Number of Previous Intubations			
2	3.28	<0.001	(2.40 – 4.48)
≥3	26.02	<0.001	(13.18 – 51.24)

Table 3 – Adjusted Estimated Odds of Unplanned Extubation (Multivariate Analyses)

Variable	Odds Ratio (OR)	P-Value	95% CI
Nasal Intubation	0.41	<0.001	(0.29 – 0.58)
ETT Secretions (Baseline = Small)			
Moderate	1.46	0.061	(0.98 – 2.16)
Copious	1.30	0.227	(0.81 – 2.12)
Muscle Relaxed	0.30	<0.001	(0.18 – 0.50)
Restraints	1.38	0.054	(0.99 – 1.90)
Sedated	0.64	0.044	(0.42 – 0.99)
Shared Room	0.66	0.025	(0.46 – 0.95)
Number of Previous Intubations			
2	3.22	<0.001	(2.13 – 4.87)
≥3	32.3	<0.001	(13.22 – 78.88)

Should I Give Two Units of Red Blood Cells to My Overweight Patient with an Hemoglobin of 58 g/L?

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Introduction: It is common medical knowledge that a single unit of red blood cells (RBC) transfusion increases the hemoglobin (Hb) by 10 g/L of (Hb). This practice was recently validated in a big study of over 38000 transfusions¹ in all types of patients. Choosing Wisely Canada recommends to transfuse one unit of RBC in stable anemic patients and wait for an Hb control before transfusion additional units.² However, in acute situations where the Hb level is lower than the usual thresholds of 70-80 for RBC transfusion (for example 50g/L), it may be tempting to transfuse two units of RBC to raise the Hb level above that threshold without delay.

Objectives: The objective of this study was to investigate the effect on Hb levels of transfusing one RBC unit in stable anemic patients in the critical care unit (CCU).

Methods: We conducted a retrospective analysis using the eICU Collaborative Research Database³, a multicenter database of CCU admission in 2014-2015. We analyzed transfusions of one RBC unit in adult patients without evidence of hemodynamic instability, recent bleeding or acute ischemic heart issues. We included all transfusions of patients with both pre-transfusion and post transfusion Hb value. First, we analyzed data in a univariate and a multivariate approach, using a generalized linear mixed effect model controlling for gender, age, height, weight, pre-transfusion Hb value and reason for admission (specifically bleeding, trauma, surgical or infection). Second, we selected anemic (HB < 60 g/L) patients who received a single order of two units RBC units and used our model to predict the potential post-transfusion Hb if the patient had received one unit instead of two.

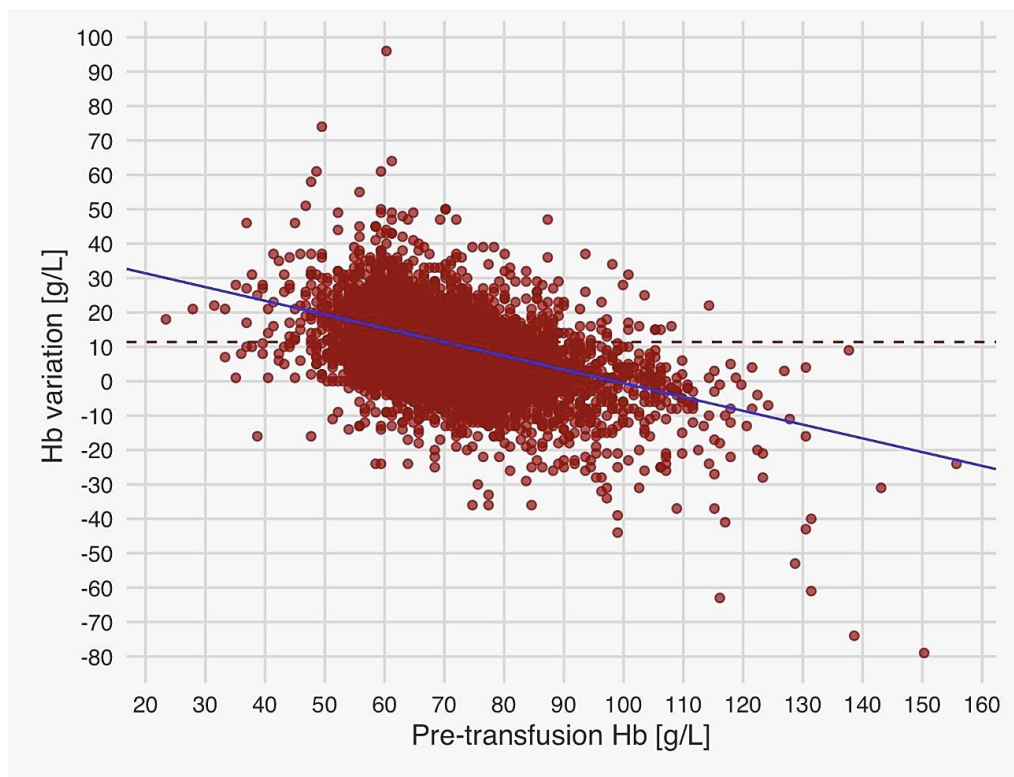
Results: There were 6308 transfusions of one unit RBC among 4421 patients. The median volume of transfusion was 350 mL (IQR 300-350) for 1 unit. The patients were male (52%) of median age of 66 years old (IQR 54-75) with a median Hb pre-transfusion of 72 g/L (IQR 67-82). The Hb variation from pre-transfusion Hb level was non-linear. At baseline Hb of 70 g/L, average Hb variation post-transfusion was 11.4 g/L (95%CI 11.1-11.7) while controlling for age, sex, weight, height, surgical status. Variation was statistically higher in elderly (0.4 g/L/10y female (0.9 g/L) in surgical patients (0.8 g/L), lower body weight (0.5 g/L/10 kg) and smaller patients (0.6 g/L/10cm) but likely not clinically significant. Hb variation increased by 4.0 g/L (CI95% 3.8-4.2) for every 10 g/L decrease of pre-transfusion Hb (Figure 1). However, the model explained only 30% of the variance, leaving a standard error on the residual of 9.4 g/L. On the 244 patients with less than 60 g/L of Hb that received two units of RBC, 24.5% still had an Hb of less than 70 g/L after transfusion. If we apply the results of our model to those patients, simulating giving them only one unit instead of two, 41.4% would still had an Hb of less than 7 g/L at control.

Conclusion: This study show that in stables CCU patients one unit of RBC increases in average the Hb of 11.4 g/L. This variation is slightly affected by gender, age, height, weight, surgical status and mostly by pre-transfusion Hb level. In the more severely anemic patients that received two units, applying the model showed that although a significant proportion of patients may not reach the target threshold with one unit, more than 50% may not have required a second RBC unit after receiving only one. This supports the recommendation of transfusing only one unit of RBC in anemic and sable patients in the CCU.

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Figure 1 – Effect of 1 Unit of RBC



Technology-Mediated Communication at the End-of-Life During Pandemic Times: What is Gained, What is Lost

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Introduction: Restricted hospital visiting policies during the COVID-19 pandemic has ushered in an era of technology-mediated communication.

Objective: To evaluate whether the 3 Wishes Project (3WP) is *feasible* and *valuable* for patients during the pandemic in 3 hospital units at St. Joseph's Healthcare in Hamilton. Herein, we focus on technology-mediated connections at the end-of-life (EOL).

Methods: In an embedded mixed-methods study, we enrolled decedents who had $\geq 95\%$ probability of death or a decision to withdraw life support. We recorded patient, wish and clinician characteristics. We interviewed clinicians caring for ≥ 1 patient 2-10 weeks postmortem. Interview transcripts were analyzed using a qualitative descriptive approach.

Results: From March 16-July 1, 2020, 45 patients were enrolled in the 3WP in the ICU (n=34); COVID ward (n=7) or medical step-down unit (n=4). We interviewed 45 clinicians (16 nurses, 10 physicians, 8 residents, 9 others) with 13.7 (11.5) [mean (SD)] years of clinical experience. Interviews were conducted by videoconference (n=25) or phone (n=20).

A third (28.9%) of patients had an antemortem virtual visit with a relative or friend.

Though few (4.2%) terminal wishes were for a real-time technology-mediated connection, this was more common than in pre-pandemic times (0.5%, $p < 0.001$).

Our main finding in the qualitative data related to **increased use of technology-mediated connection at the EOL**. Themes included: a) **What, when and how technology-mediated communication was used:** Clinicians described mainly using phone communication with families, and using baby monitors to communicate with other clinicians and patients in isolation rooms. The video platforms facilitated patient-family connections, and was used on the COVID ward for virtual staff huddles. b)

Gains realized with technology-mediated communication: Clinicians reported more frequent family phone calls to provide updates, offer support and review goals of care (GOC). Videoconferencing was described as the 'next best thing' to an in-person family visit, allowing images of their loved one including pets, their room, and sometimes their clinicians. The introduction of video technology was identified as a positive feature of

the pandemic, as many clinicians highlighted its future potential when relatives are geographically distant. c) **Losses experienced with technology-mediated communication:** Regarding phone and video platforms, clinicians spoke to the loss of human touch, and limited ability to detect non-verbal cues or convey empathy. Fewer opportunities for scheduled or impromptu in-person rapport-building bedside family conversation made clinician-initiated phone calls seem relatively more instrumental, making GOC discussions difficult. d) **Video platform cautions and considerations:** Clinicians sometimes found video visits technically and/or emotionally difficult for patients, families and themselves. They also wondered if unconscious patients would want to be viewed this way. Loss of privacy with clinician-facilitated virtual visits concerned some clinicians; others were distressed bearing witness to family member angst when seeing their dying loved one on screen for the last time. **Conclusions:** During the pandemic, the limited presence of family members at the EOL has catalyzed technology-mediated verbal and visual communication. Clinicians identify both gains and losses, sharing cautions and considerations for future practice including pandemic waves.

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The Association Between Patient Ethnicity and Family Satisfaction with the Quality and Provision of End-of-Life Care

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Introduction/Objectives: Quality care at the end of life (EOL) is an espoused right of every Canadian. Among decedents in Ontario, recently immigrated and ethnic minority patients are more likely to die in ICU and receive more aggressive life-prolonging treatment in the last six months of life in comparison to other Canadians [1]. It is not clear whether differences are attributable to diverse preferences for EOL care, or whether they are a result of specific disparities in the quality of care that occur along the EOL trajectory. This observational survey-based analysis seeks to evaluate the quality and provision of EOL care for patients of diverse ethnocultural backgrounds.

Methods: The End of Life survey (validated 52-item tool) is routinely administered to next-of-kin of all decedents at Sunnybrook Hospital to measure satisfaction with inpatient EOL care. The primary outcome is the global measure of satisfaction (10-point Likert scale). We performed a stratified analysis using modified Poisson regression to identify specific patient ethnic groups with important differences in family satisfaction with quality of EOL care. Secondary predictors of family satisfaction included: patient religion, level of religiosity, primary language, language barriers, care perceived to be consistent with patient wishes and location of death. Univariate Poisson regression was applied to each predictor variable to determine preliminary associations (at $p < 0.2$) for inclusion in the final adjusted model with a significance threshold level of $\alpha < 0.05$.

Results: Among 1384 surveys (2012-2019), 21.4% ($n=295$) of patients were identified as non-Caucasian. Overall, 76.2% of family members of Caucasian patients and 71.9% of non-Caucasian patients were "very/completely satisfied" with the overall quality of EOL care. Family members of patients who died in ICU more likely to be "very/completely satisfied" in comparison to patients who died in other units ($p=0.007$). There were no differences in rates of dying in ICU among patient ethnic groups. Examining specific ethnicities, family members of Muslim patients and those of Middle Eastern descent were less likely to be satisfied in comparison to other patients (OR 0.81 95%CI 0.60-1.09, $p=0.158$; OR 0.73 95%CI 0.52-1.03, $p=0.073$, respectively). The relationship between patient religion (Muslim vs. non-Muslim) and family satisfaction was not significantly influenced by level of patient religiosity (OR 0.76 CI 95% 0.49-1.14, $p=0.185$). In the adjusted model, family members of patients of Middle Eastern descent had lower satisfaction with quality of EOL care ($B=-0.678$, $SE=0.327$, $p=0.038$). Family satisfaction increased by 2.9x for patients whose care was consistent with their wishes, and decreased by 39.5% for those who experienced language barriers. Location of death (ICU vs. other) was a non-significant predictor of family satisfaction ($p=0.087$).

Conclusions: Our findings suggest that family members of patients who died in ICU were most commonly very/completely satisfied with the quality and provision of EOL, regardless of patient ethnicity or religious background. Dying in ICU setting with more intensive care may therefore not be an appropriate indicator for measuring quality of EOL care for patients and families. Family members of patients from certain ethnic and

cultural backgrounds may experience less satisfaction with quality of care at the EOL. More research is needed to validate and understand the quality and experience of EOL care that is provided to patients and families from diverse ethnocultural backgrounds.

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The Impact of End of Life Care on Burnout and Moral Distress in an Academic ICU

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Introduction: Burnout results from chronically high levels of stress in the workplace and is characterized by emotional exhaustion, depersonalization and reduced personal accomplishment.¹ Moral distress occurs when individuals are placed in situations that are at odds with their core values and have little power to make change.² Both have a significant negative impact on healthcare providers, their families as well as patients.^{3,4} Causes are numerous, however provision of end of life care (EOLC) has been identified as a significant contributor.⁵⁻⁷

Objective: Within our ICU team, previous research quantified high rates of burnout and moral distress.⁸ The objective of this study was to describe the impact that EOLC has on burnout and moral distress for the team at an academic Intensive Care Unit in Halifax, Nova Scotia.

Methods: This qualitative study used focus groups to elicit a better understanding of stakeholder perspectives on EOLC contributing to burnout and moral distress in the ICU team. Research Ethics Board approval was obtained (REB File #1024175, 2019). A thematic analytic approach was used to guide analysis of the data⁹ with respect to issues, impact and suggestions to build resilience.

Results: 6 focus groups, each with 4-8 participants, were conducted. A total of 35 participants (6 MDs, 21 RNs and 8 RTs) represented 43% of the MDs, 18.8% of the RNs and 20.0% of the RTs.

EOLC was recognized by all to be a vital aspect of ICU, however, the cumulative frequency with which this occurs was identified as a cause of burnout and moral distress. Compounding the volume of exposure was the lack of time during a shift to process the death of a patient before moving on to caring for the next critically ill admission.

Advocating for appropriate goals of care, either in the form of perceived futility or violation of patient autonomy caused significant burnout and distress. These occurred within the medical team and/or between the team and the patient's substitute decision maker. Discordance within the team was in part due to differences in professional roles and responsibilities. In collaboration with families, physicians write the order for withdrawal of life sustaining measures which has an emotional burden and legal responsibility. However, nurses are left to implement a patient care plan which they had little input in establishing and may not agree with. Discord between the ICU team and primary medical provider goals for care was also identified as an issue.

EOLC dynamics negatively impacted participant's emotional and physical well-being, their personal relationships as well as delivery of patient care. Many reported feeling isolated as family and friends are ill equipped to provide support.

Previous experiences with debriefing sessions held in the ICU were considered very valuable and regular debriefing was suggested to build resilience. Other suggestions include mental health recovery days and destigmatizing the need for help.

Conclusion: EOLC is a significant source of burnout and moral distress for our ICU team. Although it is highly regarded as an integral part of ICU care, the volume of exposure to death and dying, discordance within the healthcare team or between the team and patient's decision makers regarding level of treatment and a lack of support services were predominate sources of burden. Suggestions to build resilience focused on developing a culture of awareness, support and communication.

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The Impact of Frailty on Outcomes in the Cardiac Intensive Care Unit

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Introduction: Frailty is a syndrome characterized by physiological decline and marked increase in vulnerability to adverse health outcomes.¹ While there is an association between aging and frailty, the two concepts are not synonymous and the gradual decline in physiological reserve seen with aging is accelerated in frail individuals.² Frailty is common in patients admitted to medical intensive care units (ICUs) and is associated with worse clinical outcomes.³ Cardiac intensive care units (CICUs) have evolved in response to an increasingly complex and diverse patient population admitted with acute cardiac pathology.⁴ The prevalence of frailty and its association with clinical outcomes among patients admitted to the CICU remains unknown.

Objectives: We sought to describe the characteristics and outcomes of patients with frailty admitted to a dedicated CICU.

Methods: This retrospective cohort study was performed using the CICU registry at the University of Ottawa Heart Institute - a 14-bed unit servicing a population of ~1.3 million residents in eastern Ontario. All adult patients admitted to the CICU between November 1, 2018 and April 30, 2020 were included in the data analysis. Patients were excluded if they had missing data related to baseline frailty or clinical outcomes. The presence and severity of frailty was assessed prospectively using the Clinical Frailty Score (CFS)⁵ at time of admission. In accordance with existing ICU literature³, a CFS \geq five was used to classify a patient as "frail". Baseline demographic data and clinical outcomes were obtained from the registry. Multivariable logistic regression modeling was used to adjust for predefined variables including age, sex, and reason for admission. All statistical analyses were performed using SAS v9.4.

Results: A total of 1,642 patients were admitted to the CICU during the study period, of which 1,610 (98.1%) patients had a baseline CFS score available. Of these, 370 (23.0%) patients had frailty. Patients with frailty were older (73.9 ± 12.9 vs. 66.8 ± 14.6 years; $p < 0.001$) and included more female patients (41.1% vs. 33.6%; $p = 0.03$). The admission diagnosis was acute coronary syndrome in 23.5%, heart failure/cardiogenic shock in 28.7%, arrhythmia in 15.1%, and out-of-hospital cardiac arrest in 5.1% of patients with frailty. There was a greater comorbidity burden in the frail cohort (Figure 1).

There was no difference in the length of stay in CICU between the groups (4.0 ± 5.7 vs. 4.2 ± 5.4 days; $p = 0.51$). Following adjustment for age, sex, and admission diagnosis, patients with frailty were more likely to have cardiovascular death (OR 2.65, 95% CI 1.62-4.34), all-cause death (OR 3.06, 95% CI 1.95-4.81), require non-invasive mechanical ventilation (OR 1.70, 95% CI 1.17-2.47), vasoactive medications (OR 1.69, 95% CI 1.28-2.24), or renal replacement therapy (OR 5.24, 95% CI 3.33-8.26). There was no difference in the need for invasive mechanical ventilation or bleeding complications between the two groups (Figure 2).

Conclusion: We found that among patients admitted to a dedicated CICU in a large quaternary care hospital, frailty was associated with increased adverse clinical outcomes, including increased cardiovascular and all-cause mortality. The assessment of clinical frailty may provide important prognostic information to clinicians and patients, which may further aid in goals-of-care decision making. Further research is needed to evaluate the impact of potential interventions on outcomes in patients with frailty admitted to CICUs.

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Table 1 – Characteristics of Non-Frail and Frail Patients Admitted to the Cardiac Intensive Care Unit between November 1, 2018 and April 30, 2020

	Non-frail	Frail	P value
Age	66.8 ± 14.6	73.9 ± 12.9	<0.001
Males	823 (66.4%)	218 (58.9%)	0.03
Reason for Admission			
Acute coronary syndrome	509 (41.1%)	87 (23.5%)	<0.001
Heart failure/cardiogenic shock	149 (12.0%)	106 (28.7%)	<0.001
Out-of-hospital cardiac arrest	113 (9.1%)	19 (5.1%)	0.01
Arrhythmia	181 (14.6%)	56 (15.1%)	0.80
Post-procedure complication/monitoring	218 (17.6%)	71 (19.2%)	0.48
Other	70 (5.7%)	31 (8.4%)	0.06
Comorbidities			
History of myocardial infarction	214 (17.6%)	125 (37.0%)	<0.001
History of congestive heart failure	315 (26.5%)	225 (62.9%)	<0.001
Diabetes	319 (26.9%)	156 (44.4%)	<0.001
Chronic kidney disease	137 (11.5%)	137 (38.3%)	<0.001
Peripheral vascular disease	146 (12.3%)	157 (43.9%)	<0.001
Stroke or transient ischemic attack	96 (8.1%)	54 (15.1%)	<0.001
Dementia	9 (0.7%)	33 (9.2%)	<0.001
Malignancy	171 (14.4%)	82 (23.2%)	<0.001
Liver disease	64 (5.4%)	31 (8.8%)	0.06
Chronic obstructive pulmonary disease	152 (12.8%)	90 (25.1%)	<0.001

Table 2 – Outcomes of Non-Frail and Frail Patients Admitted to the Cardiac Intensive Care Unit between November 1, 2018 and April 30, 2020

Outcome	Non-frail	Frail	Crude OR (95% CI)	Adjusted OR* (95% CI)
Non-invasive mechanical ventilation	206 (16.6%)	72 (19.5%)	1.21 (0.90-1.64)	1.70 (1.17-2.47)
Invasive mechanical ventilation	134 (11.0%)	42 (12.0%)	1.10 (0.76-1.59)	0.76 (0.51-1.12)
Vasoactive medications	373 (30.2%)	157 (42.9%)	1.73 (1.36-2.20)	1.69 (1.28-2.24)
Renal replacement therapy	48 (3.9%)	58 (15.9%)	4.64 (3.10-6.64)	5.24 (3.33-8.26)
Bleeding	20 (1.6%)	11 (3.0%)	1.88 (0.89-3.95)	1.38 (0.61-3.11)
Cardiovascular death	62 (5.1%)	44 (12.1%)	2.58 (1.72-3.88)	2.65 (1.62-4.34)
All-cause death	71 (5.8%)	56 (15.4%)	2.96 (2.04-4.30)	3.06 (1.95-4.81)

* Model adjusted for age, sex, and reason for admission

The Proportion & Characteristics of Positive & Negative Trials in Adult Critical Care From 2013-2019, a Systematic Review/Meta Epidemiological Study

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Introduction: Negative trials are common in critical care literature. One review from 2008 found that 62 (83%) of 75 RCTs investigating mortality were negative. The most recent review was published in 2014 which includes all published RCTs in 16 high impact journal from 2007-2013 and showed that 63% (92 of 146) RCTs in critical care were negative, and 90% were negative when mortality was the primary outcome. A negative RCT is not necessarily true & indicative of lack of treatment effect but it can also be a false negative as a result of many methodologic reasons or insensitive outcome selection. It certainly requires further exploration on why this is happening and how to increase the chances of success of RCT. The impact of negative trials is rarely discussed, this may include premature abandonment of promising interventions, adding noise to the total body of evidence, increasing chance of research waste, enhancing feeling of negativism, and exposing a large number of patients to interventions with a very low yield, which may create an ethical dilemma. The views surrounding the value of conducting underpowered RCTs are variable, some feel that negative RCTs are detrimental and is a waste of resources, and others feel they are important to inform systematic reviews and that individual trials are seldom definitive.

Objectives: To better understand the proportion of negative RCTs over the past decade, and explore potential variables that could render the results of RCTs to be negative, we aim to conduct a meta-epidemiologic study looking at all published RCTs in the critical care field since 2013.

Methods: A librarian conducted the search. Two reviewers searched The Cochrane Library, MEDLINE, and EMBASE databases from June 2013 up to December 2019.

Results: 911 articles included for our systematic review. 96 articles were published in 2019 & will be presented in CCF fellow day. A higher proportion of trials were positive 61% & 39% negative. Some of the characteristics of these trials are: negative trials have almost an equal proportion of single vs multi center: 54% vs 46% respectively. While the majority positive RCT trials are single centre (80%). regarding geographic locations, Negative trials were conducted in the following areas: 14% International (includes 4 or more countries), 30% in Asia, 30% Europe, 22% USA & 3% Brazil. For positive trials the majority were done in Asia 63% vs 20% Europe, 2% Canada & Brazil, 7% USA & 5% in Africa. The primary outcomes selected in negative trials were: 14% multiple/composite, 32% physiological parameter, 32% patient important outcomes, 22% mortality outcome alone. While positive trials: 27% multiple/composite, 45% physiological parameter, 26% patient important outcome, 2% mortality outcome alone. Regarding size of the trials see the figures. Equal proportion of negative & positive trial were terminated early 8% up to 13% of negative trials has a Spin vs 25% of positive trials. 21% of negative trials has no reporting of power calculation vs 50% of positive trials.

Conclusions: The proportion of positive trials in adult critical care has increased in 2019. Positive trials tend to be of lower quality than Negative trials. The increase may reflect our comprehensive search which was not restricted to high impact journals as the previous reviews or due to a trend of less use of mortality as the sole primary outcome.

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Figure 1 – Do Negative Trials Tend to Be Larger in Size?

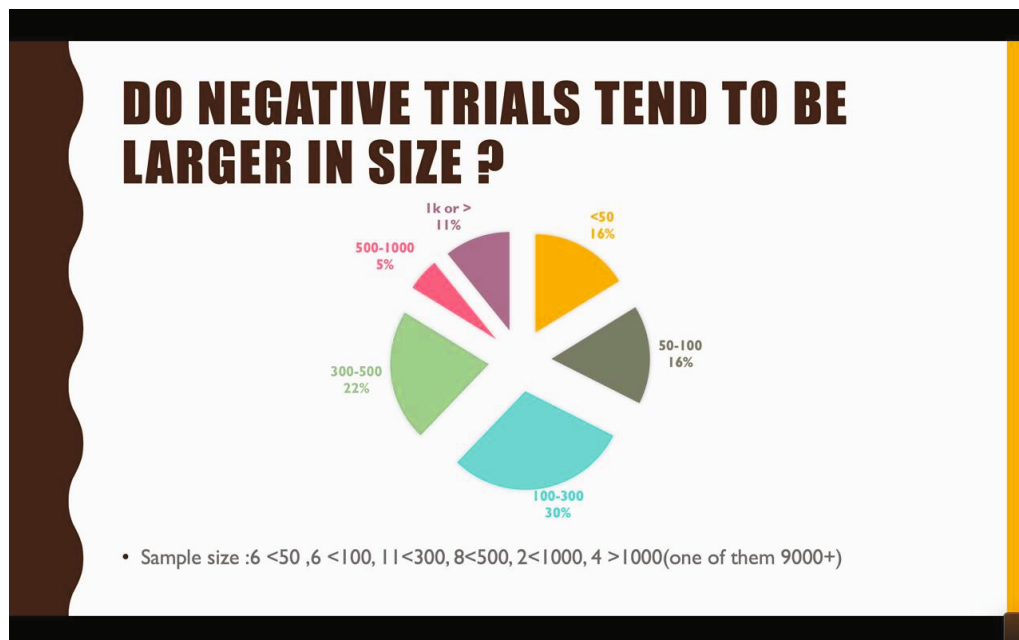
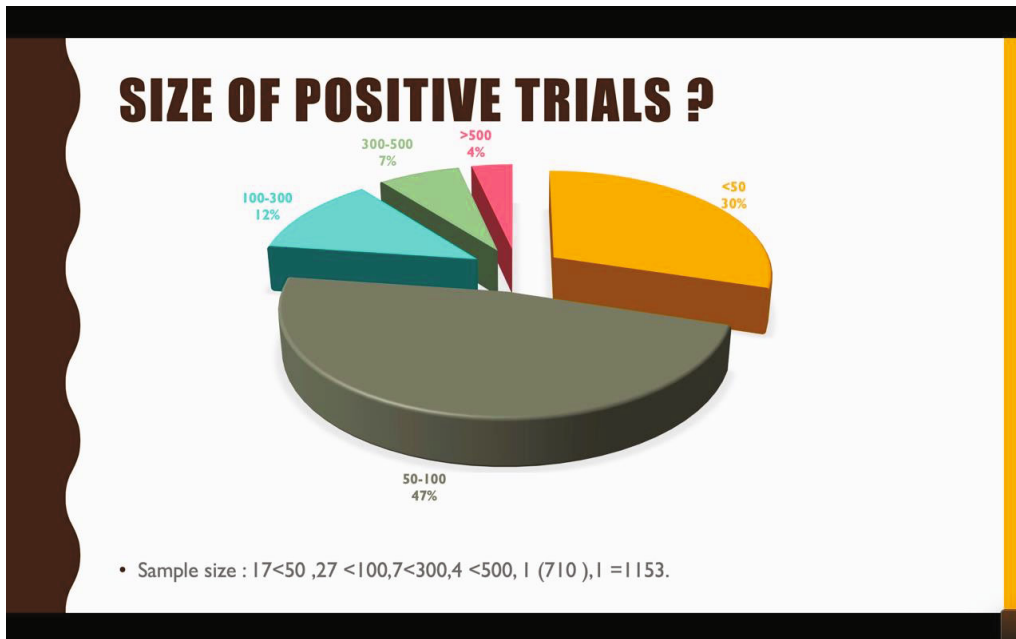


Figure 2 – Size of Positive Trails?

Upskilling Clinicians to Build Capacity to Care for Critically Ill COVID-19 Patients

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Introduction: In response to the call to increase capacity to care for critically ill COVID-19 patients, our hospital increased its number of critical care (CC) beds. This entailed assessing the organizational capability to staff critical care during critical points when staffing supply is inadequate to meet clinical demands. Upskilling healthcare professionals (HCPs) was identified as a strategy. We developed and implemented an upskilling education program for redeployed HCPs who are not currently working in CC but have useful skills to support CC teams. The upskilled HCPs are supervised by those with relevant CC training and experience.

Objectives: To describe the development and implementation of the upskilling education program of HCPs, who are not currently working in critical care, to support the care of critically ill COVID-19 patients.

Method: 1) Identification of education program developers and facilitators; 2) interdepartmental collaboration of professional practice, education, critical care, medical surgical and redeployment departments, 3) identification of HCPs by unit managers to participate in the upskilling program, and 4) implementation of the upskilling program inclusive of a) eight-hour in-class session, b) completion of on-line and simulation courses, and c) completion of three buddy shifts in CC.

Results: Eighty five HCPs participated in the program, and 79% (n=67/85) responded to the post-survey evaluation. Majority (n=65/85) did not have CC experience. Using Likert Scale (1=very poor, 2=poor, 3=good, 4=excellent), respondents rated the content and presentation excellent (range 3.49-3.73). Themes that emerged from qualitative feedback included "concise and comprehensive information on care of COVID-19 patients"; "covered nursing role and responsibilities in POD model during pandemic", and "facilitators provided safe learning space and knowledgeable, experience-based responses to questions to allay anxiety of redeployed HCPs". All 85 HCPs have completed all the elements of the upskilling education program.

Conclusion: The upskilling program showcased commitments of HCPs to patient care. The authors quickly put together the education program in under a week. As a result, we developed a pool of HCPs who are trained to support the care of critically ill patients during pandemic. It highlighted interprofessional and interdepartmental collaboration in pandemic preparedness. The program underlined the importance of professional judgement and the need to assess own level of competencies and accountabilities when redeployed to unfamiliar working environment to perform other roles or duties while ensuring patients receive safe care during pandemic.

Use of Actigraphy in Traumatic Brain Injury Patients During Intensive Care Unit Admission: A Clinical Data Analysis

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Introduction / Background: Agitation is a common behavior in intensive care patients following acute traumatic brain injury (TBI). Agitation can prolong recovery of TBI patients due to delayed mechanical ventilation weaning or mobilization.(1) TBI patients can also suffer from sleep-wake disturbances which impede the recovery of posttraumatic amnesia.(2) Actigraphy, which measures rest-wake rhythms using movements with an accelerometer, has been used as an alternative to polysomnography to estimate sleep and to measure physical activity in outpatients' settings. In the ICU setting, actigraphy has been used for the same purposes, but more studies are needed as it has only been studied in patients in whom analgosedation has been discontinued.(3, 4) Our hypothesis is that actigraphy could be a tool to objectively monitor agitation and to estimate sleep-rest cycles in TBI patients.

Objectives: The aim of the present study is to describe actigraphy data from critically ill TBI patients receiving analgosedation. Specifically, we compared the mean 24-hour activity between agitated and non-agitated TBI patients and reported consolidation of the rest-activity cycle during ICU stay.

Methods: Within 48 hours of admission at the ICU of Hôpital du Sacré-Coeur de Montréal, we prospectively enrolled adults with a TBI and abnormal CT scan between September 2018 and July 2019. Exclusion criteria included: spinal cord injury, prior history of TBI, major neurological or psychiatric disease, high risk of short-term mortality, and ICU stay <48 hours. Actiwatch-Spectrum actigraphs (Philips/Respironics, Murrysville, PA) were placed in patients' wrists; monitoring was continued till ICU discharge or limitation of therapeutic efforts. The activity level was measured with raw actigraphy counts averaged over 24h, daytime (7h00-21h59) and nighttime periods (22h-6h59). Sleep-wake consolidation was quantified by the Daytime Activity Ratio (DAR); sleep-wake is consolidated when DAR>80%.(2) RASS score was assessed by nurses minimum two times per day during patient's admission; an agitated patient has RASS>=2.

Results: A total of 30 patients were recruited with median age 64.5 years (IQR 41.3) and 73% male. TBIs were severe, moderate and mild complex in 30%, 43% and 27% of cases, respectively. We excluded five patients from the analysis who had less than 24h of data. Sixteen patients (64%) were considered agitated at least once during ICU admission. The mean level of activity over 24h was higher in participants with agitation (34.4 ± 22.5 vs 9.6 ± 12.2 ; $p<.001$). This was true for the mean activity both during daytime (38.7 ± 23.5 vs 12.01 ± 15.34 ; $p=0.002$) and nighttime (25.4 ± 20.6 vs 5.7 ± 7.3 ; $p=0.002$). The mean DAR over the period of recording was 75.2% (± 5.9). On the first day of recording, 50% of patients had a disturbed sleep-wake cycle, and 60.9% had a disturbed sleep-wake cycle for the last day of recording. No progression of the DAR between the first and last day of recording (First day: $73.98\% \pm 15.34$; Last Day: $75.36\% \pm 13.10$; $p=0.737$). Patients with or without agitation did not differ on any DAR measures.

Conclusions: This study suggests that the majority of TBI patients have altered sleep-rest cycles. In the acute phase of TBI agitated patients have higher levels of activity,

confirming the potential of actigraphy to objectively monitor agitation. Sleep-wake consolidation measures were not associated with agitation, suggesting the need to control for other variables.

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