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Impact of Family Presence on Delirium in Critically Ill Patients: A Retrospective Cohort Study

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Impact of Family Presence on Delirium in Critically Ill Patients: A Retrospective Cohort
Study

by

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A THESIS

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Abstract

Delirium, an acutely disturbed state of consciousness, manifests as a collection of symptoms such as confusion. There is potential for family members of critically ill patients to assist in non-pharmacological delirium prevention and management (e.g., re-orientation). Despite this, there are few studies on the impact of Intensive Care Unit (ICU) family presence on delirium. To bridge these knowledge gaps, our study employed a population-based retrospective cohort design to explore the association between family presence and both the incidence and duration of delirium in critically ill patients. The electronic health records of consecutive adult patients admitted to any of 14 adult medical-surgical adult ICUs in Alberta, Canada between January 1, 2014 and December 30, 2018 were examined. Family presence in the ICU (exposure), was extracted using a validated algorithm (1. family physically present, 2. family phone call only, 3. no family presence or call [reference group]). Delirium was measured using the Intensive Care Delirium Screening Checklist (ICDSC). Incident delirium was quantified (primary outcome) using an ICDSC cut-off of ≥ 4 points, after family presence (yes/no). Duration of delirium (secondary outcome) was measured as the total number of ICU days (24-hour periods) with a positive ICDSC score (≥ 4 points). Multivariable mixed-effects logistic and linear regression models (accounting for clustering by patient re-admission and ICU site, where appropriate) were used to evaluate the association between family member presence and the incidence and duration of delirium in critically ill patients in the ICU, respectively. All regression models were adjusted for relevant covariates (e.g., ICU admission type, Glasgow Coma Scale [GCS]). We included 25,537 patients. Family presence in the ICU was associated with lower incidence of delirium

during elective-surgical admissions in patients with intact GCS (OR 0.60, 95%CI:0.39-0.97, $p=0.02$) as compared to patients in the reference group. Family presence in the ICU decreased duration of delirium (adjusted mean difference -1.87 days, 95%CI: -2.01 to -1.81, $p<0.001$) as compared to patients in the reference group.

Family presence in the ICU may decrease the incidence of delirium in patients admitted for elective-surgical reasons with intact GCS and duration of delirium in all patients by up to 2 days.

Preface

The manuscript cited below will be submitted to Intensive Care Medicine for potential publication. The manuscript is described in detail as a full chapter in the thesis presented. The first author cleaned and analyzed data, discussed results, and wrote the manuscript in its entirety. Co-authors provided methodological guidance, clinically relevant suggestions, and feedback on the manuscript.

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Dedication

To my beloved mother and sister, Amany and Sarah.

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List of Abbreviations

95%CI	95% Confidence Interval
AHS	Alberta Health Services
APA	American Psychiatric Association
APACHE-II	Acute Physiology and Chronic Health Evaluation II
AUROC	Area Under the Receiver Operating Characteristic
CAD	Canadian Dollars
CAM-ICU	Confusion Assessment Method-ICU
CCI	Charlson Comorbidity Index
COVID-19	Coronavirus Disease 2019
DAD	Discharge Abstract Database
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5 th edition
EHR	Electronic Health Records
FAM-CAM	Family Confusion Assessment Method
GCS	Glasgow Coma Scale
ICDSC	Intensive Care Delirium Screening Checklist
ICU	Intensive Care Unit
IQR	Interquartile Range
MD	Mean Difference
NLP	Natural Language Processing
OR	Odds Ratio
RASS	Richmond Agitation and Sedation Scale
RECORD	REporting of studies Conducted using Observational Routinely-collected Data
SOFA	Sequential Organ Failure Assessment
STROBE	STrengthening the Reporting of OBservational studies in Epidemiology
UK	United Kingdom
US	United States

CHAPTER 1: INTRODUCTION

1.1 Background of Research Project

Delirium is an acutely disturbed state of consciousness that is associated with severe disorganization of thought [1]. Hallmarks of delirium include symptoms such as confusion and altered cognition in comparison to baseline awareness [1]. Up to 50% of critically ill patients will develop delirium at least once during their ICU stay [2]. Critically ill patients have life threatening conditions and are exposed to multiple delirium risk factors in the ICU including sedation, pain, and invasive mechanical ventilation [2]. Delirium is extremely distressing to patients during and after their ICU stay [3]. Delirium is associated with negative patient outcomes such as increased risk of mental health problems (e.g., anxiety, depression, post-traumatic stress disorder), distress, higher risk of mortality, and longer hospital stays [2-7]. Given the consequences of delirium, it is imperative for research to focus on its treatment and management.

Delirium in critically ill patients is difficult to prevent and manage, given its multiple risk factors in the ICU [8]. A systematic review studying the efficacy of pharmacological prophylaxis for the treatment and prevention of delirium found that medication for delirium was ineffective and potentially harmful (i.e., increased mortality) in critically ill patients [8, 9]. Non-pharmacological interventions such as reorientation are shown to reduce the incidence of delirium in critically ill patients [9, 10]. Efforts to implement non-pharmacological interventions in the ICU to prevent and manage delirium should be a top priority given the ineffectiveness and consequences of pharmacological delirium management.

Non-pharmacological interventions for delirium may be provided by family members. Family presence in the ICU may facilitate maintenance of a daily schedule,

early mobilization, and environmental support (e.g., sleep hygiene routine) to reduce delirium in critically ill patients [9]. Through this, families may increase cognitive stimulation, reduce pain, and maintain sleep in critically ill patients, which in turn may reduce patient distress associated with delirium [9]. Family members of ICU patients reduce the burden of delirium in critically ill patients (i.e., confusion, agitation) by providing comfort and a familiar environment [9, 11]. Increased family presence in the ICU provides opportunities for collaboration and shared decision-making between critical care physicians, nurses, and family members [11, 12]. Enhanced collaboration between family members and healthcare providers may modify administration of sedatives in patient care, therefore reducing the use of benzodiazepines (common ICU sedative) which are a modifiable risk factor of delirium [11-14].

Family presence may act as a protective factor against delirium onset and duration, yet few studies have investigated the impact of family presence on delirium [15, 16]. The purpose of this population-based retrospective cohort study was to quantify the association between family presence and the incidence and duration of delirium in critically ill patients to bridge knowledge gaps on potential for family to help reduce and manage delirium in ICU settings.

1.2 Literature Review

1.2.1 Intensive Care Units

ICUs provide specialized health services to patients with complicated medical problems [17]. Canadian ICUs provide care for over two million critically ill patients per year [19] and ICU admissions account for over 12% [17] of hospital patient admissions per year [17]. Canadian ICUs can be broadly categorized as: general (e.g., medical,

surgical), specialty (e.g., burns, cardiac, neurological), or pediatric/neonatal [17]. ICU admissions may be urgent (emergent), meaning that a patient requires immediate attention upon admission (i.e., trauma from car accident), or planned (elective), meaning that the ICU admission was anticipated as part of their hospital stay (i.e., planned cardiac surgery) [17]. In Canada (2013-2014) 8 out of 10 ICU patient admissions were associated with an urgent hospital admission [17]. In 2013-2014, majority of patient admissions in Canadian ICUs (54%) were due to medical reasons such as myocardial infarction, shock and cardiac arrest, arrhythmia, and heart failure [17]. The average Canadian ICU stay is three days [17]. Males and those of lower socioeconomic status are more likely to be admitted than females and persons of higher socioeconomic status [18, 19].

Advanced life-sustaining medical technologies such as mechanical ventilation, sedative administration, and renal replacement therapy are used to address the complex medical issues that critically ill patients experience [17]. ICU patients have a wide range of needs and require both high intensity and specialized healthcare as demonstrated by the high staff-to-patient ratio in the ICU [17]. Despite advances and innovation in medical technology, the estimated unadjusted mortality in Canadian ICUs in 2013-2014 was 9% [17]. However, this mortality rate was lower than mortality in United States (US) ICUs (2008, 10%) as well as United Kingdom (UK) ICUs (2011, 29%) [20, 21].

Critically ill patients admitted to the ICU are at increased risk of developing negative outcomes such as cognitive impairment [22], intensive care unit acquired weakness [23], and delirium [2]. Cognitive impairment is a common sequela of critical

illness in ICU settings [24]. Critically ill patients may experience cognitive impairment such as deficits in memory and attention as a result of hypoxia, anemia, sepsis, fever, and delirium [24]. In addition, critically ill patients undergo muscular changes in the ICU due to bed rest and immobilization [25]. This may cause muscle atrophy, which is associated with increased ICU length of stay and delirium [26]. ICU delirium is a major risk factor of Post-Intensive Care Syndrome (PICS), which is persistent mental, cognitive, and physical impairments that may follow ICU stay [27]. PICS may lead to decreased health-related quality of life and functional status [27]. The ICU environment contains multiple delirium risk factors such as immobilization, sedation, and invasive interventions (i.e., invasive mechanical ventilation) [7], which leads to a high prevalence of delirium in ICUs (up to 50% of patients) [2]. Negative outcomes from ICU delirium may extend after patient discharge given that delirium is a risk factor for PICS.

Due to the resource-intensive environment of the ICU, the estimated average daily cost of an ICU stay is almost three times the daily cost of a general hospital ward stay in Canada (\$3,592 Canadian Dollars [CAD] per day and \$1,135 CAD per day, respectively) [17]. While estimates are not available in Canada, ICU care accounts for 1% of the US GDP [28]. In 2012, the estimated cost of care for an episode of delirium in Canadian ICUs ranged between \$3,690 and \$12,881 [29]. It is expected that ICU admissions in Canada will increase up to 80% by 2026, given the continuous innovation of technology that allows for population longevity [17]. These current projections do not account for increased ICU length of stay attributable to delirium. If delirium remains an unresolved issue in ICU care, the future burden to the healthcare system may be greater than expected.

1.2.2 Delirium in the ICU

Delirium is an acute confusional state, characterized by fluctuating course, severe disorganized thinking, and reduced ability to focus [1]. Delirium is one of the most distressing complications of critical illness for patients, families, and healthcare providers [2,3]. Delirium is linked to numerous negative health outcomes such as increased length of hospital stay, risk of long-term cognitive impairment, risk of long-term depression, anxiety, post-traumatic stress disorder, and increased mortality [2-7]. It is estimated that for every extra 48 hours of delirium in the ICU, risk of mortality increases by 11% [22]. ICU patients who recall the experience of delirium describe feelings of distress related to hallucinations and the inability to communicate [30]. Family members of critically ill patients may be distressed when witnessing their loved ones experiencing delirium and the negative outcomes associated with it [30].

Despite the high incidence of delirium and its associated adverse outcomes, up to 66% of delirium cases are missed using existing provider-administered screening tools resulting in undetected delirium [31-33]. Delirium detection may be complicated due to its fluctuating nature and multifactorial risk factors [32]. Patients in the ICU are exposed to multiple modifiable and non-modifiable risk factors of delirium. Non-modifiable risk factors associated with delirium include prior coma, older age, dementia, trauma, and higher severity of illness scores on the Acute Physiological and Chronic Health Evaluation II (APACHE-II) scale [2]. It is estimated that 30-40% of delirium cases in the ICU are preventable [8]. Modifiable risk factors of delirium include sleep deprivation, immobility, dehydration, and sedation (e.g., benzodiazepines). Delirium risk factors in the ICU may also be categorized as: 1) pre-existing, 2) illness-related, and 3)

hospital-related [34]. Pre-existing patient characteristics include substance use (e.g., drugs or alcohol) and pre-existing psychiatric disorders (e.g., depression) [35]. Illness-related factors include related medications needed to treat the reason for ICU admission, such as sedatives [2]. Lastly, hospital-related factors include environmental settings that prevent patients from resting (i.e., machine noises causing lack of sleep) [36]. Therefore, addressing modifiable risk factors of delirium may be a useful avenue to improve outcomes in critically ill patients.

The American Psychiatric Association's (APA) fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) is considered the gold standard for assessing delirium [1, 37]. DSM-5 delirium diagnostic criteria are: 1) disturbance in attention and awareness, 2) change from baseline attention and awareness in an acute and fluctuating manner, 3) disturbance in cognition, such as memory deficit, 4) the disturbances in 2 & 3 are not due to pre-existing conditions, and 5) evidence from diagnostics that this change is due to another medical condition or intervention (i.e., alcohol withdrawal) [1, 37]. Screening for delirium in the ICU is recommended by clinical practice guidelines [38]. Two common tools are used to detect delirium in the ICU: 1) the Intensive Care Delirium Screening Checklist (ICDSC) [39] and 2) the Confusion Assessment Method-ICU (CAM-ICU) [40]. The ICDSC is an 8-item delirium assessment tool. Items include altered level of consciousness and other symptoms, including inattention; disorientation; hallucination, delusion or psychosis; psychomotor agitation or retardation; inappropriate speech or mood; sleep-wake cycle disturbance; and symptom fluctuation [39]. The ICDSC is validated and commonly used in ICUs worldwide [39]. A score of 0 (not present) or 1 (present) is given per item on the ICDSC [39]. An ICDSC

score of ≥ 4 (out of 8) is indicative of delirium [39]. A meta-analysis of four studies reported that the pooled sensitivity of the ICDSC was 74% and the pooled specificity of the ICDSC was 81.9% [41]. Given the pooled sensitivity of the ICDSC, individuals that present with delirium symptoms may be misclassified as having no delirium (false negative), if their symptoms are attributed to a pre-existing disorder (e.g., neuropsychiatric disorder) rather than delirium. The CAM-ICU is another validated tool commonly used in ICUs [41]. The CAM-ICU is comprised of four delirium criteria (features): 1) fluctuation in mental state, 2) inattention in mental state, 3) altered level of consciousness, and 4) disorganized thinking [41]. A meta-analysis of seven studies reported that the pooled estimated sensitivity of the CAM-ICU was 80.0% and the pooled specificity was 95.9% [41].

Bedside nurses in all Alberta ICUs assess delirium (in eligible patients) twice per shift using the ICDSC [38]. Eligible patients for ICDSC delirium screening are those with a Richmond Agitation and Sedation Scale (RASS) greater than or equal to -3. The RASS is a scale ranging from -5 to +4 used to assess consciousness through evaluating arousal, cognition, and stimulation. RASS scores are used to assess the first item within the ICDSC tool (i.e., altered level of consciousness) [42]. Individuals with a RASS score of zero are considered calm and alert and are able to pay attention to healthcare providers. A score of -1 indicates mild sedation (responds to stimulus for more than 10 seconds) [42]. Incremental scores between -1 to -5 indicate increasing sedation. A score of -5 represents no response to any stimulus (voice or physical) [42]. Scores of +1 to +4 indicate increased agitation and anxiety. A score of +4 indicates extreme violence and potential danger to surroundings.

1.2.3 Patient and Family-Centered Care

The paradigm of medicine has shifted towards optimizing patient and family-centered care, where both patients and their families are integral to shared decision-making within the healthcare system [43]. Patient and family-centered care is defined as an approach towards healthcare that provides a mutually beneficial partnership between healthcare providers, families, patients, and all levels within the healthcare system [43]. Patients and families have unique experiences and perspectives that directly inform their needs and satisfaction with healthcare. The Institute for Patient and Family-Centered Care identified four main components of patient and family-centered care: 1) dignity and respect, 2) information sharing, 3) participation, and 4) collaboration [44]. Dignity and respect refer to active listening and honoring of patient and family decisions. This includes incorporating patient and family wishes with regard to their culture, spirituality, beliefs, and values in their care plan. Information sharing refers to healthcare providers providing complete, accurate, and timely dissemination of medical knowledge in an unbiased manner [44]. Participation refers to encouragement of patient and family engagement in all levels within the healthcare system. Lastly, collaboration refers to active shared decision-making, policy making, and program-developing between families, patients, healthcare providers, and healthcare leaders in education, research, and delivery of care [44]. In summary, patient-centered and family-centered care is an approach to planning, developing, and implementing healthcare in a manner that is inclusive to patient and family perspectives.

Research funding agencies and healthcare policy makers have been strong proponents of involving stakeholders in healthcare and research [45-47]. In this case,

stakeholders are defined as those who are responsible for or directly affected by the healthcare system. Stakeholders include but are not limited to the public, healthcare providers (e.g., physicians, nurses, pharmacists), consumers (e.g., patients and families), payers (e.g., insurance companies, government funders), policy makers, product makers, and principal investigators [47]. There are many benefits of engaging patients and their families in research and healthcare. Patients and families have novel expertise that may improve the relevance of research questions, accelerate knowledge translation, and advance research engagement [48]. Involving family in healthcare settings results in greater clinician, patient, family, and staff satisfaction, in addition to increased efficiency in resource allocation [48]. Caregivers and family members of patients may help facilitate psychological support and medication administration that healthcare providers would be unable to do alone, which may maintain medicine regime and reduce the burden of cognitive impairment, patient distress, and pain [49-51]. Engaging patient and stakeholders in research and healthcare enhances patient experience within the healthcare system [48]. Thus, partnerships between patients, families, and healthcare providers leads to improved patient care and outcomes.

1.2.4 Perspectives on Family Presence in Healthcare

Families are integral to patient well-being, comfort, and healing, leading to positive patient outcomes in hospital settings [48]. Increased family involvement and presence in hospitals has shown to improve delivery of vital information [49], patient adherence to treatment [52], and accountability of healthcare providers [53]. One study found that 46% of families in pediatric settings provided new and necessary patient information during clinical rounds [54]. Patients have voiced their desire to have their

loved one or family member by their side [10]. Family members may motivate patients towards self-management and adherence to treatment regimens during their hospital stay and post-discharge [52]. In addition, family presence in the ICU is shown to reduce adverse events [53], diagnostic tests [55], hospital length of stay [56], and hospital utilization [57].

Family presence and care in the hospital setting requires involvement from healthcare providers [49]. Nurses may have to expand their role to include, educate, and comfort family members at the bedside. Existing studies demonstrate that nurses perceive family involvement as positive despite the work needed for nurses to act as communicators with both patients and their families [58]. In multiple surveys, both nurses and families reported greater satisfaction with open hospital visitation policies as families may provide patient comfort, which is beneficial during patient care [58, 59].

1.2.5 Perspectives on Family Presence in the ICU

Family member presence in the ICU increases opportunities for shared decision-making [12, 16]. Through shared decision-making between families and healthcare providers, collaboration on patient medical treatment plans may be achieved. This collaboration may result in greater patient treatment planning [10] and reduced administration of medicine, which in turn may result in positive patient and family experience [10] such as increased recovery time [60]. In addition, family members may also help facilitate methods to calm patient distress [16]. Within the context of delirium, shared decision-making between family, critical care clinicians, and staff may reduce modifiable risk factors for delirium such as patient sleep schedule [2, 60]. Moreover, family members of critically ill patients may employ non-pharmacological interventions

for the management of delirium by providing a familiar environment that can enhance patient sleep hygiene and cognition [7, 9]. Given the benefits of family presence, it is surprising that only 17% of patients have families present in adult ICU populations [16].

Three before-and-after studies have evaluated the effects of increased family visiting hours on the incidence of delirium in critically ill patients [61-63]. Westphal *et al.* assessed the effects of a 24-hour open visitation policy on the incidence of delirium in critically ill patients [61]. Family members of 248 consecutive patients admitted to the ICU chose between having a flexible 24-hour open visitation (Phase 2) as opposed to the restricted 6-hour visitation (Phase 1) [61]. The authors found that the increase in visitation hours between Phase 1 and Phase 2 resulted in a 5.4% reduction in the cumulative incidence of delirium [61]. These results were consistent with a systematic review including two studies that evaluated flexible family visitation hours and the incidence of delirium in critically ill patients [63-65]. The systematic review found that flexible family visitation hours were associated with both a reduced incidence of delirium and patient anxiety [64]. The above studies used small sample sizes ($n < 400$) and were single-center [64], which decreases the generalizability of these findings. Rosa *et al.* assessed the effects of extended (12 hour/day) versus restricted (4 hour/day) family visitation hours on the incidence of delirium in a before-and-after study [62]. Results showed that 14 out of 145 (9.7%) patients in the extended visitation group developed delirium compared to 29 patients out of 141 (20.6%) in the restricted group [62]. Although the study reports a statistically significant difference between both groups, limitations must be considered. It is plausible that families of critically ill patients who chose the flexible 24-hour ICU visitation would be more involved in the healing process

of patients than families who declined to be a part of the 24-hour open visitation policy [62]. This could potentially lead to an overestimation of the reduction in the cumulative incidence of delirium. Eghbali-Babadi *et al.* compared the incidence of delirium in patients within a cardiovascular surgery ICU in a randomized control trial [65]. Family of patients in the intervention group were allowed to visit patients the morning after surgery (n=34) while those in the control group received standard care (visiting 24 hours after surgery) (n=34) [65]; the incidence of delirium was significantly reduced by 11.8% in the intervention group [65]. A randomized control trial exploring flexible ICU visiting hours and the incidence of delirium reported contradictory results to studies mentioned above [66]. The trial reported no association between flexible ICU visitation hours and the incidence of delirium in critically ill patients [66]. Delirium developed in 157 of 831 patients (18.9%) in the intervention group (flexible family visitation hours) and in 170 of 845 patients (20.1%) in the restricted group (limited visitation hours). Additionally, the study cannot be generalizable to Canadian ICUs, given that the standard of care in most Canadian ICUs is 24/7 ICU visitation hours (with exceptions [67]). Although the sample size was large (n=1,685), the estimated data collection time was limited (two months) [66]. The limited intervention time may not be sufficient to measure increased family presence or statistical significance since increased visitation hours might not correlate with direct ICU family presence, especially within a short time-frame. This may result in misclassification bias that underestimates the reduction of cumulative delirium incidence (adjusted difference in incidence of delirium between flexible and restrictive visitation hours, -1.7% [95% CI, -6.1% to 2.7%]; p = 0.44) [66]. Secondly, the trial was susceptible to misclassification bias since increased family visitation hours may not

correlate to increased family member presence. It is plausible that family members in the intervention group may not have engaged or utilized the extended ICU visitation hours. This may have resulted in an underestimation of the reduction in incident delirium [66].

1.2.6 Administrative Data and Documentation of Family Presence in Alberta ICUs

Administrative data is collected by the government for medical record keeping purposes [68, 69]. This data is not collected for the primary purpose of research but may be used in research studies. Therefore, administrative data used in research is often referred to as secondary data. Administrative data provides an efficient method for obtaining a large sample size given that the data was already collected for administrative or clinical purposes [68]. This allows for data collection in a feasible and economic manner compared to other study designs (i.e., prospective cohort studies). However, administrative data does have limitations. Researchers are limited to the variables collected in the administrative data. This may lead to residual confounding if important covariates are not available for use in analysis. In addition, administrative data may be prone to errors and missing data, resulting in limited quality of the dataset used [68].

In Alberta, electronic health records of ICU patients are collected in eCritical [69]. eCritical is a provincial critical care population-based bedside clinical information system which captures in real-time demographic and patient characteristics such as age, sex, severity of illness, delirium, and family presence. Findings from Brundin-Mather *et al.* support the quality of eCritical, as the median kappa between data

extraction from eCritical and manual collection by data auditors was 0.99 (Inter Quartile Range [IQR], 0.92-1.00) [69].

Family communication and visitation (i.e., presence) is recorded as free-text in eCritical [69, 70], which may lead to barriers in coding for family presence in a large cohort. To mitigate this barrier, a Natural Language Processing (NLP) algorithm was developed by Lucini *et al.* to document family presence through analyzing human language documented in eCritical [70, 71]. The algorithm incorporated rule-based classifier training. Variables included in the algorithm were: ICU outcomes (length of stay, survival, illness severity), demographics (sex, age), and specific family variables (type of contact, family documented, visit duration). The algorithm was trained to conclude family presence when a set of conditions were satisfied. If the record of a patient contained information related to the defined inclusion category (condition one, e.g. “Presence or Visit in ICU”) and sub-category (condition two, “Comment on Family Presence or Meeting”), then the record was classified as “true”, which is indicated family presence. Categories included both inclusion and exclusion criteria. For instance, documented family member presence by situation (e.g., did a healthcare provider speak to a family member?) or general documentation (e.g., significant other). Other conditions involved documentation of parameters specific (sub-category) to each patient (e.g., surname, name, or phone number of family member). If family presence was detected by the NLP algorithm (as described above) in any of the patient’s recorded ICU days of stay, family was considered present for that patient. The algorithm also captured the mode of family presence (i.e., separating in-person ICU visits and phone calls) [70]. The algorithm was validated by comparing the performance of the rule-based

classifier with a reference standard. The reference standard for family communication was established by an independent and blinded researcher who manually reviewed all records within a random sample of 280 patients [70]. The sensitivity, specificity, and area under the receiver operator curve (AUROC) was high (above 80%) for classification of family physical visits [70] and phone calls between patients and families.

1.2.7 Knowledge Gap and Significance

Given the high incidence of delirium in the ICU and evidence of the positive impact that family presence has on critically ill patients, it is imperative to evaluate the role of family in delirium prevention. Research has shown that critically ill patients value the presence of their loved ones and family members in the ICU [72]. Despite this, there is a paucity of knowledge regarding the direct impact of ICU family presence, rather than visitation hours, on the incidence and duration of delirium in critically ill patients. Prior studies measured the impact of family presence through increased ICU visitation hours rather than estimating direct family physical presence in the ICU. Estimates reported in these studies may underestimate the impact of family presence on delirium since increased visitation hours may not correlate with increased family presence. In addition, to our knowledge none of these studies assessed the impact of family presence on the duration of delirium. To close these knowledge gaps, we used a large multi-center population-based cohort of critically ill patients to evaluate the association between family presence and the incidence and duration of delirium in critically ill patients. Stakeholders (including patients, families, providers, and decision makers) helped to identify treatment of delirium as an important area of research in the ICU [6]

and helped create the proposed study question. Stakeholders were involved during all parts of the research (proposal development, knowledge translation, and discussion), which contributed to the overall success of the project as their involvement increased knowledge and capacity for patient-oriented research. It is hypothesized that there is an association between family presence and reduced delirium incidence and duration in the ICU. Such findings can increase awareness on the importance of family presence in the ICU and thus increase active collaboration between patients, families, healthcare providers, and decision makers. Moreover, findings from this research can directly inform stakeholders, including patients, families, healthcare providers, and decision makers on policy changes that will increase family involvement in the ICU.

1.3 Aims and Objectives

1.3.1 Objectives

The study objectives are to evaluate: 1) the association between family presence and the incidence of delirium in critically ill adults admitted to the ICU; and 2) the association between family presence and the duration of delirium in critically ill adults admitted to the ICU. Objectives 1 & 2 were analyzed using mixed-effects models to compare results when data is analyzed per clusters of ICU re-admission and clustering by ICU site where appropriate.

1.3.2 Hypotheses

We hypothesize that: 1) family member presence will decrease the incidence of delirium; and 2) family member presence will decrease the duration of delirium in critically ill patients.

CHAPTER 2: IMPACT OF FAMILY PRESENCE ON DELIRIUM
IN CRITICALLY ILL PATIENTS: A RETROSPECTIVE COHORT
STUDY

2.1 Abstract

Purpose: To assess the impact of family presence on the incidence and duration of delirium in adults admitted to the intensive care unit (ICU).

Methods: We obtained electronic health records of consecutive adults (≥ 18 years) admitted to any medical-surgical ICU (in 14 hospitals) in Alberta, Canada from January 1, 2014 to December 30, 2018, using deterministic linkage of administrative databases. Family presence (exposure) was quantified using a validated algorithm and categorized as: 1) physical presence in ICU, 2) phone call only, and 3) no presence (reference group). Delirium was measured using the Intensive Care Delirium Screening Checklist (ICDSC). An ICDSC ≥ 4 , after family presence (yes/no), identified incident delirium. Multivariable mixed-effects logistic and linear regression were used to evaluate the association between family presence and incidence (binary) and duration (days) of delirium, respectively. Models were adjusted for a priori identified covariates (e.g., ICU admission type, Glasgow Coma Scale [GCS]).

Results: Family physical presence was associated with increased incidence of delirium in the overall cohort (crude odds ratio [OR] 1.19, 95%CI:1.11-1.27, $p=0.02$), and reduced incidence of delirium in elective-surgical patients with intact GCS (GCS=15) (adjusted OR 0.60, 95%CI:0.39-0.97, $p=0.02$), compared to patients in the reference group. Family physical presence decreased duration of delirium (-1.87 days, 95%CI:-2.01 to -1.81, $p<0.001$).

Conclusions: Family presence in the ICU was associated with both decreased incidence (in elective-surgical patients with intact GCS) and decreased duration (among

all ICU patients) of delirium. Findings may inform policy changes that will encourage family presence in the ICU.

2.2 Background

The Intensive Care Unit (ICU) provides health services to patients with complex and critical conditions [1]. Delirium, an acutely disturbed state of consciousness, characterized by sudden onset or fluctuating course, inattention, and disorganized thinking [2], impacts up to 50% of critically ill patients [3]. Delirium may lead to worse patient and health system outcomes, such as increased risk of long-term cognitive impairment, mental health problems (e.g., anxiety, depression), higher risk of mortality, and higher healthcare costs [3-7].

Delirium is difficult to detect and manage given its fluctuating course, numerous risk factors (e.g., age, sedatives, infection, sleep deprivation), and resistance to pharmacological management [8]. Given this, the Society of Critical Care Medicine guidelines highlight the management and treatment of delirium as top priority for future research [5]. Non-pharmacological therapies (e.g., early mobilization) are preferred over pharmacological interventions to prevent and manage delirium in the critically ill [8, 9]. A systematic review reported that pharmacological prophylaxis for the prevention and the treatment of delirium was not only ineffective, but in some cases was harmful and led to increased mortality in critically ill patients. Conversely, the use of non-pharmacological interventions such as cognitive stimulation, maintenance of sleep, and mobilization, reduce the incidence of delirium in critically ill patients [5, 10].

Family members of critically ill patients may help facilitate non-pharmacological delirium prevention and management interventions such as maintaining a day/night

schedule, promoting early mobilization, and general environmental support (e.g. hygiene routine) [11, 12]. Additionally, family member presence in the ICU may relieve patient anxiety [13]. As such, family presence may help minimize delirium burden among patients admitted to ICUs. Few studies have investigated the impact of family presence on the incidence of delirium, and to our knowledge, none have assessed the impact of family presence on the duration of delirium in critically ill patients [14, 15]. The purpose of this study was to evaluate the association between family presence and: 1) delirium incidence and 2) duration of delirium among adults admitted to an ICU.

2.3 Methods

This retrospective cohort study was reported according to STrengthening of Reporting of OBservational studies in Epidemiology (STROBE) [16], and REporting of studies Conducted using Observational Routinely-collected Data (RECORD) statement (Appendix 1) [17]. The project was approved by the Conjoint Health Research Ethics Board at the University of Calgary (REB17-0389).

2.3.1 Study Population

The study population consisted of patients admitted to any of 14 general medical-surgical ICUs in Alberta, Canada between January 1, 2014 and December 30, 2018. All ICUs utilized the same standard of care which includes open visitation hours and routine delirium assessment, prevention, and management [18]. Patients were included if they met the following criteria: 1) aged 18 years or older; 2) had at least one assessment of delirium using the Intensive Care Delirium Screening Checklist (ICDSC) during their ICU stay; 3) stayed at least 24 hours in the ICU; 4) had data that was linked

to the Discharge Abstract Database (DAD); and 5) resided in Alberta at the time of ICU admission (to ensure population from Alberta).

2.3.2 Data Sources

Patient clinical information was extracted from eCritical, a population-based bedside clinical information system which captures real-time clinical data for all adult ICU patients in Alberta [19]. eCritical was linked to the DAD, which includes demographic, diagnostic, and procedural data on all patients discharged from the hospital [20]. Using deterministic linkage to eCritical, the DAD was used to confirm Alberta residency status [20].

2.3.3 Measurement of Exposure: Family Presence

Family presence was recorded in eCritical as free-text, making it time-consuming to categorize manually [21, 22]. To eliminate this barrier, a Natural Language Processing (NLP) algorithm was developed by our team (KK, FL) to determine family presence from the medical record [21]. The NLP algorithm was developed by analyzing human language documented in eCritical [21, 23] using a rule-based classifier training, which uses IF-THEN rules [21]. If a record for a patient contained information related to the defined inclusion category (condition one, e.g. “Phone Calls”) and sub-category (condition two, e.g. “Comment on Family Phone Call”), then the record was classified as “true”, which was indicative of family presence (See Appendix 2 for conditions). The algorithm also captured the mode of family presence (e.g., in-person or phone call), yielding a three-level exposure (physical presence in ICU, phone call only (direct between patient and family), no presence or phone call [reference group]; details in

Appendix 3). The algorithm was validated by comparing the performance of the rule-based classifier with a reference standard (area under the curve above 80%) [21].

2.3.4 Measurement of Outcomes: ICDSC (Intensive Care Delirium Screening Checklist)

Among eligible patients with a Richmond Agitation and Sedation Scale (RASS) score ≥ -4 , bedside nurses in all Alberta ICUs assess delirium twice per shift (morning and night) [24], using the ICDSC [25]. The ICDSC is a validated 8-item delirium assessment tool for use in the ICU (1 point per item [i.e., inattention, disorientation, hallucination] minimum 0 and maximum 8) [26]. Scores of ≥ 4 out of 8 on the ICDSC are indicative of delirium (sensitivity: 99%; specificity: 64%) [26]. For the primary outcome, incident delirium was defined as an ICDSC score of ≥ 4 , that occurred after documentation of family presence. The secondary outcome, duration of delirium (in patients who had delirium), was measured as the total number of ICU days (24-hour periods) with a positive ICDSC score (≥ 4 points) . Proportion of days with delirium (secondary analysis) was calculated by dividing the number of days with a positive ICDSC score by the total length of ICU stay and subsequently reported in the following strata: 0%-24.99%, 25-49.99%, 50%-74.99%, 75%-100%.

2.3.5 Measurement of Delirium Risk factors, Modifiers, Confounders

Selected covariates to include in the regression models were informed by previous studies [4, 15, 27, 28]. Patient characteristics from eCritical included age (continuous and dichotomous [≥ 65 , < 65]), sex (dichotomous [female, male]), patient chronic health conditions upon admission dichotomized as ever/never (heart failure, respiratory insufficiency, metastatic cancer, immune suppression, cirrhosis, and diabetes mellitus), Clinical Frailty Scale (scores ranging from 0-9, [continuous]) [29],

admission Acute Physiology And Chronic Health Evaluation II [APACHE-II] score (ordinal) [30] and Sequential Organ Failure Assessment [SOFA] (ordinal), clinical characteristics assessed upon admission such as the Glasgow Coma Scale (GCS) (dichotomous, intact GCS [GCS=15], impaired GCS [GCS <15]) [31], and, Charlson Comorbidity Index (CCI) score (ordinal), ICU admission type (elective-surgical, emergency-surgical, medical), ICU interventions such as invasive mechanical ventilation, non-invasive mechanical ventilation, dialysis, vasoactive medication, continuous renal replacement therapy (dichotomized, ever/never), RASS (Agitated [+1 to +4], Alert and Calm [0], Sedated [-1 to -4], and Comatose [-5]) [24], and ICDSC (continuous and ordinal scores of 0, 1-3, 4-5, 6-8) [32]. Hospital characteristics were also included, such as teaching status (dichotomous, yes/no), hospital type (tertiary, community, and regional), and hospital size (median number of ICU and hospital beds).

2.3.6 Data Analysis

Statistical analyses were performed using Stata Version 16.0 (StataCorp, Texas) and the two-sided significance level was set at 5%, with 95% confidence intervals (CIs) accompanying estimates. Patient characteristics were summarized using descriptive statistics (i.e., mean, median, proportions). Methods of data handling and cleaning are described in Appendices 4 & 5 respectively [20, 33, 34].

Multivariable mixed-effects logistic regression was used to evaluate the association between family presence (physically present in the ICU, phone call only, no presence or phone calls [reference group]) and incidence of delirium; outcomes of association are presented as odds ratios (OR). Multivariable mixed-effects linear regression was used to evaluate the association between family presence and delirium

duration, wherein regression estimates reflect the difference in mean days of delirium comparing family presence with no family presence or phone calls (reference group). Family presence was categorized as family physical presence in the ICU during or prior to patient delirium onset. The above models were performed using a mixed-effects modeling to compare estimates when data were analyzed after accounting for clustering by ICU site and ICU re-admission and standard errors of repeated measures. The analysis accounted for both random and fixed effects [34]. Random effects represent shared effects of each patient [34, 35], which means the outcomes of patients were allowed to vary in defined aggregated group means (ICU re-admission, ICU site). Results from the mixed-effects analysis (for logistic and linear regression) were reported where the omnibus test was significant, for either clustering by re-admission or ICU site, meaning it is necessary to adjust estimates for either patient re-admission, ICU site, or both. Covariates in models were assessed as potential effect measure modifiers prior to an assessment of confounding by examining the significance of interaction terms in each model. If an interaction term was statistically significant ($p < 0.05$), effect modification was deemed present. Sensitivity analyses were performed: 1) excluding those who died in the ICU and 2) comparing family presence as a binary variable (grouping physical presence and call). Secondary analyses were completed to explore granular patient diagnoses (e.g., cancer, trauma) for each admission type and percentage days with delirium stratified by family presence [36].

2.4 Results

2.4.1 Study Population

Between January 1st, 2014 and December 31st, 2018, 47,195 unique patients were admitted at least once to an Alberta ICU. A total of 36,496 unique patients met initial inclusion criteria (Figure 1). Of those patients, 10,396 patients did not have the data required for the family presence algorithm, leaving 14,847 patients with delirium for the secondary outcome (Appendix 6). For the primary outcome, 563 patients had delirium prior to family exposure, leaving 25,537 unique patients in the study population. Included patients had a median age of 59 years (interquartile range [IQR], 46-70), were predominately male (n=14,690, 57.5%), and admitted for medical reasons (74.7%) (Table. 1). The median ICDSC score during ICU stay was 4 (IQR, 2-6) and 14,284 had delirium at least once during their ICU stay (55.9%, 95%CI: 55.3-56.5%) (Table 2). Patients who had family members present in the ICU had a median admission APACHE-II score of 19 (IQR, 14-25), while those with a family phone call or no ICU family present had a median APACHE-II score of 17 (IQR, 12-22) and 14 (IQR, 10-19), respectively (Table 3). The most common ICU admitting diagnoses by admission type are shown in Appendix 7.

2.4.2 Family Presence and Incidence of Delirium

The omnibus test from the mixed-effects model, adjusting for ICU re-admission, had a p-value of 0.04, suggesting that adjustment of results by ICU re-admissions was necessary to assess the relationship between family presence and incidence of delirium. The omnibus test for the mixed-effects model clustering by ICU site was non-significant (p=0.89). Family physical presence was associated with increased incidence

delirium in the overall cohort (unadjusted odds ratio [OR] 1.19, 95%CI:1.11-1.27, $p=0.02$), compared to patients in the reference group (Table 3). When stratified by admission type (elective-surgical, emergency-surgical, medical; effect modifier, $p=0.01$) and whether the patient's GCS score was intact (GCS=15 vs < 15; effect modifier, $p<0.001$) (concurrent effect modification by GCS and admission type, $p<0.001$), family physical presence was associated with lower incidence of delirium for patients admitted following elective surgery with intact GCS (GCS=15) (OR 0.60, 95%CI:0.39-0.97), compared to patients in the reference group (Table 3). There was no significant difference in incidence of delirium among patients with intact or impaired GCS (GCS=15 vs < 15) in medical and emergency-surgical admissions given family presence compared to patients in the reference group (Table 3 and Figure 2).

2.4.3 Family Presence and Duration of Delirium

The omnibus test from the mixed-effects regression, adjusting for ICU re-admission, had a p-value of 0.01, suggesting that adjusting for ICU re-admission was necessary to assess the relationship between family presence and delirium duration. The omnibus test for mixed-effects by ICU site clustering was non-significant ($p=0.09$). After adjusting for covariates, both family physical presence and a family call significantly decreased the duration of delirium (MD [Mean Difference] -1.87, 95%CI: -2.01 to -1.81) and (MD -1.41, 95%CI: -1.52 to -1.31) respectively, as compared to patients in the reference group (Table 4).

2.4.5 Sensitivity Analyses

Sensitivity analysis excluding patients who died in the ICU showed similar results for the association between family presence and the incidence and duration of

delirium (Appendices 8 & 9). The adjusted MD (-1.90 days, 95%CI: -2.13 to -0.73) in patient delirium days comparing family presence (as a binary variable) and the reference group was similar to ICU family physical presence when coded as a three-level exposure (Appendix 10). The association between family presence and percentage days with delirium are shown in Appendix 11.

2.5 Discussion

This retrospective population-based cohort study among 25,537 adults admitted to the ICU found that compared to no family visits or phone call, family physical presence was associated with increased incidence of delirium among all patients and reduced incidence of delirium in patients admitted following elective surgery with intact GCS at the time of admission. In all patients, family presence was associated with reduced duration of delirium compared to when no family physical visits or phone calls were observed. In general, sicker patients had more in-person visit than those with less severe illness. Our findings suggest that in select critically ill patients, family presence is associated with reduced incidence and duration of patient delirium.

Few studies have evaluated the effect of family presence on delirium in critically ill patients [37-40]. A before-and-after study by Westphal et al. found that an increase in visitation hours resulted in a significant (5.4%) reduction in the cumulative incidence of delirium in critically ill patients [37]. A systematic review reported that flexible visitation policies were associated with reduced frequency of delirium in critically ill patients (pooled OR 0.39; 95%CI:0.22-0.69; I² = 0%) [40]. Similarly, our findings support that family presence may reduce incidence of delirium in elective-surgical critically ill patients with intact GCS. In contrast, a randomized controlled trial of flexible ICU visitation hours

reported no association between flexible ICU visitation hours and the incidence of delirium in critically ill patients [41]. We found that family presence decreased delirium duration by two days when adjusting for patient re-admission. Patients who were previously admitted to the ICU may be predisposed to experiencing delirium in their next admission, thereby underestimating the effect of recurrent delirium when analyzing per patient admission [42]. If patients are re-admitted to an ICU, it may be important for family members to be present to aid in delirium management.

The association between family presence and incidence of delirium in the ICU is complex, with major differences observed among strata defined by patient admission type, and GCS on admission. As such, family absence could be a modifiable risk factor for incident delirium in elective-surgical patients with intact GCS. Patients admitted for elective-surgical reasons have lower risk of developing delirium, compared to patients admitted for emergency-surgical or medical reasons, given that they have less risk factors for delirium such as reduced illness severity [27]. ICU patients admitted for medical reasons may have limited benefit from family member presence given their high exposure to non-modifiable delirium risk factors (i.e., high comorbidity level) [27]. Patients admitted with intact GCS (i.e., high GCS scores indicating normal consciousness and brain function) can receive cognitive stimulation from family members through family interaction [43]. Conversely, patients with impaired GCS (low GCS scores) may not be able to meaningfully engage with their family members due to the patient's limited capacity [44], thereby restricting potential benefit from interaction with the family member. Our study was only able to measure family presence in the

ICU; family ability to engage with patients (i.e., who have intact GCS [31]) encourages further interaction, which may in turn reduce incident delirium.

Given the high incidence of delirium and its detrimental outcomes, it is imperative to understand how family member presence impacts patient delirium. Our findings highlight the importance of family presence in the ICU. However, more research is needed on increasing opportunities for meaningful family engagement. For example, a recent study showed that it is feasible for family to aid in the detection of delirium, therefore increasing opportunities for them to provide bedside care and aid in shared decision-making [45]. Lastly, future studies may explore mechanisms between family presence on different ICU admission types (e.g., elective-surgical, medical) and patient consciousness level on delirium in critically ill patients.

This study has strengths and limitations. Our large population-based sample size (n=25,537) from all 14 adult ICUs in Alberta is a major strength, increasing the precision of our results. This may allow generalization to other ICUs with similar healthcare systems and populations. Family presence was captured using a novel NLP algorithm developed by our team [16], yielding an accurate representation of family presence compared to quantifying family presence according to visitation policy alone, however family presence may have been underreported as its documentation was optional for nursing staff to complete. This may have led to misclassification of exposure status (i.e., family presence) irrespective of outcome status, thereby biasing estimates of effect toward the null value. The study is also limited in that family presence was coded when family met with ICU nurses or healthcare staff. We assumed that families would visit their loved ones before or after these meetings. Additionally, we did not have data on

what activities, if any, the family members engaged in. For example, some family members may not have actively engaged with the patient, thus underestimating the effect of active family engagement on incidence and duration of delirium. Lastly, we did not assess for time-dependent change in the incidence of delirium associated with family presence (exposure). Thus, our results may be a conservative estimate of the effect of family presence on delirium in critically ill patients.

2.6 Conclusion

ICU family presence was associated with a reduction in the incidence of ICU delirium in patients with intact GCS admitted following elective surgery. In all patients, family presence in the ICU and phone call was associated with reduced duration of delirium of up to two days and one day, respectively. Family member presence (and involvement in care) in the ICU may be an important mechanism to achieve better delirium-related outcomes for critically ill patients. Findings may inform stakeholders and future research on policy changes that will encourage family presence in ICU care.

2.7 References

1. Canadian Institute for Health Information, (2016) Care in Canadian ICUs. Care in Canadian ICUs. Canadian Institute for Health Information.
2. American Psychiatric Association, (2000) Diagnostic and statistical manual of mental disorders: DSM-IV. American Psychiatric Association, Washington, D.C
3. Salluh JI, Wang H, Schneider EB, Nagaraja N, Yenokyan G, Damluji A, Serafim RB, Stevens RD, (2015) Outcome of delirium in critically ill patients: systematic review and meta-analysis. *BMJ* 350: h2538
4. Ely E, Shintani A, Truman B, Speroff T, Gordon S, Harrell F, Inouye S, Bernard G, Dittus R, (2004) Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA* 292: 1753-1752
5. Devlin JW, Skrobik Y, Gélinas C, Needham DM, Slooter AJC, Pandharipande PP, Watson PL, Weinhouse GL, Nunnally ME, Rochwerg B, Balas MC, van den Boogaard M, Bosma KJ, Brummel NE, Chanques G, Denehy L, Drouot X, Fraser GL, Harris JE, Joffe AM, Kho ME, Kress JP, Lanphere JA, McKinley S, Neufeld KJ, Pisani MA, Payen JF, Pun BT, Puntillo KA, Riker RR, Robinson BRH, Shehabi Y, Szumita PM, Winkelman C, Centofanti JE, Price C, Nikayin S, Misak CJ, Flood PD, Kiedrowski K, Alhazzani W, (2018) Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. *Crit Care Med* 46: e825-e873

6. Collinsworth AW, Priest EL, Campbell CR, Vasilevskis EE, Masica AL, (2016) A Review of Multifaceted Care Approaches for the Prevention and Mitigation of Delirium in Intensive Care Units. *J Intensive Care Med* 31: 127-141
7. Wolters AE, Peelen LM, Welling MC, Kok L, de Lange DW, Cremer OL, van Dijk D, Slooter AJ, Veldhuijzen DS, (2016) Long-Term Mental Health Problems After Delirium in the ICU. *Crit Care Med* 44: 1808-1813
8. Serafim RB, Bozza FA, Soares M, do Brasil PE, Tura BR, Ely EW, Salluh JI, (2015) Pharmacologic prevention and treatment of delirium in intensive care patients: A systematic review. *J Crit Care* 30: 799-807
9. van Eijk MM, Roes KC, Honing ML, Kuiper MA, Karakus A, van der Jagt M, Spronk PE, van Gool WA, van der Mast RC, Kesecioglu J, Slooter AJ, (2010) Effect of rivastigmine as an adjunct to usual care with haloperidol on duration of delirium and mortality in critically ill patients: a multicentre, double-blind, placebo-controlled randomised trial. *Lancet* 376: 1829-1837
10. Teixeira C, Rosa RG, (2018) The rationale of flexible ICU visiting hours for delirium prevention. *Journal of Emergency and Critical Care Medicine* 2
11. Gonzalez CE, Carroll DL, Elliott JS, Fitzgerald PA, Vallent HJ, (2004) Visiting preferences of patients in the intensive care unit and in a complex care medical unit. *Am J Crit Care* 13: 194-198
12. Martinez FT, Tobar C, Beddings CI, Vallejo G, Fuentes P, (2012) Preventing delirium in an acute hospital using a non-pharmacological intervention. *Age Ageing* 41: 629-634

13. Burns KEA, Misak C, Herridge M, Meade MO, Oczkowski S, (2018) Patient and Family Engagement in the ICU. Untapped Opportunities and Underrecognized Challenges. *Am J Respir Crit Care Med* 198: 310-319
14. Davidson JE, (2013) Family presence on rounds in neonatal, pediatric, and adult intensive care units. *Ann Am Thorac Soc* 10: 152-156
15. Van Rompaey B, Elseviers MM, Schuurmans MJ, Shortridge-Baggett LM, Truijen S, Bossaert L, (2009) Risk factors for delirium in intensive care patients: a prospective cohort study. *Crit Care* 13: R77
16. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.*
17. Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, (2015) The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. *PLoS Med* 12: e1001885
18. Bowker SL, Stelfox HT, Bagshaw SM, (2019) Critical Care Strategic Clinical Network: Information infrastructure ensures a learning health system. *Cmaj* 191: S22-s23
19. Brundin-Mather R, Soo A, Zuege DJ, Niven DJ, Fiest K, Doig CJ, Zygun D, Boyd JM, Parsons Leigh J, Bagshaw SM, Stelfox HT, (2018) Secondary EMR data for quality improvement and research: A comparison of manual and electronic data

collection from an integrated critical care electronic medical record system.

Journal of Critical Care 47: 295-301

20. Canadian Institute for Health Information (2012) CIHI Data Quality Study of the 2009–2010 Discharge Abstract Database. CIHI Data Quality Study of the 2009–2010 Discharge Abstract Database.
21. Lucini FR, Krewulak KD, Fiest KM, Bagshaw SM, Zuege DJ, Lee J, Stelfox HT, (2021) Natural language processing to measure the frequency and mode of communication between healthcare professionals and family members of critically ill patients. J Am Med Inform Assoc 28: 541-548
22. Au SS, Roze des Ordons A, Soo A, Guienguere S, Stelfox HT, (2017) Family participation in intensive care unit rounds: Comparing family and provider perspectives. J Crit Care 38: 132-136
23. Kreimeyer K, Foster M, Pandey A, Arya N, Halford G, Jones SF, Forshee R, Walderhaug M, Botsis T, (2017) Natural language processing systems for capturing and standardizing unstructured clinical information: A systematic review. J Biomed Inform 73: 14-29
24. Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, Tesoro EP, Elswick RK, (2002) The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. Am J Respir Crit Care Med 166: 1338-1344
25. Alberta Health Services (2017) Provincial Clinical Knowledge Topic Delirium, Adult – Critical Care. Book Provincial Clinical Knowledge Topic Delirium, Adult – Critical Care. Alberta Health Services.

26. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y, (2001) Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. *Intensive Care Med* 27: 859-864
27. Cherak S, Rosgen B, Mungunzul A, Wollny K, Doig C, Patten S, Stelfox HT, Fiest KM, (2020) Mental Health Interventions to Improve Psychological Outcomes in Informal Caregivers of Critically Ill Patients: A Systematic Review and Meta-Analysis. Manuscript under peer review
28. Pisani MA, Kong SY, Kasl SV, Murphy TE, Araujo KL, Van Ness PH, (2009) Days of delirium are associated with 1-year mortality in an older intensive care unit population. *Am J Respir Crit Care Med* 180: 1092-1097
29. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A, (2005) A global clinical measure of fitness and frailty in elderly people. *CMAJ* 173: 489-495
30. Wong DT, Crofts SL, Gomez M, McGuire GP, Byrick RJ, (1995) Evaluation of predictive ability of APACHE II system and hospital outcome in Canadian intensive care unit patients. *Crit Care Med* 23: 1177-1183
31. Teasdale G, Jennett B, (1974) Assessment of coma and impaired consciousness: A practical scale. *Lancet* 2: 81-84
32. Fiest KM, Soo A, Hee Lee C, Niven DJ, Ely EW, Doig CJ, Stelfox HT, (2021) Long-Term Outcomes in Intensive Care Unit Patients with Delirium: A Population-Based Cohort Study. *Am J Respir Crit Care Med*

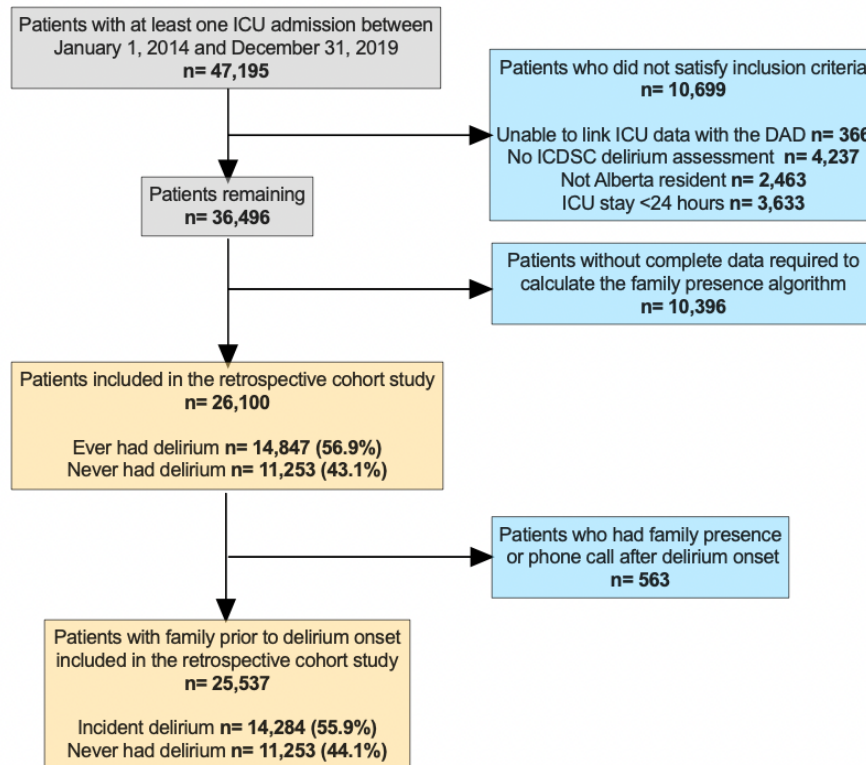
33. Lee T, Shi D, (2021) A comparison of full information maximum likelihood and multiple imputation in structural equation modeling with missing data. *Psychol Methods*
34. He H, Tang W, Wang W, Crits-Christoph P, (2014) Structural zeroes and zero-inflated models. *Shanghai Arch Psychiatry* 26: 236-242
35. Helen Brown RP (2013) *Applied Mixed Models in Medicine*, 2nd Edition. John Wiley & Sons, Hoboken, NJ
36. Stelfox HT, Soo A, Niven DJ, Fiest KM, Wunsch H, Rowan KM, Bagshaw SM, (2018) Assessment of the Safety of Discharging Select Patients Directly Home From the Intensive Care Unit: A Multicenter Population-Based Cohort Study. *JAMA Intern Med* 178: 1390-1399
37. Westphal GA, Moerschberger MS, Vollmann DD, Inácio AC, Machado MC, Sperotto G, Cavalcanti AB, Koenig Á, (2018) Effect of a 24-h extended visiting policy on delirium in critically ill patients. *Intensive Care Med* 44: 968-970
38. Eghbali-Babadi M, Shokrollahi N, Mehrabi T, (2017) Effect of Family-Patient Communication on the Incidence of Delirium in Hospitalized Patients in Cardiovascular Surgery ICU. *Iran J Nurs Midwifery Res* 22: 327-331
39. Rosa RG, Tonietto TF, da Silva DB, Gutierrez FA, Ascoli AM, Madeira LC, Rutzen W, Falavigna M, Robinson CC, Salluh JI, Cavalcanti AB, Azevedo LC, Cremonese RV, Haack TR, Eugênio CS, Dornelles A, Bessel M, Teles JMM, Skrobik Y, Teixeira C, (2017) Effectiveness and Safety of an Extended ICU Visitation Model for Delirium Prevention: A Before and After Study. *Crit Care Med* 45: 1660-1667

40. Nassar Junior AP, Besen B, Robinson CC, Falavigna M, Teixeira C, Rosa RG, (2018) Flexible Versus Restrictive Visiting Policies in ICUs: A Systematic Review and Meta-Analysis. *Crit Care Med* 46: 1175-1180
41. Rosa RG, Falavigna M, Robinson CC, da Silva DB, Kochhann R, de Moura RM, Santos MMS, Sganzerla D, Giordani NE, Eugênio C, Ribeiro T, Cavalcanti AB, Bozza F, Azevedo LCP, Machado FR, Salluh JIF, Pellegrini JAS, Moraes RB, Hocheegger T, Amaral A, Teles JMM, da Luz LG, Barbosa MG, Birriel DC, Ferraz IL, Nobre V, Valentim HM, Corrêa ECL, Duarte PAD, Tregnago R, Barilli SLS, Brandão N, Giannini A, Teixeira C, (2018) Study protocol to assess the effectiveness and safety of a flexible family visitation model for delirium prevention in adult intensive care units: a cluster-randomised, crossover trial (The ICU Visits Study). *BMJ Open* 8: e021193
42. Cho SH, (2003) Using multilevel analysis in patient and organizational outcomes research. *Nurs Res* 52: 61-65
43. Bombard Y, Baker GR, Orlando E, Fancott C, Bhatia P, Casalino S, Onate K, Denis J-L, Pomey M-P, (2018) Engaging patients to improve quality of care: a systematic review. *Implementation Science* 13: 98
44. Mena JH, Sanchez AI, Rubiano AM, Peitzman AB, Sperry JL, Gutierrez MI, Puyana JC, (2011) Effect of the modified Glasgow Coma Scale score criteria for mild traumatic brain injury on mortality prediction: comparing classic and modified Glasgow Coma Scale score model scores of 13. *J Trauma* 71: 1185-1192; discussion 1193

45. Fiest KM, Krewulak KD, Ely EW, Davidson JE, Ismail Z, Sept BG, Stelfox HT, (2020) Partnering With Family Members to Detect Delirium in Critically Ill Patients*. Critical Care Medicine 48

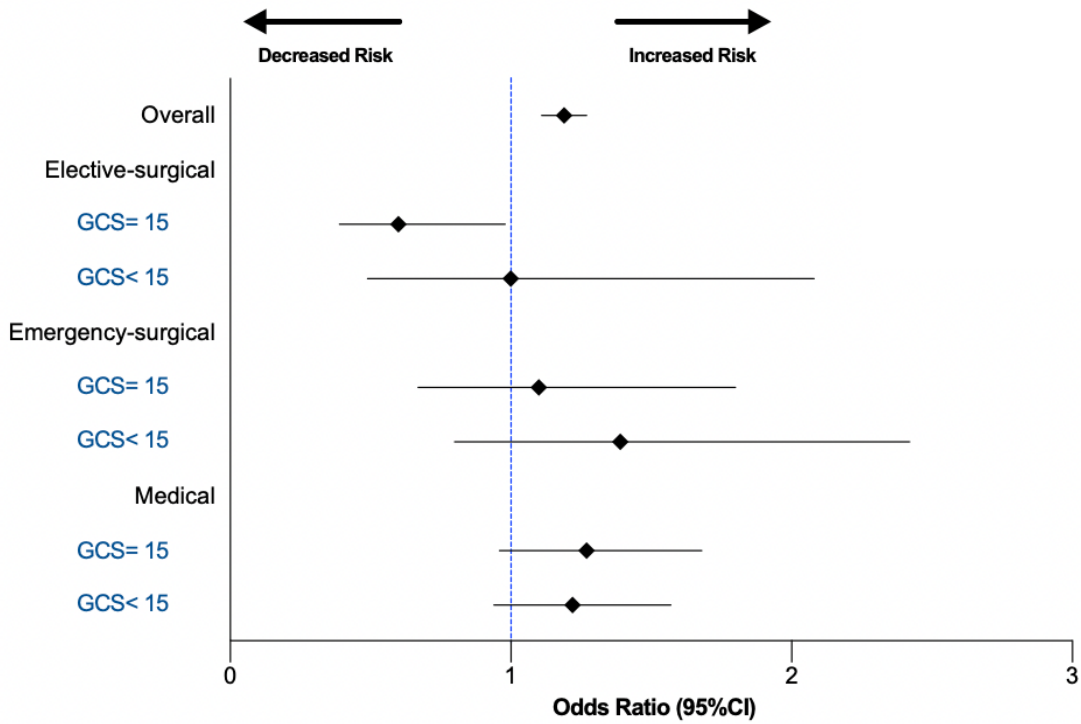
2.8 Figures

Figure 1. Participant Flow Chart



Abbreviations: DAD, Discharge Abstract Database; ICDSC, Intensive Care Delirium Checklist; ICU, Intensive Care Unit

Figure 2. Forest plot of odds ratio of delirium associated with in-person family presence compared to no family presence or phone call in the intensive care unit



Abbreviations: GCS, Glasgow Coma Scale; CI, Confidence Intervals

2.9 Tables

Table 1. Demographic and clinical characteristics of the study population (primary outcome)

Characteristics	Total (n=25,537)	Family presence		
		Physical presence ¹ (n= 23,121)	Family call only ² (n= 591)	No visit ³ (n= 1,825)
Age, yr, median (IQR)	59 (46-70)	59 (46-70)	59 (49-68)	58 (47-67)
≥65 years, n (%)	9,580 (37.5)	8,789 (38.0)	201 (34.0)	590 (32.3)
Sex, female, n (%)	10,847 (42.5)	9,980 (43.2)	202 (34.2)	665 (36.4)
Patient admitting type, n (%) ^a				
Elective-surgical	2,018 (8.1)	1,597 (7.0)	65 (11.4)	356 (21.5)
Emergency-surgical	4,285 (17.2)	3,904 (17.2)	107 (18.7)	274 (16.5)
Medical	18,600 (74.7)	17,171 (75.7)	400 (69.9)	1,029 (62.0)
Comorbidities, n (%)				
Diabetes	5,194 (20.3)	4,725 (20.4)	126 (21.3)	343 (18.8)
Cirrhosis	1,427 (5.6)	1,328 (5.7)	42 (7.1)	57 (3.1)
Heart failure	1,456 (5.7)	1,347 (5.8)	40 (6.8)	69 (3.8)
Hepatic failure	796 (3.1)	754 (3.3)	14 (2.4)	28 (1.5)
Metastatic cancer	889 (3.5)	799 (3.5)	23 (3.9)	67 (3.7)
Immune suppression	2,044 (8.0)	1,889 (8.2)	45 (7.7)	110 (6.0)
Respiratory insufficiency	3,082 (12.1)	2,844 (12.3)	78 (13.2)	160 (8.8)
Acute Physiology and Chronic Health Disease Classification System II ⁴				
Score, median (IQR)	19 (14-25)	19 (14-25)	17 (12-22)	14 (10-19)
Score, by quartile, n (%)				
Quartile 1 (<14)	6,330 (24.8)	5,292 (22.9)	181 (30.6)	857 (47.0)
Quartile 2 (≤19 & ≥14)	7,150 (28.0)	6,409 (27.7)	199 (33.7)	541 (29.6)
Quartile 3 (<25 & >19)	5,376 (21.1)	5,012 (21.7)	111 (18.8)	253 (13.9)
Quartile 4 (≥25)	6,682 (26.2)	6,408 (27.7)	100 (17.0)	174 (9.5)
Charlson Comorbidity Index, median (IQR) ⁴	1 (0-3)	1 (0-2)	1 (0-2)	0 (0-2)
Sequential Organ Failure Assessment, median (IQR) ⁴	6 (4-9)	6 (4-9)	5 (3-8)	4 (2-6)
Glasgow Coma Scale, median (IQR) ⁴	14 (10-15)	14 (10-15)	15 (13-15)	15 (14-15)
Score, by severity, n(%)				
Glasgow Coma Scale 15	10,239 (40.1)	8,955 (38.7)	292 (49.4)	992 (54.4)
Glasgow Coma Scale <15	15,298 (60.0)	14,166 (61.3)	299 (50.6)	833 (45.6)
Frailty Score, median (IQR) ^{4,b}	3 (2-5)	3 (2-5)	3 (2-4)	4 (2-4)
ICU interventions, n (%) ⁵				
Dialysis	642 (2.5)	575 (2.5)	17 (2.9)	50 (2.7)
Vasoactive medication	11,504 (47.4)	10,929 (47.3)	205 (34.7)	369 (20.2)
Invasive mechanical ventilation	16,398 (64.2)	15,440 (6.8)	305 (51.6)	653 (35.8)
Non-invasive ventilation	3,624 (14.2)	3,415 (14.8)	72 (12.2)	136 (7.5)
Continuous renal replacement therapy	1,506 (5.9)	1,485 (6.4)	3 (0.5)	18 (1.0)
Hospital length of stay, days, median (IQR)	12 (6-26)	13 (6-27)	10 (5-20.5)	9 (4-17)
ICU length of stay, median (IQR) days	4.2 (2.3-8.0)	4.5 (2.6-8.6)	2.7 (1.9-4.1)	2.1 (1.6-3.4)
Score, by quartile, n (%)				
Quartile 1 (<2.4)	6,501 (25.5)	5,221 (22.6)	254 (43.0)	1,026 (56.2)
Quartile 2 (≤4.2 & ≥2.4)	6,426 (25.2)	5,734 (24.8)	195 (33.0)	497 (27.2)
Quartile 3 (<8.1 & >4.2)	6,320 (24.8)	5,999 (26.0)	113 (19.1)	208 (11.4)
Quartile 4 (≥8.1)	6,290 (24.6)	6,167 (26.7)	29 (4.9)	94 (5.2)
Patient mortality, n (%)				
Died in ICU	2,107 (8.3)	2,076 (9.0)	11 (1.9)	20 (1.1)

Died in hospital	3,579 (14.0)	3,479 (15.1)	32 (5.4)	68 (3.7)
Hospital characteristics				
Teaching hospital, n (%)	19,936 (78.1)	18,167 (78.6)	465 (78.7)	1,304 (71.5)
Number of hospital beds, median (IQR)	695 (367-890)	695 (365-890)	695 (367-890)	695 (288-695)
Number of ICU beds, median (IQR)	18 (10-28)	18 (10-28)	25 (10-28)	14 (10-28)
Hospital type, n (%)				
Community	8,395 (35.0)	7,841 (35.9)	153 (26.5)	401 (25.6)
Regional	3,421 (14.3)	2,894 (13.3)	96 (16.6)	431 (27.5)
Tertiary	12,167 (50.7)	11,103 (50.8)	329 (56.9)	735 (46.9)

¹Family physical presence as defined by physical presence at any time during ICU stay

²Family call only as defined by telephone communication, without physical presence

³No visit means that the patient did not receive any in-person family ICU presence or phone call

⁴Score reported from assessment during admission to the ICU

⁵At any point during ICU admission

^a634 missing admission type

^b23,502 missing frailty score

Abbreviations: ICU, Intensive Care Unit; IQR, Interquartile Range

Table 2. Intensive Care Delirium Screening Checklist and Richmond Agitation Sedation Scale upon ICU admission

Characteristics	Total (n=25,537)	Family presence		
		Physical presence ¹ (n= 23,121)	Family phone call only ² (n= 591)	No visit ³ (n= 1,825)
Delirium Prevalence ⁴	56.9% (95%CI: 56.3-57.4)			
Intensive Care Delirium Screening Checklist ⁵				
Score, median (IQR)	4 (2-6)	4 (2-6)	3 (1-6)	1 (2-4)
Score, by severity, n (%)				
Scores of 0	1,144 (4.5)	901 (3.9)	35 (5.9)	208 (11.4)
Scores of 1-3	10,109 (39.6)	8,772 (37.9)	294 (50.0)	1,043 (57.2)
Scores of 4-5	5,184 (20.3)	4,830 (20.9)	106 (17.9)	248 (13.6)
Scores of 6-8	9,100 (35.6)	8,618 (37.3)	156 (26.4)	326 (17.9)
Richmond Agitation Sedation Scale, n (%)				
Agitated (scores of +1 to +4)	3,374 (13.2)	3,141 (13.6)	71 (12.0)	162 (8.9)
Alert and calm (score of 0)	11,966 (46.9)	10,506 (45.4)	299 (50.6)	1,161 (63.6)
Sedated (scores of -1 to -4)	9,484 (37.1)	8,786 (38.0)	209 (35.4)	489 (26.8)
Comatose (scores of -5)	713 (2.8)	688 (3.0)	12 (2.0)	13 (0.7)

¹Family physical presence as defined by physical presence at any time during ICU stay

²Family call only as defined by telephone, without physical presence

³No visit means that the patient did not receive any in-person family ICU presence or phone call

⁴Maximum score reported from assessment during admission to the ICU

^aTwo missing RASS score

Abbreviations: ICU, Intensive Care Unit; IQR, Interquartile Range

Table 3 Incident delirium and family presence in the intensive care unit

Family presence	Crude Odds Ratio (95% CI) (n=25,537)	Adjusted Odds Ratios* (95% CI) (n=25,537)	Adjusted Odds Ratios** (95% CI)					
			Elective-surgical Admission (n=2,018)		Emergency-surgical Admission (n=4,285)		Medical admission (n= 18,600)	
			GCS 15	GCS < 15	GCS 15	GCS < 15	GCS 15	GCS < 15
Physical presence ¹ (n=23,121)	4.20 (3.63-4.78) <i>p</i> <0.001	1.19 (1.11-1.27) <i>p</i> =0.02	0.60 (0.39-0.97) <i>p</i> =0.02	1.00 (0.49-2.08) <i>p</i> =0.88	1.10 (0.67-1.80) <i>p</i> =0.13	1.39 (0.80-2.42) <i>p</i> =0.78	1.27 (0.96-1.68) <i>p</i> =0.77	1.22 (0.94-1.57) <i>p</i> =0.13
Family call only ² (n=591)	2.00 (1.58-2.52) <i>p</i> <0.001	1.14 (0.87-1.48) <i>p</i> =0.34	0.84 (0.35-1.79) <i>p</i> =0.61	0.75 (0.03-1.88) <i>p</i> =0.90	1.28 (0.52-2.69) <i>p</i> =0.59	0.92 (0.30-2.84) <i>p</i> =0.89	1.28 (0.52-1.40) <i>p</i> =0.59	1.31 (0.81-1.88) <i>p</i> =0.32
No visit ³ (n=1,825)	--	--	--	--	--	--	--	--

¹Family physical presence as defined by physical presence at any time during ICU stay

²Family call only as defined by telephone, without physical presence

³No visit means that the patient did not receive any in-person family ICU presence or phone call

*Adjusted for age, sex, hospital type, admission type, Acute Physiology and Chronic Health Disease Classification System II score at ICU admission, Richmond Agitation Sedation Scale score at ICU admission, hospital length of stay, ICU length of stay, number of ICU beds, any receipt of invasive mechanical ventilation, Charlson Comorbidity Index score at ICU admission, Sequential Organ Failure Assessment score at admission, and Glasgow Coma Scale score at admission

**Adjusted for age, sex, hospital type, Acute Physiology and Chronic Health Disease Classification System II score at ICU admission, Richmond Agitation Sedation Scale score at ICU admission, hospital length of stay, ICU length of stay, number of ICU beds, any receipt of invasive mechanical ventilation, Charlson Comorbidity Index score at ICU admission, Sequential Organ Failure Assessment score at admission

Dashes indicate reference group for multivariable logistic regression analyses

Multilevel mixed effect model accounts for patient repeated ICU admission

Abbreviations: ICU, Intensive Care Unit; IQR, Interquartile Range; GCS, Glasgow Coma Scale

Table 4 Association between delirium duration and family presence in the intensive care unit

Family presence	Adjusted Model* (95% CI)	
	Crude Model (95% CI) (n=14,847)	All patient admissions* (n=14,847)
Physical presence ¹ (n=13,984)	1.33 (1.26-1.41) <i>p</i> <0.001	-1.87 (-2.01 to -1.81) <i>p</i> <0.001
Family call only ² (n=289)	-0.74 (-0.86 to -0.63) <i>p</i> <0.001	-1.41 (-1.52 to -1.31) <i>p</i> <0.001
No visit ³ (n=574)	--	--

¹Family physical presence as defined by physical presence at any time during ICU stay

²Family call only as defined by telephone, without physical presence

³No visit means that the patient did not receive any in-person family ICU presence or phone call

*Adjusted for age, sex, hospital type, Acute Physiology and Chronic Health Disease Classification System II score at ICU admission, Richmond Agitation Sedation Scale score at ICU admission, hospital length of stay, ICU length of stay, number of ICU beds, any receipt of invasive mechanical ventilation, Charlson Comorbidity Index score at ICU admission, Sequential Organ Failure Assessment score at admission, and Glasgow Comma Scale score at admission

Dashes indicate reference group for multilevel mixed-effects linear regression analyses

Abbreviations: ICU, Intensive Care Unit; CI, Confidence Intervals

2.10 Appendices

Appendix 1. STROBE and RECORD items checklist

	Item No.	STROBE items	RECORD items	Paper
Title and abstract				
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	<p>RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included.</p> <p>RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract.</p> <p>RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.</p>	Abstract
Introduction				
Background rationale	2	Explain the scientific background and rationale for the investigation being reported		
Objectives	3	State specific objectives, including any prespecified hypotheses		
Methods				
Study Design	4	Present key elements of study design early in the paper		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		
Participants	6	(a) <i>Cohort study</i> - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided.	Methods and Appendix 4

		<p><i>Case-control study</i> - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls</p> <p><i>Cross-sectional study</i> - Give the eligibility criteria, and the sources and methods of selection of participants</p> <p>(b) <i>Cohort study</i> - For matched studies, give matching criteria and number of exposed and unexposed</p> <p><i>Case-control study</i> - For matched studies, give matching criteria and the number of controls per case</p>	<p>RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided.</p>	Methods and Appendix 2-4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	Figure 1
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group		
Bias	9	Describe any efforts to address potential sources of bias		
Study size	10	Explain how the study size was arrived at		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Appendix 2-4

		<p>(b) Describe any methods used to examine subgroups and interactions</p> <p>(c) Explain how missing data were addressed</p> <p>(d) <i>Cohort study</i> - If applicable, explain how loss to follow-up was addressed</p> <p><i>Case-control study</i> - If applicable, explain how matching of cases and controls was addressed</p> <p><i>Cross-sectional study</i> - If applicable, describe analytical methods taking account of sampling strategy</p> <p>(e) Describe any sensitivity analyses</p>		
Data access and cleaning methods		..	<p>RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.</p>	Appendix 5
			<p>RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.</p>	Appendix 4 & 5
Linkage		..	<p>RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.</p>	Methods & Appendix 5
Results				
Participants	13	<p>(a) Report the numbers of individuals at each stage of the study (e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed)</p>	<p>RECORD 13.1: Describe in detail the selection of the persons included in the study (<i>i.e.</i>, study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.</p>	Figure 1

Descriptive data	14	<p>(b) Give reasons for non-participation at each stage.</p> <p>(c) Consider use of a flow diagram</p> <p>(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders</p> <p>(b) Indicate the number of participants with missing data for each variable of interest</p> <p>(c) <i>Cohort study</i> - summarise follow-up time (e.g., average and total amount)</p>
Outcome data	15	<p><i>Cohort study</i> - Report numbers of outcome events or summary measures over time</p> <p><i>Case-control study</i> - Report numbers in each exposure category, or summary measures of exposure</p> <p><i>Cross-sectional study</i> - Report numbers of outcome events or summary measures</p>
Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included</p> <p>(b) Report category boundaries when continuous variables were categorized</p> <p>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</p>
Other analyses	17	<p>Report other analyses done—e.g., analyses of subgroups and</p>

		interactions, and sensitivity analyses		
Discussion				
Key results	18	Summarize key results with reference to study objectives		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Discussion
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		
Generalisability	21	Discuss the generalisability (external validity) of the study results		
Other Information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based		
Accessibility of protocol, raw data, and programming code		..	RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	Appendix 2-5

*Reference: Benchimol EI, Smeeth L, Guttman A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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Appendix 2. Sub-Category and category of algorithm code

Dataset	Category	Sub-Category	Granularity	Occurrences Class "False"	Occurrences Class "True"	Dataset Status
1	Documented family or friends	Any family documented?	macro	129	151	Included
2	Documented family or friends	Significant other	macro	206	74	Included
3	Documented family or friends	Significant other – man	macro	252	28	Included
4	Documented family or friends	Significant other – woman	macro	235	45	Included
5	Documented family or friends	Significant other – unknown	macro	279	1	Excluded
6	Documented family or friends	Child	macro	203	77	Included
7	Documented family or friends	Child – boy/man	macro	241	39	Included
8	Documented family or friends	Child – girl/woman	macro	235	45	Included
9	Documented family or friends	Child – unknown	macro	277	3	Excluded
10	Documented family or friends	Parent	macro	258	22	Included
11	Documented family or friends	Parent – man	macro	271	9	Excluded
12	Documented family or friends	Parent – woman	macro	263	17	Included
13	Documented family or friends	Parent – unknown	macro	279	1	Excluded
14	Documented family or friends	Siblings	macro	250	30	Included
15	Documented family or friends	Siblings – boy/man	macro	267	13	Included
16	Documented family or friends	Siblings – girl/woman	macro	259	21	Included

17	Documented family or friends	Siblings – unknown	macro	280	0	Excluded
18	Documented family or friends	Other	macro	244	36	Included
19	Documented family or friends	Other – boy/man	macro	274	6	Excluded
20	Documented family or friends	Other – girl/woman	macro	255	25	Included
21	Documented family or friends	Other – unknown	macro	269	11	Included
22	Documented family or friends	Not specified	macro	276	4	Excluded
23	Visits	Any documented visit?	macro	50	230	Included
24	Visits	Any documented visit?	micro	52	1621	Included
25	Visits	Significant other	macro	149	131	Included
26	Visits	Significant other	micro	1180	493	Included
27	Visits	Significant other – man	macro	234	46	Included
28	Visits	Significant other – man	micro	1515	158	Included
29	Visits	Significant other – woman	macro	195	85	Included
30	Visits	Significant other – woman	micro	1341	332	Included
31	Visits	Significant other – unknown	macro	277	3	Excluded
32	Visits	Significant other – unknown	micro	1670	3	Excluded
33	Visits	Child	macro	149	131	Included
34	Visits	Child	micro	1140	533	Included
35	Visits	Child – boy/man	macro	201	79	Included
36	Visits	Child – boy/man	micro	1423	250	Included
37	Visits	Child – girl/woman	macro	185	95	Included
38	Visits	Child – girl/woman	micro	1346	327	Included
39	Visits	Child – unknown	macro	266	14	Included
40	Visits	Child – unknown	micro	1653	20	Included
41	Visits	Parent	macro	242	38	Included
42	Visits	Parent	micro	1532	141	Included
43	Visits	Parent – man	macro	260	20	Included
44	Visits	Parent – man	micro	1613	60	Included
45	Visits	Parent – woman	macro	247	33	Included
46	Visits	Parent – woman	micro	1562	111	Included
47	Visits	Parent – unknown	macro	280	0	Excluded
48	Visits	Parent – unknown	micro	1673	0	Excluded

49	Visits	Siblings	macro	205	75	Included
50	Visits	Siblings	micro	1427	246	Included
51	Visits	Siblings – boy/man	macro	243	37	Included
52	Visits	Siblings – boy/man	micro	1534	139	Included
53	Visits	Siblings – girl/woman	macro	228	52	Included
54	Visits	Siblings – girl/woman	micro	1550	123	Included
55	Visits	Siblings – unknown	macro	276	4	Excluded
56	Visits	Siblings – unknown	micro	1669	4	Excluded
57	Visits	Other	macro	158	122	Included
58	Visits	Other	micro	1289	384	Included
59	Visits	Other – boy/man	macro	225	55	Included
60	Visits	Other – boy/man	micro	1566	107	Included
61	Visits	Other – girl/woman	macro	209	71	Included
62	Visits	Other – girl/woman	micro	1458	215	Included
63	Visits	Other – unknown	macro	222	58	Included
64	Visits	Other – unknown	micro	1566	107	Included
65	Visits	Pet	macro	278	2	Excluded
66	Visits	Pet	micro	1670	3	Excluded
67	Visits	Not specified	macro	163	117	Included
68	Visits	Not specified	micro	1299	374	Included
69	Visits	Not specified – boy/man	macro	276	4	Excluded
70	Visits	Not specified – boy/man	micro	1668	5	Excluded
71	Visits	Not specified – unknown	macro	163	117	Included
72	Visits	Not specified – unknown	micro	1317	356	Included
73	Visits	Not specified – girl/woman	macro	277	3	Excluded
74	Visits	Not specified – girl/woman	micro	1659	14	Excluded
75	Visits	Did social work speak with family?	macro	235	45	Included
76	Visits	Did social work speak with family?	micro	1595	78	Included
77	Visits	Is this a family meeting / conference?	macro	241	39	Included
78	Visits	Is this a family meeting / conference?	micro	1608	65	Included
79	Visits	Does this discuss goals of care?	macro	249	31	Included
80	Visits	Does this discuss goals of care?	micro	1631	42	Included

81	Visits	Did a doctor speak with the family?	macro	188	92	Included
82	Visits	Did a doctor speak with the family?	micro	1503	170	Included
83	Visits	Did allied health speak with the family?	macro	275	5	Excluded
84	Visits	Did allied health speak with the family?	micro	1668	5	Excluded
85	Visits	Did bedside nurse speak with the family?	macro	229	51	Included
86	Visits	Did bedside nurse speak with the family?	micro	1595	78	Included
87	Visits	Is family meeting at beside?	macro	270	10	Excluded
88	Visits	Is family meeting at beside?	micro	1661	12	Excluded
89	Visits	Is family meeting at the conference room?	macro	278	2	Excluded
90	Visits	Is family meeting at the conference room?	micro	1669	4	Excluded
91	Visits	Is family meeting unspecified?	macro	265	15	Included
92	Visits	Is family meeting unspecified?	micro	1657	16	Included
93	Visits	Did the meeting discuss organ donation?	macro	278	2	Excluded
94	Visits	Did the meeting discuss organ donation?	micro	1670	3	Excluded
95	Visits	Did family attend rounds?	macro	260	20	Included
96	Visits	Did family attend rounds?	micro	1648	25	Included
97	Phone calls	Any documented phone calls?	macro	128	152	Included
98	Phone calls	Any documented phone calls?	micro	129	437	Included
99	Phone calls	Significant other	macro	233	47	Included
100	Phone calls	Significant other	micro	447	119	Included
101	Phone calls	Significant other – man	macro	268	12	Included
102	Phone calls	Significant other – man	micro	539	27	Included
103	Phone calls	Significant other – woman	macro	245	35	Included

104	Phone calls	Significant other – woman	micro	474	92	Included
105	Phone calls	Significant other – unknown	macro	280	0	Excluded
106	Phone calls	Significant other – unknown	micro	566	0	Excluded
107	Phone calls	Child	macro	220	60	Included
108	Phone calls	Child	micro	439	127	Included
109	Phone calls	Child – boy/man	macro	258	22	Included
110	Phone calls	Child – boy/man	micro	528	38	Included
111	Phone calls	Child – girl/woman	macro	241	39	Included
112	Phone calls	Child – girl/woman	micro	479	87	Included
113	Phone calls	Child – unknown	macro	279	1	Excluded
114	Phone calls	Child – unknown	micro	564	2	Excluded
115	Phone calls	Parent	macro	263	17	Included
116	Phone calls	Parent	micro	542	24	Included
117	Phone calls	Parent – man	macro	275	5	Excluded
118	Phone calls	Parent – man	micro	561	5	Excluded
119	Phone calls	Parent – woman	macro	266	14	Included
120	Phone calls	Parent – woman	micro	546	20	Included
121	Phone calls	Parent – unknown	macro	280	0	Excluded
122	Phone calls	Parent – unknown	micro	566	0	Excluded
123	Phone calls	Siblings	macro	244	36	Included
124	Phone calls	Siblings	micro	490	76	Included
125	Phone calls	Siblings – boy/man	macro	264	16	Included
126	Phone calls	Siblings – boy/man	micro	543	23	Included
127	Phone calls	Siblings – girl/woman	macro	255	25	Included
128	Phone calls	Siblings – girl/woman	micro	513	53	Included
129	Phone calls	Siblings – unknown	macro	280	0	Excluded
130	Phone calls	Siblings – unknown	micro	566	0	Excluded
131	Phone calls	Other	macro	245	35	Included
132	Phone calls	Other	micro	509	57	Included
133	Phone calls	Other – boy/man	macro	275	5	Excluded
134	Phone calls	Other – boy/man	micro	559	7	Excluded
135	Phone calls	Other – girl/woman	macro	255	25	Included
136	Phone calls	Other – girl/woman	micro	526	40	Included
137	Phone calls	Other – unknown	macro	271	9	Excluded
138	Phone calls	Other – unknown	micro	555	11	Excluded
139	Phone calls	Not specified	macro	253	27	Included
140	Phone calls	Not specified	micro	524	42	Included
141	Phone calls	Not specified – boy/man	macro	279	1	Excluded
142	Phone calls	Not specified – boy/man	micro	565	1	Excluded

143	Phone calls	Not specified – girl/woman	macro	278	2	Excluded
144	Phone calls	Not specified – girl/woman	micro	564	2	Excluded
145	Phone calls	Not specified – unknown	macro	255	25	Included
146	Phone calls	Not specified – unknown	micro	527	39	Included
147	Phone calls	Did social work speak with the family?	macro	276	4	Excluded
148	Phone calls	Did social work speak with the family?	micro	562	4	Excluded
149	Phone calls	Did a doctor speak with the family?	macro	276	4	Excluded
150	Phone calls	Did a doctor speak with the family?	micro	561	5	Excluded
151	Phone calls	Did bedside nurse speak with the family?	macro	273	7	Excluded
152	Phone calls	Did bedside nurse speak with the family?	micro	558	8	Excluded
153	Phone calls	Did allied health speak with the family?	macro	280	0	Excluded
154	Phone calls	Did allied health speak with the family?	micro	566	0	Excluded
155	Phone calls	Was a message left for the family?	macro	267	13	Included
156	Phone calls	Was a message left for the family?	micro	551	15	Included

Appendix 3. Summary of inclusion and exclusion criteria for the rule-based classifier

Category / Sub-Category	Inclusion Criteria	Exclusion Criteria
Documented family or friends	[note parameter = Family Quick View Summary OR note parameter = Contact Information Family]	Not applicable
Visits	[note parameter = OLD_Family Visit Comment OR note parameter = Comment Family In OR note parameter = Comment Family Conference OR note parameter = MD Comment Family Conference OR note parameter = OLD_MD Present During Family Conference OR note parameter = Comment Family Out] OR [token = accompanied OR token = accompanying OR token = appear OR token = appeared OR token = appears OR token = arrive OR token = arrived OR token = arrives OR token = assisted to chair OR token = at bedside OR token = at the bedside OR token = attain OR token = attained OR token = attains OR token = aware of transfer OR token = bringing OR token = brought in OR token = came by OR token = check in OR token = checked in OR token = come by OR token = conference room OR token = discharged OR token = discussion with family OR token = drop by OR token = drop in OR token = drop over OR token = dropped by OR token = dropped in OR token = dropped over OR token = enter	[note parameter = Comment Family Phone Call]

	OR token = entered OR token = enters OR token = explained to pt family OR token = explained to the family OR token = family appreciative OR token = family aware OR token = family conference OR token = family is in OR token = family is requesting OR token = family meeting OR token = family room OR token = family wanting OR token = for pt OR token = found cry outside OR token = given to #any known relation# OR token = given to pt s OR token = giving encouragement to pt OR token = goal of care OR token = gold bracelet taken OR token = hearing aid OR token = in the room OR token = in to OR token = in waiting room OR token = introduced OR token = left OR token = look around OR token = look in on OR token = look up OR token = looked around OR token = looked in on OR token = looked up OR token = met with OR token = out to OR token = packed all valuable in room OR token = parking pas OR token = patient and #any known relation# OR token = patient s #any known relation# OR token = patient sent home via wheelchair with OR token = plan of care OR token = pop in OR token = pop up OR token = popped in OR token = popped up OR token = present OR token = presently in OR token = provided the patient s	
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	OR token = pt s #any known relation# OR token = pt #any known relation# OR token = reviewed with both pt and his OR token = show up OR token = showed up OR token = spoke to family OR token = stay with OR token = stayed with OR token = step in OR token = stepped in OR token = stop by OR token = stop off OR token = stopped by OR token = stopped off OR token = swing by OR token = swung by OR token = take in OR token = to discus OR token = to speak with OR token = took belonging OR token = took in OR token = updated OR token = visit OR token = visited OR token = wa here OR token = were here OR token = will return OR token = with #any known relation# OR token = writer discussed OR token = writer explained OR token = writer provided OR token = writer supporting family]	
Phone calls	[note parameter = Comment Family Phone Call] OR [token = called OR token = calling OR token = telephoned]	[note parameter = OLD_Family Visit Comment OR note parameter = Comment Family In OR note parameter = Comment Family Conference OR note parameter = MD Comment Family Conference OR note parameter = OLD_MD Present During Family Conference OR note parameter = Comment Family Out] OR [token = blue called OR token = called ems

		OR token = code called OR token = ems called OR token = met call OR token = met called OR token = research coordinator called OR token = writer called]
Significant other	Any occurrence of significant other – male, significant other – female or significant other - unknown	Not applicable
Significant other – male	[token = boyfriend OR token = ex_boyfriend OR token = ex_husband OR token = fiance OR token = husband]	Not applicable
Significant other – female	[token = ex_girlfriend OR token = ex_wife OR token = fiancée OR token = girlfriend OR token = wife]	Not applicable
Significant other – unknown	[token = common_law OR token = partner OR token = significant_other OR token = spouse]	Not applicable
Child	Any occurrence of child – male, child – female or child – unknown	Not applicable
Child – male	[token = son]	Not applicable
Child – female	[token = daughter]	Not applicable
Child – unknown	[token = child]	Not applicable
Parent	Any occurrence of parent – male, parent – female or parent - unknown	Not applicable
Parent – male	[token = father]	Not applicable
Parent – female	[token = mother]	Not applicable
Parent – unknown	[token = parent]	Not applicable
Siblings	Any occurrence of siblings – male, siblings – female or siblings - unknown	Not applicable
Siblings – male	[token = brother]	Not applicable
Siblings – female	[token = sister]	Not applicable
Siblings – unknown	[token = sibling]	Not applicable
Other	Any occurrence of other – male, other – female or other – unknown	Not applicable
Other – male	[token = brother_in_law OR token = father_in_law OR token = grandfather OR token = grandson OR token = great_grandfather OR token = great_grandson OR token = great_grandfather	Not applicable

	OR token = great_great_grandson OR token = half_brother OR token = nephew OR token = son_in_law OR token = stepbrother OR token = stepfather OR token = stepson OR token = uncle]	
Other – female	[token = aunt OR token = daughter_in_law OR token = granddaughter OR token = grandmother OR token = great_granddaughter OR token = great_grandmother OR token = great_great_granddaughter OR token = great_great_grandmother OR token = half_sister OR token = mother_in_law OR token = niece OR token = sister_in_law OR token = stepdaughter OR token = stepmother OR token = stepsister]	Not applicable
Other – unknown	[token = cousin OR token = friend OR token = godparent OR token = grandchild OR token = grandparent OR token = guardian OR token = other OR token = roommate OR token = visitors]	Not applicable
Not specified	Any occurrence of not specified – male, not specified – female or not specified – unknown	Not applicable
Not specified – male	[Documented family or friends = True OR Visits = True OR Phone Calls = True] AND [Unknown male name = True]	[Any other relation = True]
Not specified – female	[Documented family or friends = True OR Visits = True OR Phone Calls = True] AND [Unknown female name = True]	[Any other relation = True]
Not specified – unknown	[Documented family or friends = True]	[Any other relation = True OR Not specified – male = True]

	OR Visits = True OR Phone Calls = True]	OR Not specified – female = True]
Pet	[token = cat OR token = dog OR token = pet]	Not applicable
Did a doctor speak with the family?	[token = doctor OR token = dr OR token = md OR token = physician]	Not applicable
Did allied health speak with the family?	[token = ot OR token = physio OR token = rt]	Not applicable
Did bedside nurse speak with the family?	[token = bedside nurse OR token = nurse OR token = rn]	Not applicable
Did family attend rounds?	[token = round]	Not applicable
Did social work speak with family?	[token = social work OR token = sw]	Not applicable
Did the meeting discuss organ donation?	[token = donation OR token = organ OR token = organ donation]	Not applicable
Does this discuss goals of care?	[token = C1 OR token = C2 OR token = comfort care OR token = end of life OR token = end of life care OR token = goal of care OR token = GOC OR token = M1 OR token = M2 OR token = palliative OR token = R1 OR token = R2 OR token = R3]	Not applicable
Is family meeting at bedside?	Is this a family meeting / conference? = True AND [token = at bedside OR token = at the bedside]	Not applicable
Is family meeting at the conference room?	Is this a family meeting / conference? = True AND [token = conference room OR token = family room]	Not applicable
Is family meeting unspecified?	Is this a family meeting / conference? = True	[token = at bedside OR token = at the bedside OR token = conference room OR token = family room]
Is this a family meeting / conference?	[note parameter = MD Comment Family Conference	Not applicable

	OR note parameter = Comment Family Conference OR note parameter = OLD_MD Present During Family Conference] OR [token = explained to the family OR token = family conference OR token = family meeting OR token = in waiting room]	
Was a message left for the family?	[token = message]	Not applicable

*Reference: Lucini FR, Krewulak K, Stelfox HT. Natural language processing to evaluate documented family presence and mode of communication in Alberta ICUs. In Press.

Appendix 4. Variables and covariates included in study objectives and their coding

Variable	Description of Parameter	Coding
eCritical		
Age	Age recorded upon ICU admission Older Adults	Continuous Categorical >65=1 <65=0
Sex	Identified patient sex as female or male.	Female=1 Male=0
Admission Category	Medical, Surgical, Neuro, Trauma	Medical=0 Surgical=1 Neuro=2 Trauma=3
Admission Type	Elective post-surgery, Emergency post-surgery, and Nonsurgical	Elective post-surgery=0 Nonsurgical=1 Emergency post-surgery=2
Comorbidities	Flagged 1 for present or Null for not present upon admission: diabetes, heart failure, respiratory insufficiency, metastatic cancer immune suppression, cirrhosis, hepatic failure.	Diabetes Yes=1 No=0 Heart failure Yes=1 No=0 Respiratory insufficiency Yes=1 No=0 Metastatic cancer Yes=1 No=0 Immune suppression Yes=1 No=0 Cirrhosis Yes=1 No=0 Hepatic failure Yes=1 No=0
Acute Physiology and Chronic Health Evaluation II score (APACHE-II)	Illness severity score at ICU admission	Continuous Categorical Score, by quartile Quartile 1 <25% Quartile 2 >25% and <50% Quartile 3 >50% & <75%

		Quartile 4 >75%
Sequential Organ Failure assessment (SOFA)	Illness severity score at ICU admission	Continuous
Charlson Comorbidity Index (CCI)	score at ICU admission	Continuous
Glasgow Coma Scale (GCS)	assessment of consciousness at admission	Continuous Categorical High Glasgow Coma Scale (≥ 15) Low Glasgow Coma Scale (< 15)
ICU Interventions		
Invasive mechanical ventilation	In minutes at admission, binary variable formed	Minutes greater than 0 is coded as 1 Minutes of zero is coded as 0
Non-Invasive mechanical ventilation	In minutes at admission, binary variable formed	Minutes >0 = 1 Minutes 0 = 0
Vasoactive medication	If patient is administered any of the following drugs upon admission (dopamine, dobutamine, epinephrine, isoproterenol, milrinone, norepinephrine, phenylephrine or vasopressin) flagged for 1. Variable in minutes; therefore, cleaned to compose one binary yes/no variable that is inclusive of any of the above drugs.	Yes=1 No=0
Dialysis	Flagged 1 for present or Null for not present.	Yes=1 No=0
Continuous renal replacement therapy	In minutes at admission, binary variable formed	Minutes >0 = 1 Minutes 0 = 0
Hospital Type	A key is used to create a variable that translates ICU site to hospital type (Tertiary, Community, Regional)	Tertiary=0 Community=1 Regional=2
Hospital length of stay	Total length of stay in days in first admission	Continuous
Teaching hospital	A key is used to create a variable that translates ICU site to teaching hospital (binary)	Yes=1 No=0
Number of ICU beds	A key is used to create a variable that translates ICU site to number of ICU beds	Continuous
Number of hospital beds	A key is used to create a variable that translates ICU site to number of hospital beds	Continuous
Length of ICU stay	Total length of stay in days in first admission	Continuous Categorical Score, by quartile

		Quartile 1 <25% Quartile 2 >25% and <50% Quartile 3 >50% & <75% Quartile 4 >75%
Length of hospital stay	Total length of stay in days in first admission	Continuous
Died in ICU	Anytime during ICU stay	Yes=1 No=0
Died in hospital	Anytime during hospital stay	Yes=1 No=0
Objective outcomes and exposure		
ICDSC, Obj 1	Intensive Care Delirium Screening Checklist, delirium identified after family visit.	Score of ≥ 4 = 1 Score of < 4 = 0
ICDSC, Obj 2	Count of days during ICU admission with a delirium present (ICDSC, Obj 1). Variable created to calculate total number of delirium days during ICU stay.	Ordinal
Family presence	Algorithm code was used to explore ecritical and determine if family member was present via call, in-person, or not present.	Mutually exclusive three variable exposure. Family in-person Family phone call No family presence or call
DAD		
Patient residency	Province of patient residency	Alberta (AB)=1 Other=0

Abbreviations: DAD, Discharge Abstract Database; ICDSC, Intensive Care Delirium Checklist; ICU, Intensive Care Unit

Appendix 5. Supplement text for data handling and merging

Data was received de-identified with scrambled unique identifiers from Alberta Health Services (AHS, data custodian). Deterministic data linkage was used to link the two patient-level databases (eCritical and DAD) via a unique identifier [20], which was assigned to each patient by the custodian. Given that all administrative data were recorded for administration of health services, the study anticipated missing variables to be missing at random or due to random human error. However, if missing data exceeded 10% for covariates, listwise deletion was used when applicable [33]. Covariate cell sizes less than 5 were excluded from the analysis described below to prevent over-fitting the models [34]. All patients had complete outcome and exposure data.

Appendix 6. Demographic and clinical characteristics of the study population (secondary outcome)

Characteristics	Total (n=26,100)	Family presence		
		Physical presence ¹ (n= 23,657)	Family call only ² (n= 618)	No visit ³ (n= 1,825)
Age, yr, median (IQR)	59 (46-67)	58 (47-67)	59 (49-68)	58 (47-57)
≥65 years, n (%)	9,789 (37.5)	8,988 (38.0)	211 (34.1)	590 (32.3)
Sex, female, n (%)	11,059 (42.4)	10,181 (43.0)	213 (34.5)	665 (36.4)
Patient admitting type, n (%) ^a				
Elective-surgical	2,051 (7.9)	1,629 (7.0)	66 (11.0)	356 (21.5)
Emergency-surgical	4,374 (16.8)	3,991 (17.2)	109 (18.2)	274 (16.5)
Medical	19,032 (72.9)	17,580 (75.8)	423 (70.7)	1,029 (62.0)
Comorbidities, n (%)				
Diabetes	5,330 (20.4)	4,855 (29.5)	132 (21.4)	343 (18.8)
Cirrhosis	1,473 (5.6)	1,368 (5.8)	48 (7.8)	57 (3.1)
Heart failure	1,487 (5.7)	1,396 (5.9)	37 (6.0)	40 (2.2)
Hepatic failure	816 (3.3)	773 (3.3)	15 (2.4)	28 (1.5)
Metastatic cancer	904 (3.5)	813 (3.4)	24 (3.9)	67 (3.7)
Immune suppression	2,083 (8.0)	1,927 (8.2)	46 (7.4)	110 (6.0)
Respiratory insufficiency	3,139 (12.0)	2,889 (12.3)	80 (13.0)	160 (8.8)
Acute Physiology and Chronic Health Disease Classification System II ⁴				
Score, median (IQR)	19 (14-25)	19 (14-25)	17 (12-22)	14 (10-19)
Score, by quartile, n (%)				
Quartile 1 (<14)	6,414 (24.6)	5,373 (22.7)	184 (29.8)	857 (47.0)
Quartile 2 (≤19 & ≥14)	7,300 (28.0)	6,552 (27.7)	207 (33.5)	541 (29.6)
Quartile 3 (<25 & >19)	5,506 (21.1)	5,136 (21.7)	117 (18.9)	253 (13.9)
Quartile 4 (≥25)	6,880 (26.4)	6,596 (27.9)	110 (17.8)	174 (9.5)
Charlson Comorbidity Index, median (IQR) ⁴	1 (0-3)	1 (0-3)	1 (0-2)	0 (0-2)
Sequential Organ Failure Assessment, median (IQR) ⁴	6 (4-9)	6 (4-9)	5 (3-8)	4 (2-6)
Glasgow Coma Scale, median (IQR) ⁴	14 (10-15)	14 (10-15)	14 (12-15)	15 (14-15)
Score, by severity, n(%)				
Glasgow Coma Scale 15	10,888 (41.7)	9,430 (39.9)	312 (50.5)	992 (54.4)
Glasgow Coma Scale <15	15,213 (58.3)	14,227 (60.1)	306 (49.5)	833 (45.6)
Frailty Score, median (IQR) ^{4,b}	3 (2-5)	3 (2-5)	3 (2-4)	4 (2-4)
ICU interventions, n (%) ^{5,c}				
Dialysis	654 (2.5)	585 (2.5)	19 (3.1)	50 (2.7)
Vasoactive medication	11,224 (47.4)	10,645 (45.0)	210 (34.0)	369 (20.2)
Invasive mechanical ventilation	16,837 (64.5)	15,858 (67.0)	326 (52.8)	653 (35.8)
Non-invasive ventilation	3,714 (14.2)	3,504 (14.8)	74 (12.0)	136 (7.5)
Continuous renal replacement therapy	1,552 (6.0)	1,529 (6.5)	5 (0.8)	18 (1.0)
Hospital length of stay, days, median (IQR)	12 (6-27)	13 (6-27)	10 (5-20.5)	9 (4-17)
ICU length of stay, median (IQR) days	4.2 (2.4-8.1)	4.6 (2.6-8.6)	2.7 (1.9-4.4)	2.1 (1.6-3.4)
Score, by quartile, n (%)				
Quartile 1 (<2.4)	6,533 (25.0)	5,250 (22.2)	257 (41.6)	1,026 (56.2)
Quartile 2 (≤4.2 & ≥2.4)	6,537 (25.1)	5,838 (25.0)	202 (32.7)	497 (27.2)
Quartile 3 (<8.1 & >4.2)	6,513 (25.0)	6,179 (26.1)	126 (20.4)	208 (11.4)
Quartile 4 (≥8.1)	6,518 (25.0)	6,390 (27.0)	33 (5.3)	94 (5.2)
Patient mortality, n (%)				
Died in ICU	2,188 (8.4)	2,157 (9.1)	11 (1.8)	20 (1.1)
Died in hospital	3,701 (14.2)	3,599 (15.2)	35 (5.7)	68 (3.7)
Hospital characteristics ^d				
Teaching hospital, n (%)	20,394 (78.1)	18,603 (78.6)	487 (78.8)	1,304 (71.5)

Number of hospital beds, median (IQR)	695 (367-890)	695 (365-890)	695 (367-890)	695 (288-695)
Number of ICU beds, median (IQR)	18 (10-28)	18 (10-28)	25 (10-28)	14 (10-28)
Hospital type, n (%)				
Community	8,527 (34.8)	7,968 (35.7)	158 (26.2)	401 (25.6)
Regional	3,496 (14.3)	2,965 (13.3)	100 (16.6)	431 (27.5)
Tertiary	12,461 (50.9)	11,378 (51.0)	346 (57.3)	735 (46.9)

¹Family physical presence as defined by physical presence at any time during ICU stay

²Family call only as defined by telephone communication, without physical presence

³No visit means that the patient did not receive any in-person family ICU presence or phone call

⁴Score reported from assessment during admission to the ICU

⁵At any point during ICU admission

^a657 missing admission category

^b643 missing admission type

^c23,502 missing frailty score

^dTwo missing ICU interventions

^eTwo missing all hospital characteristics

Abbreviations: ICU, Intensive Care Unit; IQR, Interquartile Range

Appendix 7. Secondary analyses for admission diagnosis upon admission to ICU by patient admission type

Admission Diagnosis ^{1,a}	Total (n=24,736)	Patient Admission		
		Elective- surgical (n= 1,948)	Emergency- surgical (n= 4,208)	Medical admission (n= 18,575)
Cancer	1,060 (4.3)	705 (36.2)	205 (4.9)	148 (0.80)
Cardiovascular	3,189 (12.9)	274 (14.21)	420 (10.0)	2,493 (13.4)
Gastrointestinal	2,927 (11.8)	187 (9.7)	1,421 (33.8)	1,319 (7.1)
Medical other	2,259 (9.1)	270 (13.9)	613 (14.6)	1,375 (7.4)
Neurological other	1,564 (6.3)	66 (3.4)	209 (5.0)	1,289 (6.9)
Overdose, withdrawal, seizures, or metabolic coma	2,653 (10.7)	7 (0.4)	8 (0.19)	2,638 (14.2)
Pneumonia	3,530 (14.3)	11 (0.6)	22 (0.5)	3,499 (18.9)
Pregnancy or genitourinary	843 (3.4)	90 (4.6)	252 (6.0)	501 (2.7)
Respiratory other	2,947 (11.9)	127 (6.5)	243 (5.8)	2,577 (13.8)
Trauma	1,814 (7.3)	87 (4.5)	659 (15.7)	1,068 (5.8)
Orthopedic	247 (1.0)	116 (5.9)	122 (2.9)	9 (0.05)
Sepsis	1,703 (6.9)	8 (0.4)	36 (0.86)	1,659 (8.9)

¹Diagnosis upon admission to ICU

^a801 missing admission category

Abbreviations: ICU, Intensive Care Unit

Appendix 8. Sensitivity analysis of incident delirium and family presence excluding those who died in the intensive care unit

Family presence	Crude Odds Ratio (95% CI) (n=21,958)	Adjusted Odds Ratios* (95% CI) (n=21,958)	Adjusted Odds Ratios** (95% CI)					
			Elective-surgical admission (n=21,920)		Emergency-surgical admission (n=3,710)		Medical admission (n= 15,745)	
			GCS 15	Low < 15	GCS 15	GCS <15	GCS 15	GCS <15
Physical presence ¹ (n=19,642)	4.18 (3.95-4.41) <i>p</i> <0.001	1.18 (1.11-1.27) <i>p</i> <0.001	0.59 (0.38-0.92) <i>p</i> =0.02	0.83 (0.41-1.72) <i>p</i> =0.62	0.92 (0.58-1.48) <i>p</i> =0.74	1.37 (0.82-2.31) <i>p</i> =0.07	1.16 (0.87-1.54) <i>p</i> =0.31	1.04 (0.82-1.33) <i>p</i> =0.72
Family call only ² (n=559)	1.99 (1.80-2.21) <i>p</i> <0.001	1.29 (1.80-2.21) <i>p</i> <0.001	0.58 (0.25-1.37) <i>p</i> =0.22	0.63 (0.16-2.54) <i>p</i> =0.52	1.13 (0.53-2.40) <i>p</i> =0.75	1.10 (0.43-2.80) <i>p</i> =0.07	1.39 (0.85-2.3) <i>p</i> =0.196	0.99 (0.67-1.47) <i>p</i> =0.96
No visit ³ (n=1,757)	--	--	--	--	--	--	--	--

¹Family physical presence as defined by physical presence at any time during ICU stay

²Family call only as defined by telephone, without physical presence

³No visit means that the patient did not receive any in-person family ICU presence or phone call

*Adjusted for age, sex, hospital type, admission type, Acute Physiology and Chronic Health Disease Classification System II score at ICU admission, Richmond Agitation Sedation Scale score at ICU admission, hospital length of stay, ICU length of stay, number of ICU beds, any receipt of invasive mechanical ventilation, Charlson Comorbidity Index score at ICU admission, Sequential Organ Failure Assessment score at admission, and Glasgow Coma Scale score at admission

** Adjusted for age, sex, hospital type, Acute Physiology and Chronic Health Disease Classification System II score at ICU admission, Richmond Agitation Sedation Scale score at ICU admission, hospital length of stay, ICU length of stay, number of ICU beds, any receipt of invasive mechanical ventilation, Charlson Comorbidity Index score at ICU admission, Sequential Organ Failure Assessment score at admission

Dashes indicate reference group for multivariable logistic regression analyses

Abbreviations: ICU, Intensive Care Unit; CI, Confidence Intervals

Appendix 9. Sensitivity analysis of delirium duration and family presence excluding those who died in the intensive care unit

Family presence	Adjusted Model* (95% CI)	
	Crude Model (95% CI) (n=13,153)	All patient admissions (n=13,153)
Physical presence ¹ (n= 12,313)	1.25 (1.26-2.30) <i>p</i> <0.001	-1.58 (-1.94 to -1.40) <i>p</i> <0.001
Family call only ² (n= 182)	-0.70 (-0.50 to -0.91) <i>p</i> <0.001	-1.00 (-2.18 to -1.80) <i>p</i> <0.001
No visit ³ (n=558)	--	--

¹Family physical presence as defined by physical presence at any time during ICU stay

²Family call only as defined by telephone, without physical presence

³No visit means that the patient did not receive any in-person family ICU presence or phone call

*Adjusted for age, sex, hospital type, Acute Physiology and Chronic Health Disease Classification System II score at ICU admission, Richmond Agitation Sedation Scale score at ICU admission, hospital length of stay, ICU length of stay, number of ICU beds, any receipt of invasive mechanical ventilation, Charlson Comorbidity Index score at ICU admission, Sequential Organ Failure Assessment score at admission, and Glasgow Comma Scale score at admission

Dashes indicate reference group for multivariable linear regression analyses

Abbreviations: ICU, Intensive Care Unit; CI, Confidence Intervals

Appendix . Sensitivity analyses of delirium duration and family presence (coded as binary) in the intensive care unit

Family presence	Crude Model (95% CI) (n=26,100)	Adjusted Models* (95% CI)
		All patient admissions (n=26,100)
Physical Presence and call ¹ (n= 14,273)	1.35 (1.26-2.30) <i>p</i> <0.001	-1.90 (-2.13 to -0.73) <i>p</i> =0.004
No visit ² (n= 574)	--	--

¹Family physical presence as defined by physical presence at any time during ICU stay and family call as defined by telephone call.

²No visit means that the patient did not receive any in-person family ICU presence or phone call

*Adjusted for age, sex, hospital type, Acute Physiology and Chronic Health Disease Classification System II score at ICU admission, Richmond Agitation Sedation Scale score at ICU admission, hospital length of stay, ICU length of stay, number of ICU beds, any receipt of invasive mechanical ventilation, Charlson Comorbidity Index score at ICU admission, Sequential Organ Failure Assessment score at admission, and Glasgow Comma Scale score at admission

Dashes indicate reference group for multilevel mixed-effects linear regression analyses

Abbreviations: ICU, Intensive Care Unit

Appendix 11. Secondary analyses for percentage days of delirium and family presence

Percentage Days of Delirium ¹	Total (n=26,100)	Family Presence		
		Physical presence ² (n= 23,657)	Family call only ³ (n= 618)	No Visit ⁴ (n= 1,825)
Percentage, by quartile, n (%)				
Quartile 1 (<25%)	16,587 (63.6)	14,763 (62.4)	402 (65.1)	1,422 (77.9)
Quartile 2 (≤50% & ≥25%)	3,212 (12.3)	3,075 (13.0)	57 (9.2)	80 (4.4)
Quartile 3 (<75% & >50%)	3,722 (14.3)	3,722 (14.3)	73 (11.8)	165 (9.0)
Quartile 4 (≥75%)	2,579 (9.9)	2,579 (9.9)	86 (13.9)	158 (8.7)

¹Total days delirium divided by total ICU length of stay

²Family physical presence as defined by physical presence at any time during ICU stay

³Family call only as defined by telephone, without physical presence

⁴No visit means that the patient did not receive any in-person family ICU presence or phone call

CHAPTER 3: DISCUSSION

3.1 Summary of Main Findings

The work presented in this thesis examined the associations between family presence of critically ill adult patients admitted to ICU and the incidence and duration of delirium. Family presence was categorized as: 1) family physically present in the ICU, 2) family phone call only, and 3) no family presence or phone call (reference group). The study presented in Chapter 2 employed a multi-center population-based retrospective cohort design to examine these two objectives. Less than 10% of patients included in the study had no family member presence nor a phone call during their ICU stay. In general, patients who were sedated or had higher illness severity were more likely to have family member present in the ICU or receive a family phone call. The majority of patients included in the study were admitted for medical reasons followed by emergency-surgical reasons, and elective-surgical reasons. Over half of patients did not have an intact GCS (limited eye, verbal, or motor response). Family physical presence in the ICU was associated with increased incidence of delirium in all patients compared to patients receiving no family presence or phone call (unadjusted). Reasons for admission to the ICU as well as GCS score (intact GCS versus without intact GCS) were found to modify the association between family presence and the incidence of delirium in critically ill patients. After adjusting for concurrent effect modification by admission type and GCS score, family presence reduced incidence of delirium during elective-surgical admissions in patients with intact GCS compared to patients with no family presence or phone call (reference group), adjusted for patient re-admission. Family presence was not associated with incidence of delirium in patients without intact GCS admitted for elective-surgical and medical reasons as compared to patients in the

reference group, adjusted for patient re-admission. Family phone calls were not associated with incidence of delirium in any ICU patient.

Among all patients in the cohort, regardless of admission type and GCS score, family member presence was associated with reduced duration of delirium by up to two days compared to patients in the reference group, adjusted for patient re-admission. Additionally, a family phone call (to a patient) was associated with reduced duration of delirium by up to one day compared to patients in the reference group, adjusted for patient re-admission. For the association between family presence and both the incidence and duration of delirium, clustering by ICU re-admission was necessary. However, clustering by ICU site was not found to affect the association between family presence and both the incidence and duration of delirium. Therefore, exposure to delirium during an ICU admission may be a risk factor to subsequent delirium in future ICU admissions.

A sensitivity analysis estimating the association between family member presence and duration of delirium excluding those who died during either the ICU admission or subsequent hospitalization found similar associations as the main findings. However, estimates had wider confidence intervals, and the impact of family presence compared to family phone call only did not statistically differ in their effect on duration of delirium. Overall family member presence (combining both family member presence and family phone call as one category) was associated with reduced duration of delirium by up to two days. This is similar to results seen with family member presence in the ICU alone. Secondary analyses exploring reasons for ICU admission found that elective-surgical patients were less likely to be diagnosed with neurological problems as

compared to their counterparts admitted for emergency-surgical and medical reasons. This further supports the observed effect modification between ICU admission type and GCS score (measure of intact consciousness) found in the association between family member presence and the incidence of delirium in critically ill patients. Secondary analyses exploring percentage patient days with delirium demonstrated that patients with family presence or a phone call had the highest odds of having delirium during three-quarters or greater of their ICU stay, as compared to patients in reference group. Family members may be more likely to be present when their loved ones are experiencing prolonged delirium.

3.2 Findings in Context of Existing Literature

The prevalence of delirium in the current study (55.9%) was congruent with other studies using Alberta ICU data [73, 74], but was higher than the pooled prevalence of delirium reported in a meta-analysis that included studies conducted in North America, Europe, and Asia (n=42 studies; 31.8%) [2]. The meta-analysis identified delirium in 5280 of 16,595 (31.8%) critically ill patients by multiple screening or diagnostic instruments (i.e., CAM-ICU, ICDSC, DSM-5) and excluded patients with prior primary central nervous system disorder (i.e., stroke, brain trauma, brain injury), cardiac surgery, and alcohol or drug withdrawal. The exclusion of patients in these groups may account for the discrepancies between delirium prevalence estimates from our study and the international meta-analysis. Patients with central nervous system disorders or alcohol and drug withdrawal have a higher risk of developing delirium in the ICU [15]; therefore, the meta-analysis may have included less cases of ICU patients with delirium than our study [15]. Given that our study encompassed the majority of patient groups in

the ICU (i.e., did not exclude based on diagnosis or illness severity), it is understandable that the estimated prevalence of delirium was greater than that reported in the meta-analysis.

The findings from the retrospective cohort study add to the limited body of literature regarding the impact of family presence on delirium in the ICU. Few studies have investigated the impact of family presence on delirium in critically ill patients [61, 62, 64-66, 75]. A meta-analysis of two studies reported that flexible family visitation hours in the ICU reduced the odds of delirium (pooled OR 0.39; 95% CI:0.22-0.69; $I^2 = 0\%$) compared to patients with restricted ICU visitation hours [62, 64, 65]. An RCT by Eghbali-Babadi *et al.* found that patients within a cardiovascular surgical ICU had lower incidence of delirium when their family visited them the morning after the operation than when family members visited 24-hours after surgery (OR 0.33; 95% CI:0.21-0.82) [65]. A before-and-after study by Rosa *et al.* found that a 12-hour extended ICU visitation policy, as opposed to a 4-hour restricted visitation policy, resulted in a significant reduction in the odds of delirium in critically ill patients (OR 0.50; 95% CI:0.21-0.82) [62]. A subgroup analysis of the Rosa *et al.* study found that patients with extended family visitation had a higher reduction (compared to patients with restricted family visitation) in the odds ratio of delirium (OR 0.43; 95% CI:0.22-0.87) when they were admitted for medical reasons compared to the odds ratio (comparing incidence of delirium in patients with flexible visitation hours versus restricted hours) of patients admitted for elective and emergency-surgical reasons [62]. Rosa *et al.* reported that patients with extended flexible family visitation hours admitted for both elective and emergency-surgical reasons (combined as one category) did not have significantly

reduced odds of delirium compared to patients with restricted family ICU visitation. Our study stratified ICU admission type into three groups: 1) elective-surgical, 2) emergency-surgical and 3) medical and similarly found that family presence was not associated with incidence of delirium in critically ill patients admitted for emergency-surgical reasons. However, our findings highlight that family presence reduced the incidence of delirium in critically ill patients with intact GCS admitted for elective reasons. It is possible that the Rosa *et al.* study found no significant association in the reduction of delirium in patients admitted for elective-surgical and emergency-surgical reasons because the two admission types were combined as one group when each ICU type alone could have a different effect (i.e., increase/decrease delirium). It is also possible that our study's findings were due to chance. Findings from our study are also supported by results from Westphal *et al.* [61]. Westphal *et al.* found that patients in a 24-hour open visitation policy group, compared to a restricted visitation policy group, had a lower incidence of delirium (by 5.4%) [61]. We found that family presence reduced the incidence delirium in some critically ill patients (elective-surgical with intact GCS). In contrast, a randomized controlled trial by Rosa *et al.* reported no association between flexible ICU visitation hours and the incidence of delirium in critically ill patients [66]. The randomized controlled trial was performed over a study period of two months and compared an open 24-hour ICU visitation intervention group to a restricted ICU visitation control group [66]. The randomized controlled trial may have underestimated the incidence of delirium (adjusted difference in incidence of delirium between flexible and restrictive visitation hours, -1.7% [95% CI, -6.1% to 2.7%], given the limited intervention time (two months), which may not have been sufficient to estimate

statistical significance [66]. In addition, the study measured increased family ICU visitation hours, which may not correlate with increased family presence or engagement, potentially further underestimating the adjusted difference in incidence of delirium between flexible and restrictive visitation hours (-1.7% [95% CI, -6.1% to 2.7%]).

Our study found that the association between family presence and delirium was modified by two clinical factors (i.e., admission type and GCS score at admission). Family presence decreased the incidence of delirium during elective-surgical admissions in patients with intact GCS, compared to patients in the reference group, after adjusting for patient readmission. Patients admitted for elective-surgical reasons are likely to have less risk factors for delirium such as lower illness severity (compared to patients admitted for medical or emergency-surgical reasons) [73]. Current literature supports that patients with intact GCS (i.e., high GCS scores indicating normal consciousness and brain function) are able to better engage with their family member in hospital settings [76, 77]. Additionally, patients with intact GCS are able to receive emotional (i.e., care, calming effect), environmental (i.e., opening windows to increase daylight), and cognitive support (i.e., active neurological stimulation) through interacting with their family member during their ICU stay, which may reduce delirium [12]. In addition, critically ill patients admitted for medical and emergency-surgical reasons may have limited benefit from family members even with intact GCS. ICU patients admitted for emergency-surgical and medical reasons likely have more delirium risk factors such as illness severity and comorbidity, when compared to patients admitted for elective-surgical reasons [73]. The association between family presence and incidence of

delirium was not statistically significant in medical patients, irrespective of GCS scores. Conversely, patients without intact GCS (indicated by lower GCS scores) may have limited cognitive capacity, which is a barrier to effective family engagement [76, 77]. In a qualitative study, some nurses reported limiting family interaction in patients with severe impaired consciousness or medical conditions for safety reasons [76]. However, as patients recovered from impaired consciousness, family were re-introduced to engage in mental, physical, and emotional patient support [76]. Family members may be more likely to engage and support critically ill patients when they are conscious (i.e., high GCS score).

While the majority of previous studies assessed the impact of flexible visitation hours on the incidence of delirium, research gaps pertaining to the impact of family presence on the duration of delirium in critically ill patients still remain. Our study addressed this gap, and found that among all ICU patients, both family presence and family phone call significantly reduced the duration of delirium in critically ill patients by up two days and one day compared to patients in the reference group, respectively. Estimates were adjusted by ICU re-admission (to account for clustering) as patients previously exposed to delirium in ICU settings may have a higher risk of experiencing delirium in subsequent admissions [78]. It is plausible that family member presence in the ICU may reduce the duration of delirium by providing non-pharmacological interventions such as reorientation [9, 12]. Family members may provide emotional support and sensory stimulation through direct phone calls with critically ill patients [79], which may be a plausible mechanism in reducing delirium after onset [79].

3.3 Strengths

The study has several strengths. This study employed a large, multi-centered population-based cohort from all 14 adult medical-surgical ICUs in Alberta. The feasible obtainment of a large sample size also increased power, precision, and minimized type II error. This also allows for generalization to other ICUs with similar healthcare structures and ICU populations. Patients were merged using deterministic linkage by a unique patient identifier (Medical Record Number), which increased the reliability of data linkage and limited selection bias associated with unlinked (therefore excluded) patients. In addition, family presence was recorded in a novel manner with the use of an NLP algorithm developed by our team. Although eCritical contains a check box for family presence/absence, sometimes the check box is left unrecorded. The algorithm is able to interpret free-text recorded (in eCritical) by healthcare providers (e.g., nurses, physicians, social workers) on family member presence. This enables the NLP to capture a more accurate representation of family presence than increased unit-wide visitation hours alone. In addition, the NLP algorithm enables categorization of family presence as a three-level exposure: 1) family physical presence in the ICU, 2) family phone call only, and 3) no family presence or call. This allowed for reporting estimates for patients receiving telephone contact and direct family presence in the ICU, which adds to the clinical relevance of our findings. The rule-based AUROC for visits by family or friends was 0.882 95%CI: 0.82–0.94 and for patient receiving a family phone call was 0.975, 95%CI: 0.95–0.99 [70]. The rule-based classifier excluded phone calls that were between family members and hospital staff. Additionally, this study examined multiple covariates, informed by the literature, as potential effect modifiers and confounders.

Concurrent modification was identified by both ICU admission type (elective-surgical, emergency-surgical, and medical) and GCS scores in the association between family presence and the incidence of delirium in critically ill patients. No effect modification was found in the association between family presence and the duration of delirium in critically ill patients. Using rigorous methodology, estimates of the association between family presence and both the incidence and duration of delirium in critically ill patients were adjusted for clustering by patient re-admission to eliminate bias associated with repeated ICU admissions.

3.4 Limitations

This project has limitations that must be considered. First, selection bias may have been introduced since patients who died in the ICU and hospital were included in the analysis. Patients with complex medical problems and delirium have higher mortality rates and patients are more likely to have family visit in-person near the end-of-life. The duration of delirium for these patients would be underestimated since they would die earlier (survival bias), leading to selection bias. This would lead to a decrease in exposed individuals with the outcome (duration of delirium), thereby overestimating the numerator of the mean duration of delirium estimate and overestimating the overall difference in mean duration of delirium between exposed (family presence) and unexposed (no family presence) patients. However, this bias would be minimal, as a sensitivity analysis excluding patients who died in the ICU or hospital showed similar results to the full cohort (i.e., including those who died). Second, there is a risk of underreporting family presence in eCritical because it is not required that bedside nurses or physicians document this variable. In addition, the algorithm did not quantify

meaningful family engagement or family presence at the bedside alone (rather physical presence in the ICU). We assumed that family visiting the ICU would also visit their loved one at the bedside or that their presence increased collaboration with healthcare providers, which may positively impact ICU patient outcomes. Family members who were present in the ICU may or may not have engaged with the patient at the bedside. Classification of family presence using the algorithm may have led to non-differential misclassification bias. Family members providing limited to no engagement would be classified as present rather than not present, irrespective of outcome status, thereby biasing estimates of effect toward the null value (i.e., closer to 1 for OR and closer to 0 for duration). Despite this limitation in classifying family presence, the novel use of the NLP algorithm enabled a comprehensive view of family presence, which is more informative than quantifying family presence through visitation hours alone. Another limitation to this study is the moderate specificity of the ICDSC tool, which can result in an increase in false positive delirium identification. For instance, a nurse using the ICDSC who does not know a patient's baseline mental state could mistakenly identify a critically ill patient with delirium if the patient presents with inattention symptoms that are attributable to dementia or other psychiatric problems, rather than delirium. Given that the ICDSC is used on both patients with family (exposed) and patients without family (unexposed), the low specificity of the ICDSC would lead to a non-differential misclassification bias resulting in an estimate of effect that is closer to the null value (i.e., closer to 1 for OR and closer to 0 for duration). Given that only one estimate was significant in our study (the association between family presence and incidence of delirium), it is plausible that this effect was due to chance (random error). It is also

possible that the study did not control for all potential confounders (e.g., frailty score), due to limitations in administrative data sources, leading to residual confounding. Due to limited reporting of frailty scores in the dataset, frailty was not used in the analysis to prevent overfitting of models. Though, frailty could have potentially been a confounder in the association between family presence and the incidence and duration of delirium, the magnitude of bias may have been low. If those with higher frailty scores were more likely to have delirium and family present in the ICU for support, the direction of bias would be negative and lack of accounting for frailty scores would thus underestimate the OR. Taken together, these potential sources of bias would have underestimated the results of the present study, and the true effect may be larger than reported.

3.5 Implications on Clinical Practice and Public Health

The main aims of public health are to increase overall population health, identifying major risks to disease, and implementing strategies to reduce disease onset, duration, and follow-up sequelae [80]. Public health within the field of critical care medicine has identified prevention, early detection, and management of delirium as a top priority [81]. Delirium is common in ICUs and is associated with worsened patient outcomes, such as long-term cognitive impairment and mortality [2]. Delirium is difficult to identify and treat [34]. Given delirium's fluctuating nature, many cases of delirium are missed in ICUs worldwide [34]. Moreover, to date, pharmacological interventions have not been shown to be effective in the treatment of delirium [8]. Conversely, non-pharmacological interventions in hospital settings have shown to reduce delirium occurrence by 30% [82]. Given the high prevalence of delirium and its associated negative outcomes, the International Drive to Illuminate Delirium seeks to implement

primary, secondary, and tertiary prevention and management strategies for delirium [81]. Primary prevention interventions involve preventing the onset of delirium through early mitigation of delirium risk factors such as immobilization, sleep deprivation, and cognitive decline [81]. Secondary prevention interventions involve early detection and management of delirium [81]. Tertiary prevention interventions involve providing therapies (e.g., treatment to prevent long-term consequences of disease) to return critically ill patients to baseline after onset of delirium [81]. Family engagement in the ICU may facilitate opportunities for both primary, secondary, and tertiary prevention of delirium through non-pharmacological interventions [12].

The current study highlights the positive impact of direct family presence on both the incidence and duration of delirium in critically ill patients. Previous studies relied on measuring the impact of family presence on delirium by comparing extended and restricted family visitation hours, which limited quantifying direct family presence [61, 62, 65]. However, our study used a validated algorithm to detect family presence that was specific to the rich administrative data from eCritical (a provincial wide, population-based, ICU bedside recording system) in Alberta, Canada. Family presence in the ICU was found to decrease the incidence of delirium in some patients (those with intact GCS admitted for elective-surgical reasons). However, family presence did not significantly reduce the incidence of delirium in patients with or without intact GCS admitted for emergency-surgical and medical reasons. These findings, combined with future research on early management of delirium, may identify patients (i.e., those without intact GCS admitted for medical or emergency-surgical reasons) that have limited benefit from non-pharmacological interventions facilitated by family in the ICU. In

addition, the study found that family presence in the ICU decreased the duration of delirium by up to two days, which can reduce the risk of mortality associated with delirium [83]. Interestingly, patients who received a family phone call only had reduced duration of delirium by up to one day compared to patients receiving no family presence or phone call. This may be relevant in situations where family presence at the bedside is not feasible. For instance, pandemics such as COVID-19 [Coronavirus Disease 2019], can result in restrictions to family visitation in ICUs worldwide (for safety reasons regarding COVID-19 transmission) [84]. A multi-center cohort study of 69 adult ICUs across 14 countries, including patients with COVID-19, found that patients receiving virtual family contact had lower risk of developing delirium than patients receiving no virtual contact [85]. Lack of family presence either in-person or by phone call is a modifiable risk factor to delirium [85]. Future policy recommendations may adapt ICUs to allow for family phone calls or virtual contact in instances where family presence at the bedside is not allowed, in order to reduce the risk of delirium in critically ill patients. Telemedicine options may provide opportunities for family to engage with patients and overcome challenges to family bedside participation in care (i.e., distance to hospitals, work/family obligations) [79]. The findings from the current study, alongside findings from the COVID-19 pandemic, highlight an additional benefit to promoting family engagement or contact in efforts to prevent and reduce ICU delirium.

There is potential for family members to aid in both the identification and management of delirium [7, 86]. Early identification of delirium is difficult and requires routine delirium screening in ICU settings [87, 88]. Identifying delirium in early stages allows for efficient management that reduces associated negative outcomes (i.e.,

cognitive impairment, post-traumatic stress disorder, longer hospital stay, and mortality) [89]. Family members may aid in early detection of delirium [86]. There are two delirium detection tools which may be used by family members in the ICU [86]. The first is the Family Confusion Assessment Method (FAM-CAM) [90] and the second is the Sour Seven questionnaire [91]. Fiest *et. al* assessed the validity of family using the FAM-CAM and Sour Seven questionnaire to detect delirium [86]. The study included 147 dyads (patient and family), and found family delirium detection tools to be feasible, with fair diagnostic accuracy (area under the receiver operating characteristic curve on the Family Confusion Assessment Method was 65.0% [95%:CI60.0–70.0%]) [86]. Family members may also aid in the management of delirium by employing non-pharmacological management strategies such as patient mobilization, sleep maintenance, and cognitive stimulation to manage delirium in critically ill patients [92]. The Society of Critical Care Medicine recommends the use of the ABCDEF (A = Assessment and treatment of pain; B = Both spontaneous awakening and breathing trials; C = Medication choice and de-escalation; D = Delirium screening and prevention; E = Early mobilization; and F = Family engagement) bundle to reduce the incidence of delirium in critically ill patients [7]. The bundle emphasizes the benefits of family engagement in the management of delirium [93]. Our study highlights the potential benefits of family presence in reducing both the incidence and duration of delirium in critically ill patients.

Encompassing patient and family engagement in clinical practice is gaining momentum, but it is not without barriers. Burns *et al.* discussed that family engagement barriers may stem from: 1) patients, 2) families, and 3) organizational critical care

structures [10]. Patients with higher illness severity, prone to longer ICU stays, may have limited ability to meaningfully engage with family in the ICU [94]. Families may experience both anxiety and depression associated with having their loved one admitted to the ICU [95]. Families reported emotional distress and suffering from seeing their relative experience pain and illness [96]. Family members may be prone to post-traumatic stress disorder up to three months after admission of a relative or loved one in the ICU [97]. This may cause reluctance of family members to participate in patient care and shared decision-making [95, 96]. There are opportunities for nurses to facilitate family participation to increase family confidence and reduce family distress associated with an ICU admission [98]. Knowledge gaps still persist regarding the positive impact of family on patient care, which may limit motivation for family to be present at the bedside [99]. Lastly, organizational barriers to family engagement may be both environmentally [100] and clinician related [101]. Environment barriers include limited ICU space, nurse work-flow interruption, and clinician time required to explain disease and care delivery [100]. There also seems to be a mismatch between clinician and family perception on family engagement [100]. In a cross-sectional survey, 97% of family members reported interest in participating in ICU rounds, while 38% of clinicians perceived moderate family interest in participating [100]. Barriers to family engagement are seen across the healthcare system. However, the challenges and barriers to ICU family engagement can be overcome through research and interventions to allow for a system that continually improves patient and family-centered care.

3.6 Directions for Future Research

Future research should focus on: 1) increasing knowledge translation to stakeholders (i.e., clinicians, researchers, patients, families, and policy makers) on the impact of family engagement in the ICU; 2) creating metrics that accurately measure the impact of meaningful family involvement on delirium outcomes; 3) understanding the complex association between family presence and delirium; 4) implementing family interventions that are safe, inclusive, and specific to assist delirium management in critically ill patients.

Knowledge translation of findings alongside further research on the impact of family presence on delirium in critically ill patients may promote family presence in the ICU. Family member engagement may be underutilized in ICU settings [100]. This may stem from general lack of knowledge pertaining to family importance in patient well-being across all levels of stakeholders [102]. Clinicians may underestimate the willingness of family interest in participation [100]. In addition, family members may not be aware of their potentially positive effect on patient outcomes in critical care [103]. Therefore, public health and policy makers may target education on the multiple benefits of family presence in ICU settings through journal articles, conferences, and mandatory clinician training, as a means to promote knowledge within the healthcare system. It is important to note the complex dynamic of hospital settings and the key players involved in the healthcare system (i.e., federal and provincial governments, nurses, pharmacists, doctors, educational institutions, social workers, policy makers, medical researchers, patient advocacy groups, and social media) [104]. Integrated knowledge translation, encompassing involvement of all key stakeholders may enhance

the translation of research into clinical practice [105]. For instance, engagement of patients and families in knowledge translation may directly inform key mechanisms to improve the relevance, impact, and efficiency of public knowledge efforts [105]. Integrated knowledge translation research can utilize the unique experiences of families and patients to highlight their importance in ICU settings amongst the general public and the healthcare system [105].

While efforts have increased over the past decade to call for greater family engagement in ICU settings, there is a paucity in research on how to define and measure family engagement [10]. While the findings from our study highlight the impact of family presence on delirium in the ICU, limitations on measuring meaningful engagement persist. Therefore, future research may assess the definition of family engagement in the management and prevention of delirium through both qualitative and quantitative studies to generate holistic metrics [10]. Grading *et al*, proposed three ways to quantify engagement in a system: 1) accountability and transparency of research and change, 2) quality and validity of measurements, and 3) partnership and respect among stakeholders [106]. Metrics quantifying the dose-response of family engagement may also be clinically relevant. For example, a study may measure the duration, frequency, and quality of meaningful family engagement on delirium outcomes in critically ill patients. Meaningful family engagement could be determined through administration of a questionnaire to family members on the activities they participate in. The definition of engagement may vary by the culture of the ICU [107], family dynamics and personalities [108], and patient values [109]. Therefore, defining family engagement may require continuous evaluation and assessment of patient and family satisfaction

and values through qualitative methods [76]. Research on quantifying the impact of meaningful family engagement is required to develop appropriate system-level interventions that may utilize family members as partners in reducing ICU patient delirium.

After identifying and assessing effective family engagement in ICU settings, future research may focus on family-facilitated delirium interventions. Family conceptions of engagement may differ across race [110], culture [110], gender [111], and spirituality [112]. Family engagement metrics may be used in a prospective cohort study to assess the relationship between meaningful family engagement on the incidence and duration of delirium. Future research may then personalize intervention strategies to enhance support provided by family members on delirium in ICU settings. For instance, clinicians may tailor family-facilitated delirium interventions based on family needs, values, and perspectives [11]. This may be facilitated through patient aid tools that assess willingness, comfort, and perspectives of family participating in delirium interventions. Feasibility and work-load capacity to implement such interventions will also be needed to ensure sustainability [113].

3.7 Conclusions

The study conducted in this thesis found that family presence at the bedside of critically ill patients reduced the incidence of ICU delirium in patients with intact GCS admitted for elective-surgical reasons. In all patients, family presence in the ICU was associated with reduced duration of delirium (up to two days). Additionally, in all patients, a family phone call was associated with reduced duration of delirium (up to one day). Family members of critically ill patients may be important partners to prevent and

manage delirium in the ICU. Findings may inform stakeholders and future research on knowledge translation, measuring family engagement, and family-facilitated delirium interventions to increase family engagement in the ICU and reduce ICU delirium. This in turn may improve delirium-related patient and healthcare outcomes, such as mortality and costs, respectively, and allow for an ICU system that continually incorporates patients and families as partners in care.

REFERENCES

1. American Psychiatric Association (2000) Diagnostic and statistical manual of mental disorders: DSM-IV. American Psychiatric Association, Washington, D.C
2. Salluh JI, Wang H, Schneider EB, Nagaraja N, Yenokyan G, Damluji A, Serafim RB, Stevens RD, (2015) Outcome of delirium in critically ill patients: systematic review and meta-analysis. *BMJ* 350: h2538
3. Ely E, Shintani A, Truman B, Speroff T, Gordon S, Harrell F, Inouye S, Bernard G, Dittus R, (2004) Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA* 292: 1753-1752
4. Davidson JE, Aslakson RA, Long AC, Puntillo KA, Kross EK, Hart J, Cox CE, Wunsch H, Wickline MA, Nunnally ME, Netzer G, Kentish-Barnes N, Sprung CL, Hartog CS, Coombs M, Gerritsen RT, Hopkins RO, Franck LS, Skrobik Y, Kon AA, Scruth EA, Harvey MA, Lewis-Newby M, White DB, Swoboda SM, Cooke CR, Levy MM, Azoulay E, Curtis JR, (2017) Guidelines for Family-Centered Care in the Neonatal, Pediatric, and Adult ICU. *Crit Care Med* 45: 103-128
5. Collinsworth AW, Priest EL, Campbell CR, Vasilevskis EE, Masica AL, (2016) A Review of Multifaceted Care Approaches for the Prevention and Mitigation of Delirium in Intensive Care Units. *J Intensive Care Med* 31: 127-141
6. Stelfox HT, Niven DJ, Clement FM, Bagshaw SM, Cook DJ, McKenzie E, Potestio ML, Doig CJ, O'Neill B, Zygun D, (2015) Stakeholder Engagement to Identify Priorities for Improving the Quality and Value of Critical Care. *PLoS One* 10: e0140141

7. Devlin JW, Skrobik Y, G  linas C, Needham DM, Slooter AJC, Pandharipande PP, Watson PL, Weinhouse GL, Nunnally ME, Rochweg B, Balas MC, van den Boogaard M, Bosma KJ, Brummel NE, Chanques G, Denehy L, Drouot X, Fraser GL, Harris JE, Joffe AM, Kho ME, Kress JP, Lanphere JA, McKinley S, Neufeld KJ, Pisani MA, Payen JF, Pun BT, Puntillo KA, Riker RR, Robinson BRH, Shehabi Y, Szumita PM, Winkelman C, Centofanti JE, Price C, Nikayin S, Misak CJ, Flood PD, Kiedrowski K, Alhazzani W, (2018) Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Crit Care Med 46: e825-e873
8. Serafim RB, Bozza FA, Soares M, do Brasil PE, Tura BR, Ely EW, Salluh JI, (2015) Pharmacologic prevention and treatment of delirium in intensive care patients: A systematic review. J Crit Care 30: 799-807
9. Martinez FT, Tobar C, Beddings CI, Vallejo G, Fuentes P, (2012) Preventing delirium in an acute hospital using a non-pharmacological intervention. Age Ageing 41: 629-634
10. Burns KEA, Misak C, Herridge M, Meade MO, Oczkowski S, (2018) Patient and Family Engagement in the ICU. Untapped Opportunities and Underrecognized Challenges. Am J Respir Crit Care Med 198: 310-319
11. Goldfarb MJ, Bibas L, Bartlett V, Jones H, Khan N, (2017) Outcomes of Patient- and Family-Centered Care Interventions in the ICU: A Systematic Review and Meta-Analysis. Crit Care Med 45: 1751-1761

12. Teixeira C, Rosa RG, (2018) The rationale of flexible ICU visiting hours for delirium prevention. *Journal of Emergency and Critical Care Medicine* 2
13. Reade MC, Finfer S, (2014) Sedation and delirium in the intensive care unit. *N Engl J Med* 370: 444-454
14. Ogundele O, Yende S, (2010) Pushing the envelope to reduce sedation in critically ill patients. *Crit Care* 14: 339
15. Van Rompaey B, Elseviers MM, Schuurmans MJ, Shortridge-Baggett LM, Truijen S, Bossaert L, (2009) Risk factors for delirium in intensive care patients: a prospective cohort study. *Crit Care* 13: R77
16. Davidson JE, (2013) Family presence on rounds in neonatal, pediatric, and adult intensive care units. *Ann Am Thorac Soc* 10: 152-156
17. Information ClfH (2020) Care in Canadian ICUs. Book Care in Canadian ICUs.
18. Fowler RA, Abdelmalik P, Wood G, Foster D, Gibney N, Bandrauk N, Turgeon AF, Lamontagne F, Kumar A, Zarychanski R, Green R, Bagshaw SM, Stelfox HT, Foster R, Dodek P, Shaw S, Granton J, Lawless B, Hill A, Rose L, Adhikari NK, Scales DC, Cook DJ, Marshall JC, Martin C, Juvet P, (2015) Critical care capacity in Canada: results of a national cross-sectional study. *Crit Care* 19: 133
19. Fowler RA, Sabur N, Li P, Juurlink DN, Pinto R, Hladunewich MA, Adhikari NK, Sibbald WJ, Martin CM, (2007) Sex-and age-based differences in the delivery and outcomes of critical care. *Cmaj* 177: 1513-1519
20. Wunsch H, Angus DC, Harrison DA, Collange O, Fowler R, Hoste EA, de Keizer NF, Kersten A, Linde-Zwirble WT, Sandiumenge A, Rowan KM, (2008) Variation

- in critical care services across North America and Western Europe. *Crit Care Med* 36: 2787-2793, e2781-2789
21. Wunsch H, Angus DC, Harrison DA, Linde-Zwirble WT, Rowan KM, (2011) Comparison of medical admissions to intensive care units in the United States and United Kingdom. *Am J Respir Crit Care Med* 183: 1666-1673
 22. Cavallazzi R, Saad M, Marik PE, (2012) Delirium in the ICU: an overview. *Ann Intensive Care* 2: 49
 23. Hermans G, Van den Berghe G, (2015) Clinical review: intensive care unit acquired weakness. *Crit Care* 19: 274
 24. Wilcox ME, Brummel NE, Archer K, Ely EW, Jackson JC, Hopkins RO, (2013) Cognitive dysfunction in ICU patients: risk factors, predictors, and rehabilitation interventions. *Crit Care Med* 41: S81-98
 25. Dos Santos C, Hussain SN, Mathur S, Picard M, Herridge M, Correa J, Bain A, Guo Y, Advani A, Advani SL, Tomlinson G, Katzberg H, Streutker CJ, Cameron JI, Schols A, Gosker HR, Batt J, (2016) Mechanisms of Chronic Muscle Wasting and Dysfunction after an Intensive Care Unit Stay. A Pilot Study. *Am J Respir Crit Care Med* 194: 821-830
 26. Elliott D, Davidson JE, Harvey MA, Bemis-Dougherty A, Hopkins RO, Iwashyna TJ, Wagner J, Weinert C, Wunsch H, Bienvenu OJ, Black G, Brady S, Brodsky MB, Deutschman C, Doepp D, Flatley C, Fosnight S, Gittler M, Gomez BT, Hyzy R, Louis D, Mandel R, Maxwell C, Muldoon SR, Perme CS, Reilly C, Robinson MR, Rubin E, Schmidt DM, Schuller J, Scruth E, Siegal E, Spill GR, Sprenger S, Straumanis JP, Sutton P, Swoboda SM, Twaddle ML, Needham DM, (2014)

- Exploring the scope of post-intensive care syndrome therapy and care: engagement of non-critical care providers and survivors in a second stakeholders meeting. *Crit Care Med* 42: 2518-2526
27. Rawal G, Yadav S, Kumar R, (2017) Post-intensive Care Syndrome: an Overview. *J Transl Int Med* 5: 90-92
 28. Halpern NA, Bettles L, Greenstein R, (1994) Federal and nationwide intensive care units and healthcare costs: 1986-1992. *Crit Care Med* 22: 2001-2007
 29. Zywielski MG, Hurley RT, Perruccio AV, Hancock-Howard RL, Coyte PC, Rampersaud YR, (2015) Health economic implications of perioperative delirium in older patients after surgery for a fragility hip fracture. *J Bone Joint Surg Am* 97: 829-836
 30. Morita T, Hirai K, Sakaguchi Y, Tsuneto S, Shima Y, (2004) Family-Perceived Distress From Delirium-Related Symptoms of Terminally Ill Cancer Patients. *Psychosomatics* 45: 107-113
 31. Ryan D, O'Regan N, Caoimh R, Clare J, O'Connor M, Leonard M, McFarland J, Tighe S, O'Sullivan K, Trzepacz P, Meagher D, Timmons S, (2013) Delirium in an adult acute hospital population: predictors, prevalence and detection. *BMJ Open* 3: e001772
 32. Spronk PE, Riekerk B, Hofhuis J, Rommes JH, (2009) Occurrence of delirium is severely underestimated in the ICU during daily care. *Intensive Care Med* 35: 1276-1280

33. Brummel NE, Vasilevskis EE, Han JH, Boehm L, Pun BT, Ely EW, (2013) Implementing delirium screening in the ICU: secrets to success. *Crit Care Med* 41: 2196-2208
34. Morandi A, Jackson JC, Ely EW, (2009) Delirium in the intensive care unit. *Int Rev Psychiatry* 21: 43-58
35. Wolters AE, Peelen LM, Welling MC, Kok L, de Lange DW, Cremer OL, van Dijk D, Slooter AJ, Veldhuijzen DS, (2016) Long-Term Mental Health Problems After Delirium in the ICU. *Crit Care Med* 44: 1808-1813
36. Farasat S, Dorsch JJ, Pearce AK, Moore AA, Martin JL, Malhotra A, Kamdar BB, (2020) Sleep and Delirium in Older Adults. *Curr Sleep Med Rep*: 1-13
37. European Delirium A, American Delirium S, (2014) The DSM-5 criteria, level of arousal and delirium diagnosis: inclusiveness is safer. *BMC Medicine* 12: 141
38. Services; AH (2020) Provincial Clinical Knowledge Topic Delirium, Adult – Critical. Provincial Clinical Knowledge Topic Delirium, Adult – Critical.
39. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y, (2001) Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. *Intensive Care Med* 27: 859-864
40. Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, Speroff T, Gautam S, Bernard GR, Inouye SK, (2001) Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med* 29: 1370-1379
41. Gusmao-Flores D, Salluh JI, Chalhub R, Quarantini LC, (2012) The confusion assessment method for the intensive care unit (CAM-ICU) and intensive care

- delirium screening checklist (ICDSC) for the diagnosis of delirium: a systematic review and meta-analysis of clinical studies. *Crit Care* 16: R115
42. Zheng J, Gao Y, Xu X, Kang K, Liu H, Wang H, Yu K, (2018) Correlation of bispectral index and Richmond agitation sedation scale for evaluating sedation depth: a retrospective study. *J Thorac Dis* 10: 190-195
 43. Institute of Patient and Family Centered Care (2020) Core Concepts
 44. Kaporiri L, (2018) Stakeholder involvement in health research priority setting in low income countries: the case of Zambia. *Research Involvement and Engagement* 4: 41
 45. Kokorelias KM, Gignac MAM, Naglie G, Cameron JI, (2019) Towards a universal model of family centered care: a scoping review. *BMC Health Services Research* 19: 564
 46. Canadian Institute of Health Research (2019) Canada's Strategy for Patient-Oriented Research. *Canada's Strategy for Patient-Oriented Research*.
 47. Howe A, Mathie E, Munday D, Cowe M, Goodman C, Keenan J, Kendall S, Poland F, Staniszewska S, Wilson P, (2017) Learning to work together – lessons from a reflective analysis of a research project on public involvement. *Research Involvement and Engagement* 3: 1
 48. Concannon TW, Fuster M, Saunders T, Patel K, Wong JB, Leslie LK, Lau J, (2014) A systematic review of stakeholder engagement in comparative effectiveness and patient-centered outcomes research. *J Gen Intern Med* 29: 1692-1701

49. Fisher C, Lindhorst H, Matthews T, Munroe DJ, Paulin D, Scott D, (2008) Nursing staff attitudes and behaviours regarding family presence in the hospital setting. *J Adv Nurs* 64: 615-624
50. Agård AS, Lomborg K, (2011) Flexible family visitation in the intensive care unit: nurses' decision-making. *J Clin Nurs* 20: 1106-1114
51. Ciufo D, Hader R, Holly C, (2011) A comprehensive systematic review of visitation models in adult critical care units within the context of patient- and family-centred care. *Int J Evid Based Healthc* 9: 362-387
52. Aggarwal B, Liao M, Mosca L, (2013) Medication adherence is associated with having a caregiver among cardiac patients. *Ann Behav Med* 46: 237-242
53. Weingart SN, Zhu J, Chiappetta L, Stuver SO, Schneider EC, Epstein AM, David-Kasdan JA, Annas CL, Fowler FJ, Jr., Weissman JS, (2011) Hospitalized patients' participation and its impact on quality of care and patient safety. *Int J Qual Health Care* 23: 269-277
54. Aronson PL, Yau J, Helfaer MA, Morrison W, (2009) Impact of family presence during pediatric intensive care unit rounds on the family and medical team. *Pediatrics* 124: 1119-1125
55. Epstein RM, Franks P, Shields CG, Meldrum SC, Miller KN, Campbell TL, Fiscella K, (2005) Patient-centered communication and diagnostic testing. *Ann Fam Med* 3: 415-421
56. Charmel PA, Frampton SB, (2008) Building the business case for patient-centered care. *Healthc Financ Manage* 62: 80-85

57. Bertakis KD, Azari R, (2011) Patient-centered care is associated with decreased health care utilization. *J Am Board Fam Med* 24: 229-239
58. Adams JA, Anderson RA, Docherty SL, Tulskey JA, Steinhäuser KE, Bailey DE, Jr., (2014) Nursing strategies to support family members of ICU patients at high risk of dying. *Heart Lung* 43: 406-415
59. Tudor K, Berger J, Polivka BJ, Chlebowy R, Thomas B, (2014) Nurses' perceptions of family presence during resuscitation. *Am J Crit Care* 23: e88-96
60. Chittle MD, Oklu R, Pino RM, He P, Sheridan RM, Martino J, Hirsch JA, (2016) Sedation shared decision-making in ambulatory venous access device placement: Effects on patient choice, satisfaction and recovery time. *Vasc Med* 21: 355-360
61. Westphal GA, Moerschberger MS, Vollmann DD, Inácio AC, Machado MC, Sperotto G, Cavalcanti AB, Koenig Á, (2018) Effect of a 24-h extended visiting policy on delirium in critically ill patients. *Intensive Care Med* 44: 968-970
62. Rosa RG, Tonietto TF, da Silva DB, Gutierrez FA, Ascoli AM, Madeira LC, Rutzen W, Falavigna M, Robinson CC, Salluh JI, Cavalcanti AB, Azevedo LC, Cremonese RV, Haack TR, Eugênio CS, Dornelles A, Bessel M, Teles JMM, Skrobik Y, Teixeira C, (2017) Effectiveness and Safety of an Extended ICU Visitation Model for Delirium Prevention: A Before and After Study. *Crit Care Med* 45: 1660-1667
63. Mitchell ML, Aitken LM, (2017) Flexible visiting positively impacted on patients, families and staff in an Australian Intensive Care Unit: A before-after mixed method study. *Aust Crit Care* 30: 91-97

64. Nassar Junior AP, Besen B, Robinson CC, Falavigna M, Teixeira C, Rosa RG, (2018) Flexible Versus Restrictive Visiting Policies in ICUs: A Systematic Review and Meta-Analysis. *Crit Care Med* 46: 1175-1180
65. Eghbali-Babadi M, Shokrollahi N, Mehrabi T, (2017) Effect of Family-Patient Communication on the Incidence of Delirium in Hospitalized Patients in Cardiovascular Surgery ICU. *Iran J Nurs Midwifery Res* 22: 327-331
66. Rosa RG, Falavigna M, da Silva DB, Sganzerla D, Santos MMS, Kochhann R, de Moura RM, Eugênio CS, Haack T, Barbosa MG, Robinson CC, Schneider D, de Oliveira DM, Jeffman RW, Cavalcanti AB, Machado FR, Azevedo LCP, Salluh JIF, Pellegrini JAS, Moraes RB, Foernges RB, Torelly AP, Ayres LO, Duarte PAD, Lovato WJ, Sampaio PHS, de Oliveira Júnior LC, Paranhos J, Dantas ADS, de Brito P, Paulo EAP, Gallindo MAC, Pilau J, Valentim HM, Meira Teles JM, Nobre V, Birriel DC, Corrêa ECL, Specht AM, Medeiros GS, Tonietto TF, Mesquita EC, da Silva NB, Korte JE, Hammes LS, Giannini A, Bozza FA, Teixeira C, (2019) Effect of Flexible Family Visitation on Delirium Among Patients in the Intensive Care Unit: The ICU Visits Randomized Clinical Trial. *Jama* 322: 216-228
67. Fiest K, Krewulak K, Hiploylee C, Bagshaw S, Burns K, Cook D, Fowler R, Kredentser M, Niven D, Olafson K, Parhar K, Patten S, Fox-Robichaud A, Rewa O, Rochweg B, Spence K, Straus S, S. S, West A, Stelfox H, Parsons Leigh J, (2021) An Environmental Scan of Visitation Policies in Canadian ICUs During the First Wave of the COVID-19 Pandemic. *CJA* (forthcoming)

68. Mazzali C, Duca P. Use of administrative data in healthcare research. *Intern Emerg Med*. 2015 Jun;10(4):517-24. doi: 10.1007/s11739-015-1213-9. Epub 2015 Feb 25. PMID: 25711312.
69. Brundin-Mather R, Soo A, Zuege DJ, Niven DJ, Fiest K, Doig CJ, Zygun D, Boyd JM, Parsons Leigh J, Bagshaw SM, Stelfox HT, (2018) Secondary EMR data for quality improvement and research: A comparison of manual and electronic data collection from an integrated critical care electronic medical record system. *Journal of Critical Care* 47: 295-301
70. Lucini FR, Krewulak KD, Fiest KM, Bagshaw SM, Zuege DJ, Lee J, Stelfox HT, (2021) Natural language processing to measure the frequency and mode of communication between healthcare professionals and family members of critically ill patients. *J Am Med Inform Assoc* 28: 541-548
71. Kreimeyer K, Foster M, Pandey A, Arya N, Halford G, Jones SF, Forshee R, Walderhaug M, Botsis T, (2017) Natural language processing systems for capturing and standardizing unstructured clinical information: A systematic review. *J Biomed Inform* 73: 14-29
72. Slota M, Shearn D, Potersnak K, Haas L, (2003) Perspectives on family-centered, flexible visitation in the intensive care unit setting. *Crit Care Med* 31: S362-366
73. Cherak SJ, Soo A, Brown KN, Ely EW, Stelfox HT, Fiest KM, (2020) Development and validation of delirium prediction model for critically ill adults parameterized to ICU admission acuity. *PLoS One* 15: e0237639

74. Brown KN, Soo A, Faris P, Patten SB, Fiest KM, Stelfox HT, (2020) Association between delirium in the intensive care unit and subsequent neuropsychiatric disorders. *Critical Care* 24: 476
75. Rosa RG, Falavigna M, Robinson CC, da Silva DB, Kochhann R, de Moura RM, Santos MMS, Sganzerla D, Giordani NE, Eugênio C, Ribeiro T, Cavalcanti AB, Bozza F, Azevedo LCP, Machado FR, Salluh JIF, Pellegrini JAS, Moraes RB, Hocheegger T, Amaral A, Teles JMM, da Luz LG, Barbosa MG, Birriel DC, Ferraz IL, Nobre V, Valentim HM, Corrêa ECL, Duarte PAD, Tregnago R, Barilli SLS, Brandão N, Giannini A, Teixeira C, (2018) Study protocol to assess the effectiveness and safety of a flexible family visitation model for delirium prevention in adult intensive care units: a cluster-randomised, crossover trial (The ICU Visits Study). *BMJ Open* 8: e021193
76. Hetland B, McAndrew N, Perazzo J, Hickman R, (2018) A qualitative study of factors that influence active family involvement with patient care in the ICU: Survey of critical care nurses. *Intensive Crit Care Nurs* 44: 67-75
77. Matamala-Gomez M, Maisto M, Montana JI, Mavrodiev PA, Baglio F, Rossetto F, Mantovani F, Riva G, Realdon O, (2020) The Role of Engagement in Teleneurorehabilitation: A Systematic Review. *Front Neurol* 11: 354
78. Cho SH, (2003) Using multilevel analysis in patient and organizational outcomes research. *Nurs Res* 52: 61-65
79. Stelson EA, Carr BG, Golden KE, Martin N, Richmond TS, Delgado MK, Holena DN, (2016) Perceptions of Family Participation in Intensive Care Unit Rounds and Telemedicine: A Qualitative Assessment. *Am J Crit Care* 25: 440-447

80. Vickers G, (1958) What sets the goals of public health. *N Engl J Med* 258: 589-596
81. Khachaturian AS, Hayden KM, Devlin JW, Fleisher LA, Lock SL, Cunningham C, Oh ES, Fong TG, Fick DM, Marcantonio ER, Iyengar V, Rockwood K, Kuchel GA, Eckenhoff RG, MacLulich AMJ, Jones RN, Davis D, D'Antonio PM, Fargo KN, Albert MS, Williamson JD, Ling SM, Weiss J, Karlawish J, Petersen RC, Blazer DG, Khachaturian ZS, Inouye SK, (2020) International drive to illuminate delirium: A developing public health blueprint for action. *Alzheimers Dement* 16: 711-725
82. Siddiqi N, Harrison JK, Clegg A, Teale EA, Young J, Taylor J, Simpkins SA, (2016) Interventions for preventing delirium in hospitalised non-ICU patients. *Cochrane Database Syst Rev* 3: Cd005563
83. Kiely DK, Marcantonio ER, Inouye SK, Shaffer ML, Bergmann MA, Yang FM, Fearing MA, Jones RN, (2009) Persistent delirium predicts greater mortality. *J Am Geriatr Soc* 57: 55-61
84. Kotfis K, Williams Roberson S, Wilson JE, Dabrowski W, Pun BT, Ely EW, (2020) COVID-19: ICU delirium management during SARS-CoV-2 pandemic. *Crit Care* 24: 176
85. Pun BT, Badenes R, Heras La Calle G, Orun OM, Chen W, Raman R, Simpson BK, Wilson-Linville S, Hinojal Olmedillo B, Vallejo de la Cueva A, van der Jagt M, Navarro Casado R, Leal Sanz P, Orhun G, Ferrer Gómez C, Núñez Vázquez K, Piñeiro Otero P, Taccone FS, Gallego Curto E, Caricato A, Woien H, Lacave G, O'Neal HR, Jr., Peterson SJ, Brummel NE, Girard TD, Ely EW, Pandharipande

- PP, (2021) Prevalence and risk factors for delirium in critically ill patients with COVID-19 (COVID-D): a multicentre cohort study. *Lancet Respir Med* 9: 239-250
86. Fiest KM, Krewulak KD, Ely EW, Davidson JE, Ismail Z, Sept BG, Stelfox HT, (2020) Partnering With Family Members to Detect Delirium in Critically Ill Patients. LID - 10.1097/CCM.0000000000004367 [doi]. *Critical Care Medicine*
 87. van den Boogaard M, Pickkers P, van der Hoeven H, Roodbol G, van Achterberg T, Schoonhoven L, (2009) Implementation of a delirium assessment tool in the ICU can influence haloperidol use. *Critical Care* 13: R131
 88. Spiegelberg J, Song H, Pun B, Webb P, Boehm LM, (2020) Early Identification of Delirium in Intensive Care Unit Patients: Improving the Quality of Care. *Crit Care Nurse* 40: 33-43
 89. Cerejeira J, Mukaetova-Ladinska EB, (2011) A clinical update on delirium: from early recognition to effective management. *Nurs Res Pract* 2011: 875196
 90. Steis MR, Evans L, Hirschman KB, Hanlon A, Fick DM, Flanagan N, Inouye SK, (2012) Screening for delirium using family caregivers: convergent validity of the Family Confusion Assessment Method and interviewer-rated Confusion Assessment Method. *J Am Geriatr Soc* 60: 2121-2126
 91. Shulman RW, Kalra S, Jiang JZ, (2016) Validation of the Sour Seven Questionnaire for screening delirium in hospitalized seniors by informal caregivers and untrained nurses. *BMC Geriatrics* 16: 44
 92. Cachón-Pérez JM, Alvarez-López C, Palacios-Ceña D, (2014) [Non-pharmacological steps for the treatment of acute confusional syndrome in the intensive care unit]. *Enferm Intensiva* 25: 38-45

93. Marra A, Ely EW, Pandharipande PP, Patel MB, (2017) The ABCDEF Bundle in Critical Care. *Crit Care Clin* 33: 225-243
94. Barry MJ, Edgman-Levitan S, (2012) shared decision-making--pinnacle of patient-centered care. *N Engl J Med* 366: 780-781
95. Azoulay E, Pochard F, Chevret S, Arich C, Brivet F, Brun F, Charles PE, Desmettre T, Dubois D, Galliot R, Garrouste-Orgeas M, Goldgran-Toledano D, Herbecq P, Joly LM, Jourdain M, Kaidomar M, Lepape A, Letellier N, Marie O, Page B, Parrot A, Rodie-Talbere PA, Sermet A, Tenaillon A, Thuong M, Tulasne P, Le Gall JR, Schlemmer B, (2003) Family participation in care to the critically ill: opinions of families and staff. *Intensive Care Med* 29: 1498-1504
96. Pochard F, Azoulay E, Chevret S, Lemaire F, Hubert P, Canoui P, Grassin M, Zittoun R, le Gall JR, Dhainaut JF, Schlemmer B, (2001) Symptoms of anxiety and depression in family members of intensive care unit patients: ethical hypothesis regarding decision-making capacity. *Crit Care Med* 29: 1893-1897
97. Azoulay E, Pochard F, Kentish-Barnes N, Chevret S, Aboab J, Adrie C, Annane D, Bleichner G, Bollaert PE, Darmon M, Fassier T, Galliot R, Garrouste-Orgeas M, Goulenok C, Goldgran-Toledano D, Hayon J, Jourdain M, Kaidomar M, Laplace C, Larché J, Liotier J, Papazian L, Poisson C, Reignier J, Saidi F, Schlemmer B, (2005) Risk of post-traumatic stress symptoms in family members of intensive care unit patients. *Am J Respir Crit Care Med* 171: 987-994
98. Brom L, Hopmans W, Pasman HR, Timmermans DR, Widdershoven GA, Onwuteaka-Philipsen BD, (2014) Congruence between patients' preferred and

- perceived participation in medical decision-making: a review of the literature.
BMC Med Inform Decis Mak 14: 25
99. Severinsson E, Holm AL, (2012) Knowledge gaps in nursing leadership - focusing on health care systems organisation. J Nurs Manag 20: 709-712
 100. McConnell B, Moroney T, (2015) Involving relatives in ICU patient care: critical care nursing challenges. J Clin Nurs 24: 991-998
 101. Au SS, Roze des Ordons A, Soo A, Guienguere S, Stelfox HT, (2017) Family participation in intensive care unit rounds: Comparing family and provider perspectives. J Crit Care 38: 132-136
 102. Haines A, Kuruvilla S, Borchert M, (2004) Bridging the implementation gap between knowledge and action for health. Bull World Health Organ 82: 724-731; discussion 732
 103. Kleinpell R, Zimmerman J, Vermoch KL, Harmon LA, Vondracek H, Hamilton R, Hanson B, Hwang DY, (2019) Promoting Family Engagement in the ICU: Experience From a National Collaborative of 63 ICUs. Crit Care Med 47: 1692-1698
 104. Braithwaite J, Herkes J, Ludlow K, Testa L, Lamprell G, (2017) Association between organisational and workplace cultures, and patient outcomes: systematic review. BMJ Open 7: e017708
 105. Banner D, Bains M, Carroll S, Kandola DK, Rolfe DE, Wong C, Graham ID, (2019) Patient and Public Engagement in Integrated Knowledge Translation Research: Are we there yet? Research Involvement and Engagement 5: 8

106. Grading F, Britten N, Wyatt K, Froggatt K, Gibson A, Jacoby A, Lobban F, Mayes D, Snape D, Rawcliffe T, Popay J, (2015) Values associated with public involvement in health and social care research: a narrative review. *Health Expect* 18: 661-675
107. Carlson EB, Spain DA, Muhtadie L, McDade-Montez L, Macia KS, (2015) Care and caring in the intensive care unit: Family members' distress and perceptions about staff skills, communication, and emotional support. *J Crit Care* 30: 557-561
108. Ackerman RA, Kashy DA, Donnellan MB, Conger RD, (2011) Positive-engagement behaviors in observed family interactions: a social relations perspective. *J Fam Psychol* 25: 719-730
109. Saha S, Beach MC, Cooper LA, (2008) Patient centeredness, cultural competence and healthcare quality. *J Natl Med Assoc* 100: 1275-1285
110. Jongen C, McCalman J, Bainbridge R, (2018) Health workforce cultural competency interventions: a systematic scoping review. *BMC* 18: 232
111. Galdas PM, Harrison AS, Doherty P, (2018) Gender differences in the factors predicting initial engagement at cardiac rehabilitation. *Open Heart* 5: e000764
112. Puchalski CM, (2001) The role of spirituality in health care. *Proc (Bayl Univ Med Cent)* 14: 352-357
113. Doody P, Lord JM, Whittaker AC, (2019) Assessing the feasibility and impact of an adapted resistance training intervention, aimed at improving the multi-dimensional health and functional capacity of frail older adults in residential care settings: protocol for a feasibility study. *BMC* 5: 86