Mental Health Sequelae in the Perioperative Period:

An Examination of Perioperative Dissociation, Postoperative Delirium, and Posttraumatic Stress

By

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A Thesis submitted to the Faculty of Graduate Studies of

The University of Manitoba

in partial fulfillment of the requirements of the degree of

MASTER OF ARTS

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Acknowledgements

This research was supported by a Canadian Institutes of Health Research Frederick Banting and Charles Best Canada Graduate Scholarship, a University of Manitoba Tri Council Master's Supplemental Award, the University of Manitoba Centre on Aging Esther and Samuel Milmont Scholarship, and a University of Manitoba Direct Aid to Achieve Award. First, I would like to thank my Master's co-supervisors, Dr. Renée El-Gabalawy and Dr. Kristin Reynolds for their dedication to this project and their continued mentorship, support, and encouragement. I would also like to thank my committee members, Dr. Corey Mackenzie and Dr. Rakesh Arora for their thoughtful input. I also acknowledge Ms. Desiree Gagnon for her assistance with transcription and coding and the ENGAGES-CANADA team, including primary investigators Drs. Eric Jacobsohn, Michael Avidan, Vincent Wourms, Tarit Saha, Alain Deschamps, and George Djaiani. Finally, I thank my loved ones for their support and encouragement.

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Abstract

Perioperative dissociation and postoperative delirium are adverse mental health outcomes that can occur in the context of surgery and are both independently associated with posttraumatic stress (PTS). Using quantitative and qualitative methodologies across two studies, this thesis aimed to identify whether symptom overlap exists between perioperative dissociation and postoperative delirium, examine how perioperative dissociation and postoperative delirium are associated with PTS (study 1; quantitative), understand how individuals describe and experience symptoms of dissociation and delirium, and examine the impact of these symptoms on the recovery process (study 2; qualitative). Both studies included a sub-sample of non-emergent surgical patients (study 1: $n = 181$; study 2: $n = 5$), aged 60 years and older, who participated in the Electroencephalography Guidance of Anesthesia to Alleviate Geriatric Syndromes (ENGAGES-CANADA; $N = 492$ at time of analysis) study. In study 1, a principal components analysis did not support symptom overlap between dissociation and delirium and multiple linear regressions revealed both symptom presentations were associated with PTS; however, differential relationships emerged according to the covariates included. Using qualitative methods informed by constructivist grounded theory, study 2 revealed a main theme of silence of perioperative mental health; participants did not describe or elaborate on perioperative mental health experiences when asked, and focused on their physical health-related experiences. Findings of these two studies highlight important similarities and differences between dissociation and delirium. In addition, results underscore the importance of communication, assessment, and monitoring of these symptoms, which may help reduce adverse perioperative mental health outcomes.

Keywords: perioperative dissociation, postoperative delirium, posttraumatic stress, surgery

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All surgical procedures carry some element of risk, ranging from mild postoperative discomfort and sleep disturbances, to intraoperative complications, postoperative infections, and mortality (e.g., Ghoneim & O'Hara, 2016; Harvey, 2012; Joshi & Kehlet, 2013; Marik & Flemmer, 2012; Semel et al., 2012). Though physical health complications are often the most salient and well-studied following surgery, a large body of research has begun investigating a range of negative mental health outcomes that are also common, including postoperative delirium (Arora, Djaiani, & Rudolph, 2017; Inouye, 2006; Inouye, Westendorp, & Saczynski, 2014; Witlox et al., 2010), perioperative dissociation (i.e., dissociation during and after surgery; Osterman, Hopper, Heran, Keane, & van der Kolk, 2001; Whitlock et al., 2015), and posttraumatic stress disorder (PTSD; Davydow, Gifford, Desai, Beedham, & Bienvenu, 2008; El-Gabalawy et al., 2019; Lesli, Chan, Myles, Forbes, & McCulloch, 2010; Whitehead, Perkins-Porras, Strike, & Steptoe, 2006). Though progress has been made toward better understanding the correlates and risk factors of perioperative mental health sequelae, little is known about their underlying features including interrelationships between these mental health outcomes. The aim of this thesis is to examine the relationships between perioperative dissociation, postoperative delirium, and posttraumatic stress (PTS; i.e., symptoms of PTSD) in a non-emergent mixed surgical sample of older adults.

Adverse Postoperative Outcomes

Worldwide, over 300 million major surgical procedures take place each year (Weiser et al., 2015). With advancements in medical technology and improvements in quality of care, there have been significant reductions in hospital patient morality rates (Zimmerman, Kramer, &

Knaus, 2013), consequentially leaving a larger proportion of individuals living with postoperative and post-discharge complications. Historically, the majority of research in this area has focused on physical health complications including acute or chronic postoperative pain (e.g., Apfelbaum, Chen, Mehta, & Gan, 2003; Joshi & Kehlet, 2013; Macrae, 2008), bleeding (e.g., Twersky, Fishman, & Homel, 1997), nausea and vomiting (e.g., Marshall & Chung, 1999), infections (e.g., Forrester et al., 2017; Marik & Flemmer, 2012; The International Surgical Outcomes Study Group, 2016), cardiovascular events (e.g., myocardial infarction, cardiac arrest, pulmonary embolism, stroke; Devereaux & Sessler, 2015; Kristensen et al., 2014; The International Surgical Outcomes Study Group, 2016), and mortality (e.g., Boehm, Baumgarten, & Hoeft, 2015; Botto et al., 2014; Hansen, Petersen, Dahl, & Wetterslev, 2016). More recently, however, there has been an increased focus on adverse mental health outcomes associated with both surgery and critical illness (e.g., Davydow et al., 2008; Pfeuffer et al., 2017; e.g., Dao et al., 2010; El-Gabalawy et al., 2019; Indja et al., 2017; Inouye, Westendorp et al., 2014; Jackson et al., 2007; Jackson et al., 2015; Kim, Kim, Kim, Park, & Choi, 2017; Latif, Shamsher Khan, & Nawaz, 2017; Theunissen et al., 2017). This shift may be in part the result of increasing recognition of the negative impact of mental health on the aforementioned physical health outcomes (e.g., Abrams, Vaughan-Sarrazin, & Rosenthal, 2010; Fox et al., 2013; Ghoneim & O'Hara, 2016; Menendez, Neuhaus, Bot, Ring, & Cha, 2014).

Relatedly, there is also growing awareness of the adverse mental health outcomes associated with being treated in the intensive care unit (ICU; e.g., Bienvenu & Neufeld, 2011; de Miranda et al., 2011; Marra, Pandharipande, & Patel, 2017; McGiffin, Galatzer-Levy, & Bonanno, 2016). Post-intensive care syndrome (PICS), defined as "new or worsening problems in physical, cognitive, or mental health status arising after a critical illness and persisting beyond

acute care hospitalization" (Needham et al., 2012, p. 505), is now commonly described in the critical care and perioperative literature (e.g., Gunderson, Walter, Ruskin, Ding, & Moore, 2016; Harvey, 2012; Jutte, Erb, & Jackson, 2015; Rawal, Yadav, & Kumar, 2017). More specific mental health sequelae that have been examined in ICU patient populations include PTSD (Davydow et al., 2008; Wade et al., 2012; Wade, Hardy, Howell, & Mythen, 2013), delirium (e.g., Bulic, Bennett, & Shehabi, 2015; Desai, Chau, & George, 2013), depression (e.g., Jackson et al., 2014), and anxiety (e.g., Nikayin et al., 2016), with prevalence estimates ranging from 8-27% (PTSD), 20-80% (delirium), 33-37% (depression), and 32-34% (anxiety; Davydow et al., 2008; Desai et al., 2013; Jackson et al., 2014; Nikayin et al., 2016; Wade et al., 2013). Thus, the increased focus on perioperative mental health in the literature may also relate to the large proportion of surgical patients who are admitted to the ICU postoperatively (e.g., 50% of Canadian ICUs were comprised of surgical patients in 2013-2014; Canadian Institute for Health Information, 2016). Mental health sequelae in the context of surgery and critical illness can be conceptualized using a diathesis-stress framework (Rosenthal, 1963), wherein a number of pre-existing vulnerabilities (i.e., diatheses; e.g., age, sex, preoperative mental health symptoms or conditions, cognitive impairment) interact with a stressor (e.g., surgery, receiving intensive care) and catalyze the expression of a mental disorder or compromised psychological state. This framework has previously been applied to understand the development of postoperative delirium (El-Gabalawy et al., 2017) and PTS (e.g., Martin, Halket, Asmundson, Flora, & Katz, 2010), among others.

Postoperative Delirium

One of the most commonly investigated adverse mental health outcomes following surgery, particularly among older adults (e.g., age 65 and older), is postoperative delirium

(Deiner & Silverstein, 2009; Indja et al., 2017; Inouye, 2006; Inouye, Robinson et al., 2014; Nguyen, Uminski, Hiebert, Tangir, & Arora, 2017; Raats, van Elijsden, Crolla, Steyerberg, & van der Laan, 2015; Reddy, Irkal, & Srinivasamurthy, 2017). The Diagnostic and Statistical Manual of Mental Disorders-5th edition (DSM-5; American Psychiatric Association, 2013) classifies delirium as a neurocognitive disorder characterized by (a) a disturbance in attention and awareness, (b) which develops over a short duration, and (c) a disturbance in cognition (e.g., perception deficit, memory deficit, disorientation). Other common symptoms of delirium include symptom fluctuation throughout the day, sleep-wake cycle disturbances, delusions, and psychomotor disturbances (Arora et al., 2017; Inouye, 2006; Inouye, Robinson et al., 2014). The DSM-5 also indicates that the disturbances cannot be explained by a pre-existing neurocognitive disorder or a state of severely reduced arousal (e.g., coma); rather symptoms are considered a direct consequence of a pre-existing medical condition, the effects of substance intoxication or withdrawal, exposure to a toxin, or multiple etiologies (American Psychiatric Association, 2013).

In contrast to other forms of delirium (e.g., delirium due to a medical condition), individuals with postoperative delirium tend to be more physically healthy prior to entering the hospital for surgery (Deiner & Silverstein, 2009); the onset of postoperative delirium typically occurs within hours, or up to a few days postoperatively (Cole, 2004). Elements associated with the surgical procedure itself including anesthetics/analgesics are considered implicated in the disorder's etiology in this context (Deiner & Silverstein, 2009; El-Gabalawy et al., 2017). However, controversy exists regarding the exact cause of postoperative delirium; some research highlights the role of anesthetic toxicity (Berger et al., 2018) whereas other studies underline the impact of anesthesia *delivery* on the brain (Mutch & El-Gabalawy, 2017; Mutch, El-Gabalawy, & Graham, 2018). The literature also suggests the complex interaction between predisposing

patient factors (i.e., diatheses; elaborated below) and exposure to both surgery and other stressors associated with perioperative care/postoperative recovery, are implicated in the development of postoperative delirium (Inouye, 2006). These stressors may include drugs (e.g., sedatives, narcotics), neurologic diseases (e.g., stroke, encephalitis), physiological stress (e.g., fever, infection, electrolyte imbalance, hypoxia, alterations in cerebral blood flow), environmental stressors (e.g., admission to the ICU), and sleep deprivation (Inouye, 2006). Some have thought of postoperative delirium as an "acute brain failure", or a signal of the brain's diminished reserve capacity, analogous to heart failure as a signal of the heart's diminished reserve capacity (Inouye, Westendorp et al., 2014). Others have suggested that postoperative delirium arises as the result of an inflammatory reaction associated with the stress of surgery (Deiner & Silverstein, 2009).

Prevalence estimates of postoperative delirium range from approximately 15-53% among surgical patients in general (Inouye, 2006), and may increase to 70% among cardiac surgical patients, depending on the specific type of procedure (Sockalingam et al., 2005). Postoperative delirium is associated with substantial financial burden, with a total estimated annual cost upwards of $150 billion in the United States (U.S.; Inouye et al., 2015; Inouye, Westendorp et al., 2014). In contrast to variations in opinion on etiology, there is general consensus surrounding risk factors (i.e., diatheses) of postoperative delirium. These include older age (typically over 65 or 70 years), premorbid cognitive impairment, poor functional status, symptoms of depression, alcohol abuse, and visual or hearing impairments at baseline (Arora et al., 2017; Deiner & Silverstein, 2009; Inouye, 2006; Inouye, Kosar et al., 2014; Inouye et al., 2015). There is also consistent evidence that postoperative delirium, including subsyndromal manifestations, is associated with a range of poor health outcomes, including increased length of hospital stay, increased risk of postoperative complications and functional decline, cognitive

impairment, post-discharge institutionalization, and mortality (e.g., Bulic et al., 2015; Girard et al., 2010; Inouye, Kosar et al., 2014; Pandharipande et al., 2013; Raats et al., 2015; Rudolph et al., 2010; Witlox et al., 2010). Postoperative delirium has also been found to be associated with adverse postoperative psychological outcomes, including PTSD (e.g., DiMartini, Dew, Kormos, McCurry, & Fontes, 2007; Drews et al., 2015), which will be discussed later in greater detail.

A growing body of literature has also begun exploring patients' experiences of delirium through qualitative research (e.g., Gaete Ortega, Papathanassoglou, & Norris, 2019; Instenes et al., 2018; Pollard, Fitzgerald, and Ford, 2015; Schmitt et al., 2019; Van Rompaey, Van Hoof, van Bogaert, Timmermans, and Dilles, 2016; Weir & O'Brien, 2019; Weissenberger-Leduc, Maier, & Iglseder, 2019). Instenes and colleagues (2018) identified six emergent themes from interviews with 10 patients who experienced delirium following cardiac surgery at 6-12 months post-discharge from hospital. These included: (1) "like dreaming while awake" (e.g., experiences did not feel real); (2) "disturbed experience of time" (e.g., difficulty figuring out the time of day); (3) "existing in a twilight zone" (e.g., the experience of frightening hallucinations); (4) "trapped in medical tubes" (e.g., restricted movement due to medical equipment); (5) moving between different surroundings (e.g., feeling as though one was no longer in the hospital); and (6) meeting with death and the deceased (e.g., the experience of having deceased relatives 'visit' while in hospital). In other qualitative research on delirium, patients recovering in the intensive care unit have described that communication with others was difficult while in a delirious state, feelings of fear, frustration, and anger were common, and sleep difficulties arose due to a disturbed experience of time (Van Rompaey et al., 2016). These emergent themes of fear and communication difficulties have also been identified from interviewing 11 individuals who experienced delirium following orthopedic surgery (Pollard et al., 2015). Patients in this study

also described feeling unsafe, trapped, and suspicious of others while delirious. A recent meta-ethnography that included nine qualitative studies of patients' experiences of delirium highlighted a main emergent theme across studies of 'experiencing an altered reality' (Gaete Ortega et al., 2019). As a whole, the qualitative literature has begun to describe the experience of having delirium, although continued investigation (qualitative and quantitative) is warranted to identify the impact these symptoms have on individuals who experience them, and features driving the associations with adverse mental health-related outcomes, such as PTSD.

Posttraumatic Stress Disorder

PTSD is prevalent in the perioperative period (El-Gabalawy et al., 2019) and rates are elevated among individuals who have experienced postoperative delirium (Drews et al., 2015). The DSM-5 classifies PTSD as a trauma and stressor-related disorder that arises following the experience of a traumatic event involving actual or threatened death, serious injury, or sexual violence (i.e., index trauma), and is characterized by symptoms of re-experiencing (e.g., intrusive memories, nightmares, flashbacks), avoidance (e.g., avoiding external reminders, avoiding thoughts and feelings), negative alternations in mood and cognition (e.g., persistent anger or guilt, inability to experience positive emotions, inability to remember important details), and hyperarousal (e.g., sleep disturbances, angry outbursts, exaggerated startle response; American Psychiatric Association, 2013). The DSM-5 criteria specifies that symptoms must be present for longer than one month, must cause clinically significant distress or functional disturbances, and are not caused by substance use or a pre-existing medical condition. If PTS symptoms resolve within one month following the index trauma, a diagnosis of acute stress disorder would be more appropriate (American Psychiatric Association, 2013).

Extant research demonstrates that serious and life-threatening medical conditions (e.g., cancer, cardiovascular disease, critical illness in general) can be considered traumatic and are capable of triggering PTSD (e.g., Cordova, Riba, & Spiegel, 2017; Edmondson, 2014; El-Gabalawy, Mota, Sommer, & Edmondson, 2018; Jackson et al., 2007; Sommer, Mota, Edmondson, & El-Gabalawy, 2018; Vilchinsky, Ginzburg, Fait, & Foa, 2017), with prevalence estimates ranging between 12-25% (among those with serious and life-threatening medical conditions; Edmondson, 2014). The traumatic nature of an adverse health condition may relate to receiving the diagnosis, invasive stages of treatment (including surgical procedures), or associated functional impairment (e.g., loss of bodily control, physical disability; Doolittle, 1991; Edmondson, 2014). Specific to surgery, prevalence estimates of PTSD have been identified that exceed double that of the general population (i.e., ~20% versus 6-7%; lifetime PTSD prevalence; El-Gabalawy et al., 2019; Kessler et al., 2005; Sommer, Mota, & El-Gabalawy, 2018; Whitlock et al., 2015). This is particularly problematic given that postoperative/post-ICU PTSD and medical condition-related PTSD are associated with a range of negative outcomes including poor quality of life (Parker et al., 2015), cognitive impairment (Davydow, Zatzick, Hough, & Katon, 2013), increased risk of cardiac events (Edmondson et al., 2012), and an increased risk of mortality (Dao et al., 2010).

As previously indicated, a diathesis-stress perspective can be applied to understand the development of PTSD (e.g., Martin, Halket, Asmundson, Flora, & Katz, 2010). This conceptualization may also extend to PTSD in the context of surgery, wherein a number of person-specific diatheses interact with surgical-related stressors. With respect to person-specific risk factors, certain sociodemographic characteristics are associated with postoperative PTS (similarly to PTSD in the general population; e.g., Goldstein at al., 2016), where females and

those who are younger in age are at increased risk (e.g., Davydow et al., 2008; El-Gabalawy et al., 2019; Gries et al., 2013; Liberzon et al., 2006). In addition, history of a mental health condition is a risk factor for postoperative PTS, including depressive disorders and anxiety disorders (e.g., Deisseroth & Hart, 2012; Jeantieu et al., 2014). In terms of surgical-related stressors, anesthetic awareness (i.e., unintentional consciousness during surgery) is a traumatic event considered capable of triggering postoperative PTS and PTSD (e.g., Leslie et al., 2010; Osterman et al., 2004; Whitlock et al., 2015). For example, among a non-emergent surgical cohort, over 40% of patients who experienced anesthetic awareness screened positive for postoperative PTSD compared to just over 15% who did not experience anesthetic awareness (Whitlock et al., 2015). Further, although many surgical procedures are elective, all surgeries are somewhat uncontrollable in nature due to their associated potential risks (El-Gabalawy et al., 2019). Prior research has noted an association between situations perceived as uncontrollable and PTS responses (Frazier, 2003), which may explain the occurrence of PTS or PTSD following surgery. In addition, acute postoperative pain has been recognized as a predictor of PTSD (e.g., Archer et al., 2016; Jeantieu et al., 2014). Another surgical-related stressor that is relevant to the development of PTS is receiving treatment in the ICU. The use of physical restraints (e.g., Jones et al., 2007), mechanical ventilation (e.g., Cuthbertson, Hull Strachan, & Scott, 2004), and benzodiazepines (e.g., Davydow et al., 2008), in addition to the recollection of frightening in-ICU experiences (e.g., Wade at al., 2015) have been identified as risk factors for post-ICU PTSD, with prevalence estimates of over 20% among ICU patients (e.g., Davydow et al., 2008; Jones et al., 2007; Parker et al., 2015). In addition to a number of stressors associated with surgery, some have suggested that surgery can be considered a stressor, in and of itself (Whitlock et al., 2015). Two other important risk factors associated with postoperative PTSD, as described

below in greater detail, are delirium and dissociation. For a more detailed description of risk factors of postoperative PTSD, see a recent review published by our group (El-Gabalawy et al., 2019).

Postoperative Delirium and Posttraumatic Stress Disorder

As indicated, postoperative delirium is also associated with, and supported as an independent risk factor for, postoperative PTS and PTSD (e.g., Bashar et al., 2017; Davydow et al., 2008; DiMartini et al., 2007; Drews et al., 2015; Jackson et al., 2015; Morrissey & Collier, 2016; Warlan, Howland, & Connelly, 2016). For example, over 80% of individuals with postoperative delirium (i.e., 62 out of 77) also screened positive for PTSD among a surgical sample of over 550 patients (Drews et al., 2015). In this study, postoperative delirium emerged as the only independent predictor of postoperative PTSD in a model with seven other hypothesized perioperative risk factors (i.e., postoperative pain, preoperative depression, age, physical health status, gender, duration of anesthesia, postoperative nausea and vomiting; Drews et al., 2015).

The relationship between postoperative delirium and PTSD is not clearly understood, however, a number of potential mechanisms in this relationship have been noted in the literature. The absence of factual postoperative memories and recollections of delusional memories from the delirious state are suggested as important mechanisms in the relationship between postoperative delirium and PTSD (e.g., Jones et al., 2007; Jones, Griffiths, Humphris, & Skirrow, 2001; Keikkas, Theodorakopoulou, Spyratos, & Baltopoulous, 2010; Marra et al., 2017; Wade et al., 2015). Delusional memories and/or lack of factual memories make it challenging for patients to piece together what they have experienced, or to differentiate delusions from facts, which may add to the traumatic nature of being hospitalized (Jones, Griffiths, & Humphris,

2000). Hallucinations and delusions of *life-threatening* events in particular may be especially traumatic (e.g., Davydow et al., 2008; DiMartini et al., 2007; Wade et al., 2015). For example, DiMartini and colleagues (2007) describe four transplant patients who had hallucinations of life-threatening events (e.g., being shot by the hospital staff while tied down by restraints in bed) while delirious and re-experienced those hallucinations as symptoms of PTSD. Wade and colleagues (2015) identified intrusive memories of frightening hallucinations and delusions (that may or may not have been attributed to delirium) as more common than factual intrusive memories among a sample of individuals with post-ICU PTSD in a mixed-methods study. Taken together, the evidence from these studies suggests that re-experiencing, particularly hallucinations and delusions, may be a predominant symptom of PTS in the context of delirium. An additional reason why these conditions commonly co-occur may be that many precipitating factors of postoperative delirium are also risk factors for postoperative PTS. As indicated above, these common factors include: history of a mental health condition, admission to the ICU, administration of sedatives, and use of physical restraints, among others. Despite the fact that these common factors and potential mechanisms have been identified, the relationship between postoperative delirium and postoperative PTSD is still largely unclear. Further investigation is needed in order to better understand how and why individuals with postoperative delirium may develop PTS or PTSD, and which symptoms of PTSD are most strongly associated with delirium.

Dissociation

Another independent risk factor of PTSD identified in the literature is dissociation (Briere et al., 2005; Candel & Merckelbach, 2004; de Miranda et al., 2011; Gandubert et al., 2016; Kangas, Henry, & Bryant, 2005; Osterman et al., 2001; Whitlock et al., 2015). Dissociation may

occur in the context of trauma (Briere, Scott, & Weathers, 2005; Choi & Seng, 2016; Dalenberg et al., 2012; Marmar et al., 1994; Marmar, Weiss, & Metzler, 1997) and can be defined as an acute psychological state characterized by constriction of consciousness or memory (i.e., restricted access to conscious awareness or memory), depersonalization (i.e., feeling detached from one's mental processes or body), derealization (i.e., experiencing unreality of surroundings), perceptual disturbances, micro-amnesias, and/or alterations in sensory-motor functioning (American Psychiatric Association, 2013). According to the DSM-5, dissociative symptoms can be classified as either "positive" or "negative". Positive dissociative symptoms (e.g., derealization, depersonalization) are experienced as intrusions into awareness and disjointed subjective experiences, whereas negative symptoms impair the ability to access information and control mental functions (e.g., amnesia; American Psychiatric Association, 2013). The term "peritraumatic dissociation" (i.e., dissociation around the time of a traumatic event) is commonly referred to in the trauma literature and has been conceptualized as an unconscious psychological response to threat, aimed at psychologically removing oneself from a traumatic experience or "detaching" from oneself during trauma; therefore increasing one's chances for survival (e.g., Dalenberg et al., 2012; McKinnon et al., 2016; Nurcombe, Scott, & Jessop, 2009). The symptom presentation of peritraumatic dissociation closely aligns with one of the other specified dissociative disorders outlined in the DSM-5, "acute dissociative reactions to stressful events". Due to the well-established relationship between dissociation and PTSD, the DSM-5 also includes a dissociative subtype of PTSD characterized by depersonalization and derealization in addition to clinically significant PTSD symptoms (American Psychiatric Association, 2013).

Although a large body of research has examined the association between trauma exposure and dissociation, few studies have investigated individuals' experiences of dissociation. A recent qualitative study identified three overarching themes that emerged through interviewing a sample of eight urban violence victims presenting with clinically significant symptoms of dissociation: (1) the inner world, (2) the outer world, and (3) observations made about the participant (Mattos, Pedrini, Fiks, & de Mello, 2016). With respect to the inner world, participants described feelings of unreality, out of body experiences, and somatic symptoms (e.g., shivering, chest pain). Gaps in memory, empty emotions, and uncertainty in judgment were outlined as subthemes related to the outer world, as they made it difficult for individuals to make sense of their surroundings and experiences (even beyond the context of the traumatic event). Within the third and final theme, Mattos and colleagues described others' observations of the individual who experienced dissociation. Caregivers had trouble grasping whether their loved ones (i.e., those exhibiting dissociative symptoms) were "going crazy" or whether they were "making up stories", and health professionals (i.e., psychiatric residents) noted that individuals who experienced dissociation seemed reluctant to embrace treatment and struggled to accept their state of impaired mental health. A second recent qualitative study examined differences in emotions, self-perception, memory, cognitive abilities, perception of time, experiences of unreality, and perception of the world between individuals with varying severity of dissociative symptoms (Gusics, Malesevic, Cardena, Bengtsson, & Sondergaard, 2018). Although a few other qualitative studies on dissociation exist (e.g., Anketell, Dorahy, & Curran, 2011; Auerbach, C. F., Mirvis, S., Stern, S., & Schwartz, 2009; Stein, Crompton, Ohry, & Solomon, 2016), very few outline how dissociative symptoms impact individuals. In addition, no research to my knowledge has qualitatively examined dissociation in a surgical context; such an investigation

may provide insight into how surgical patients describe dissociative symptoms and how other perioperative experiences (e.g., sleep deprivation, treatment in the ICU) and symptoms (e.g., delirium symptoms, PTS) may be related to dissociation. These insights may improve identification of and subsequent intervention for perioperative dissociation (i.e., dissociation during and around the time of the surgical period).

Dissociation and Posttraumatic Stress Disorder

Though research is limited on how dissociation is experienced in a peritraumatic context (and is non-existent in a perioperative context), a well-established literature has examined the mental health outcomes associated with dissociation. As indicated, peritraumatic dissociation may be considered a psychological defense mechanism to "detach" from oneself during a traumatic experience (e.g., Dalenberg et al., 2012; McKinnon et al., 2016; Nurcombe, Scott, & Jessop, 2009). Although this conceptualization of dissociation may appear adaptive in nature (i.e., at the time of the actual trauma), dissociation is a strong independent predictor of PTSD symptoms (Briere et al., 2005; Candel & Merckelbach, 2004; de Miranda et al., 2011; Gandubert et al., 2016; Kangas, Henry, & Bryant, 2005; Osterman et al., 2001; Whitlock et al., 2015) and other adverse mental health and neuropsychiatric outcomes including depression, anxiety, substance use, both suicide ideation and attempts, and decrements in executive functioning, memory, and attention (e.g., Blevins, Weathers, & Witte, 2014; McKinnon et al., 2016; Tsai, Armour, Southwick, & Pietrzak, 2015). Dissociation is also a suggested mediator in the relationship between trauma exposure (including interpersonal violence, childhood trauma, and natural disasters, among others) and PTS (Aho, Proczkowska Bjorklund, & Svedin, 2017; DeCou, Lynch, Cole, & Kaplan, 2016; Ozdemir, Boysan, Guzel Ozdemir, & Yilmaz, 2015; van Dijke, Ford, Frank, & van der Hart, 2015).

Extant research suggests that dissociation interferes with the encoding and immediate processing of traumatic memories, which increases the likelihood of developing PTSD (e.g., Briere et al., 2005; Ehlers & Clark, 2000; Peltonen, Kangaslampi, Saranpaa, Qouta, & Punamaki, 2017). For example, a content analysis of the traumatic memories of motor vehicle accident survivors with and without acute stress disorder (ASD) demonstrated substantially greater disorganization (e.g., disjointedness, confusion, unnecessary repetition) and dissociation content (e.g., description of detachment, reduced awareness, derealization, amnesia, numbing) among those with ASD compared to those without (Harvey & Bryant, 1999). Dissociation may also occur beyond the peritraumatic period in the context of the dissociative PTSD subtype, which captures an estimated 15-30% of individuals with PTSD (McKinnon et al., 2016). The dissociative PTSD subtype has been associated with increased severity of PTS, especially re-experiencing (e.g., Ross, Banik, Dedova, Mikulaskova, & Armour, 2017) and avoidance (e.g., Choi et al., 2017) symptoms, and greater rates of comorbid mental health conditions, compared to PTSD without dissociation (de Miranda et al., 2011; Hansen, Ross, & Armour, 2017; McKinnon et al., 2016; Tsai et al, 2015).

Perioperative dissociation and posttraumatic stress disorder. As indicated, perioperative dissociation refers to dissociation during or around the time of the surgical period. Research suggests an important factor implicated in those who experience dissociation is perceived physical threat during a traumatic event (e.g., McDonald et al., 2013; Morgan et al., 2001). Surgery represents a unique potentially traumatic experience in that it is a predictable stressor characterized by physical threat, and is associated with rates of PTSD that are substantially higher than what has been reported in the general population (Davydow et al., 2008; El-Gabalawy et al., 2019; Kessler at al., 2005; Sommer et al., 2018; Whitlock et al., 2015).

Research suggests that dissociation in the context of surgery may be associated with postoperative PTSD (El-Gabalawy et al., 2019; Osterman et al., 2001; Whitlock et al., 2015). For example, among a sample of 16 patients who experienced intraoperative awareness and 10 controls who did not, perioperative dissociation (defined as having "left your body at some point" or that "at some point you could mentally escape what was happening to you") was a significant predictor of postoperative PTSD in the full sample (Osterman et al., 2001). A recent study conducted by Whitlock and colleagues (2015) also found that in a large sample of over 300 adults undergoing primarily cardiac, general, or gynecologic surgery, perioperative dissociation was the strongest predictor of postoperative PTSD. Perioperative dissociation was also identified as a potential mediator in the relationship between anesthetic awareness and incident postoperative PTS. However, in both studies outlined above, dissociation was assessed using one or two individual self-report items (i.e., Osterman et al., 2001: "left your body at some point" or "at some point you could mentally escape what was happening to you"; Whitlock et al., 2015: "feeling that one is numbed, dazed, or dreaming during a real event"). No research to my knowledge has comprehensively evaluated perioperative dissociation using a well-validated measure.

Dissociation and Postoperative Delirium

Despite the strong established associations between dissociation and PTSD (both across trauma types, and in the perioperative period in particular; Briere et al., 2005; Candel & Merckelbach; Osterman et al., 2001; Whitlock et al., 2015) and postoperative delirium and PTSD, and the occurrence of all three symptom presentations in a surgical context (e.g., Drews et al., 2015; Inouye et al., 2015; Osterman et al., 2001; Raats et al., 2015; Whitlock et al., 2015), no research to my knowledge has investigated the relationship between all three conditions in a

single study. In addition to both being independent predictors of PTSD (e.g., Drews et al., 2015; Kangas et al., 2005; Osterman et al., 2001) and particularly associated with re-experiencing symptoms (e.g., DiMartini et al., 2007; Ross et al., 2017; Wade at al., 2015), postoperative delirium and dissociation exhibit many similar characteristics. Qualitative and quantitative studies of delirium or dissociation individually have demonstrated that both conditions are characterized by fragmentation of consciousness, disruption of memory consolidation, and perceptual disturbances, all of which also play important roles in the development of PTS (e.g., Briere et al., 2005; Davydow et al., 2008; DiMartini et al., 2007; Ehlers & Clark, 2000; Halligan, Michael, Clark, & Ehlers, 2003; Marra et al., 2017; Wade et al., 2015).

A number of delirious symptoms also appear to align with identified underlying factors of dissociation (see Figure 1 for a hypothesized outline of how delirium and dissociation symptoms may cluster together). For example, factor analytic studies of the Peritraumatic Dissociative Experiences Questionnaire (PDEQ; Marmar et al., 1997), a well-validated and commonly used self-report measure of peritraumatic dissociation, have supported a two-factor model of dissociation (e.g., Brooks et al., 2009; Sijbranji et al., 2012). The first factor, typically labelled “derealization and depersonalization” reflects perceptual distortions of the self and the world, similar to the positive dissociative symptoms outlined in the dissociative disorders chapter of the DSM-5. This factor was associated with poor mental health outcomes including acute stress, PTS, anxiety, and depression, whereas the second identified latent factor, “altered awareness” was not associated with these outcomes (Brooks et al., 2009; Sijbranji et al., 2012). The perceptual disturbances commonly experienced during delirium, which are suggested as a mechanism in the relationship between delirium and PTSD, appear to align conceptually with this derealization and depersonalization factor (or positive dissociative symptoms).

The second factor of dissociation, altered awareness, is characterized by disturbances in information processing (related to the trauma) and corresponds with the negative dissociative symptoms outlined in the dissociative disorders chapter of the DSM-5. In contrast to findings from factor analytic studies, this factor also may be implicated in the relationship between dissociation and PTSD; a large body of research has recognized the importance of fragmented and disorganized memories of a trauma as an important mechanism in the development of PTSD (e.g., Briere et al., 2005; Ehlers & Clark, 2000; Peltonen et al., 2017). Delirious symptoms of disorientation, inattention, memory impairment, and disorganized thinking appear closely related to the altered awareness factor (or negative dissociative symptoms). As indicated above, these symptoms (e.g., disorganized thinking, memory impairment) have been known to interfere with the cognitive processing of a traumatic event, which is associated with the development of PTS; however, this has not been explicitly investigated among individuals with delirium. In indirect support of the relevance of altered awareness in both dissociation and delirium, both conditions are associated with poor neuropsychological functioning (e.g., Bulic et al., 2015; Deiner & Silverstein, 2009; Girard et al., 2010; Halligan et al., 2003; Inouye et al., 2-15; Inouye, Westendorp et al., 2014; McKinnon et al., 2016; Pandharipande et al., 2013).

Although the latent factors of dissociation appear to be conceptually linked to symptoms of delirium, this has not yet been investigated by existing research nor has it been recognized by DSM nomenclature. Existing DSM-5 diagnostic criteria of delirium (i.e., disturbance in attention/awareness, disturbance in cognition) appear to overlap with the altered awareness factor of dissociation, so individuals with delirium likely experience negative dissociative symptoms; however, in light of the nature of these symptoms (and their impact on cognitive functioning), individuals with delirium may not recall having these symptoms, and subsequently would not

endorse them via self-report, for example. However, only subsets of individuals with delirium endorse symptoms of PTS, which may suggest the importance of additional delirious symptoms (not required for the diagnosis) in vulnerability for PTSD. Perhaps the addition of positive dissociative features to the presentation of delirium (which would likely already include negative dissociative features) represents a "dissociative subtype" of delirium, which might be a driving factor in the relationship between delirium and PTS. These positive dissociative symptoms (e.g., perceptual disturbances) are not required for a delirium diagnosis but have been described in a number of delirium cases, particularly among those who suffer from postoperative PTSD (e.g., DiMartini et al., 2007; Wade et al., 2015).

In addition to considering conceptual overlapping features, understanding transdiagnostic properties and physiological mechanisms may help elucidate the associations between dissociation, delirium, and PTS. Dissociation may be conceptualized as a transdiagnostic mechanism (e.g., McKinnon et al., 2016) in light of its occurrence in the context of various psychiatric disorders including major depressive disorder (e.g., Parlar, Frewen, Oremus, Lanius, & McKinnon, 2016), anxiety disorders (e.g., Sierra, Medford, Wyatt, & David, 2012), substance use disorders (e.g., Evren, Sar, Karadag, Tamar Gurol, & Karagoz, 2011), and bipolar disorder (e.g., Hariri et al., 2015), in addition to disorders more commonly associated with trauma such as PTSD (e.g., Armour, Karstoft, & Richardson, 2014), dissociative disorders (e.g., Spiegel et al., 2013), and borderline personality disorder (e.g., Vermetten & Spiegel, 2014). To this end, dissociation may be considered a constellation of symptoms (e.g., detachment, unreality, and fragmented consciousness) that occur transdiagnostically (i.e., shared by various disorders/diagnoses), including in the context of delirium. Similarly to dissociative PTSD (Choi et al., 2017; Hansen et al., 2017; McKinnon et al., 2016; Ross et al., 2017; Tsia et al., 2015), it is

possible that dissociation in the context of delirium may be associated with greater symptom severity and poorer outcomes, such as increased psychiatric comorbidity (e.g., PTSD). Alternatively, biological and physiological mechanisms, such as hypothalamic-pituitary adrenal axis (HPA axis) dysregulation, have been examined across these conditions and may help explain the complex relationship between dissociation, delirium, and PTS. The HPA axis is activated by stress, which triggers the release of cortisol (Kyrou, & Tsigos, 2009; Robertsson et al., 2001). Both over- and under-secretion of cortisol may be a signal of HPA axis dysfunction. Prior research has found atypical levels of cortisol on either end of the spectrum (i.e., elevated or reduced) among individuals with dissociation (Inslicht et al., 2011; McKinnon et al., 2016), postoperative delirium (Kazmierski, Banys, Latek, Bourke, & Jaszewski, 2013; McIntosh et al., 1985), and PTS (Seng et al., 2018; Zaba et al., 2015), which may suggest a common physiological mechanism at play; however, this has yet to be formally examined. Further investigation is warranted to determine the extent of the similarities between these conditions and to identify potential reasons why these similarities exist.

Limitations of Prior Research

Although the perioperative literature on mental health sequelae has recently grown considerably, this body of work is still in its infancy, and some key gaps and limitations are apparent. First, as indicated, no research to my knowledge has examined the relationship between delirium and dissociation. Considering the apparent symptom overlap and common associations with PTSD, a comprehensive understanding of the relationship between delirium and dissociation could provide valuable insight to the development of postoperative PTS. Second, only two studies to date have explicitly examined perioperative dissociation and its association with postoperative PTS, although neither utilized a validated and comprehensive

assessment of dissociation. Third, to my knowledge, no research has examined the relationship between the severity of postoperative delirium and PTS; delirium is typically assessed as either present or absent. Confusional states exist on a spectrum (rather than as a dichotomy) and recent research suggests that poor outcomes are also associated with delirium severity that does not meet full threshold levels (Inouye, Kosar et al., 2014). An assessment of delirium severity may provide further insight into the association between postoperative delirium and PTS. Fourth, although qualitative studies have begun outlining individuals' descriptions of their delirious experiences, this area of research is still in need of continued exploration. Further examination of how delirious symptoms impact individuals (e.g., psychologically, socially, physically) is warranted. Finally, there is a lack of qualitative research examining dissociation in general and no qualitative research, to my knowledge, has examined dissociation in a surgical context. Understanding individuals' dissociative experiences associated with surgery may provide insight toward how these symptoms are associated to related constructs and outcomes, namely delirium and PTS.

Summary of Objectives and Hypotheses

As a result of the above-described gaps in the literature, this thesis aimed to comprehensively examine the relationship between perioperative dissociation, postoperative delirium, and PTS in two studies using both quantitative and qualitative methodologies. Study 1 aimed to: (1) identify the symptom overlap and common components (i.e., symptom clusters formed according to shared variance) between perioperative dissociation and postoperative delirium and (2) examine the associations between perioperative dissociation and postoperative delirium components with PTS (total PTS and PTS symptom clusters). Based on the reviewed literature, I hypothesized at least two common components would be identified among

perioperative dissociation and postoperative delirium (hypothesis 1A), one of which would be characterized by feelings of unreality and perceptual disturbances (hypothesis 1B), and a second characterized by alterations in awareness (e.g., confusion, disorientation, memory impairment; hypothesis 1C). In addition, I hypothesized there would be at least two components that were condition-specific (e.g., dissociation specific [feeling on automatic pilot] or delirium specific [sleep/wake cycle disturbances, psychomotor agitation]; hypothesis 1D; see Figure 1 for hypothesized components). I also predicted that elevations in components characterized by both perioperative dissociation and postoperative delirium would be significantly and positively associated with PTS (hypothesis 2A), to a larger effect than components characterized by either condition alone (hypothesis 2B). In addition, across the PTS symptom clusters, I suspected the strongest associations would emerge for associations with re-experiencing symptoms (hypothesis 2C).

Using qualitative methodology, study 2 aimed to build on the aims of study 1 through (1) examining how individuals with postoperative delirium and perioperative dissociation describe and experience their symptoms, and (2) understanding the impact these symptoms have on postoperative recovery. I was interested in identifying whether individuals describe symptoms of delirium and dissociation in similar or distinct ways. I was also interested in whether individuals who experience these symptoms describe emotional, functional, or mental health challenges and how those challenges affect their overall health and quality of life.

Study 1 Method

Participants

Study 1 utilized a subset of secondary data from the Electroencephalography Guidance of Anesthesia to Alleviate Geriatric Syndromes (ENGAGES-CANADA; University of Manitoba,

2016; clinical trials identifier NCT02692300) study. ENGAGES-CANADA is an ongoing randomized clinical trial investigating whether the use of intraoperative electroencephalography (EEG) guidance during general anesthesia can reduce the incidence of postoperative delirium and other adverse postoperative outcomes, and is a parallel study to the ENGAGES study in the U.S. (Wildes et al., 2019). The sample consisted of 492 older adults (at the point of data analysis for this thesis; recruitment is ongoing), aged 60 years and older, who underwent a major elective surgery (cardiac: coronary artery bypass grafting, aortic valve replacement, mitral valve replacement, tricuspid valve replacement, hemiarch aortic repair; non-cardiac: vascular, laparotomy, thoracic, other) at the Health Sciences Centre in Winnipeg (n = 61), St. Boniface hospital in Winnipeg (n = 262), Kingston General Hospital in Kingston (n = 81), and the Montreal Heart Institute in Montreal (n = 88), requiring a minimum stay of two days postoperatively. Of these participants, 116 were recruited from the discontinued non-cardiac sample (from Health Sciences Centre, St. Boniface Hospital, and Kingston General Hospital); following an interim analysis that showed no differences in anesthetic depth between the intervention and control groups, the non-cardiac arm of the trial was discontinued, but analyses for secondary trial aims are still being pursued with these data. Participants were excluded if they: were unable to provide informed consent, were undergoing neurosurgical procedures, screened positive for delirium preoperatively or could not participate in delirium screening (due to being blind, deaf, illiterate, or not fluent in English), had a history of intraoperative awareness, or had a second planned surgery occurring within five days of the initial surgery. The Research Ethics Board at the University of Manitoba Bannatyne campus provided ethical approval for the ENGAGES-CANADA study and the use of these data, and all participants recruited gave witnessed informed consent.

Procedure

Participants participated in three phases of assessment. Recruitment took place approximately 1-2 weeks before surgery, at patients' regularly scheduled pre-anesthesia clinic (PAC) appointment. Consenting participants were immediately provided study measures for the preoperative phase of assessment. During this phase, patients reported demographic information (i.e., age, sex, race/ethnicity, education) and completed 13 self-report and administered measures assessing psychiatric symptoms (e.g., depressive/anxiety symptomatology, PTS, alcohol misuse) and cognitive functioning (e.g., dementia, subjective cognitive abilities, subjective cognitive concerns). Those who were able completed measures independently, however if needed, research personnel were available to provide assistance and answer any questions that arose during assessment. Trained personnel also administered certain cognitive assessments (e.g., Short Blessed Test) and a structured clinical interview to assess delirium (described below) preoperatively. During in-hospital recovery, postoperative delirium was assessed daily (at a time of convenience until discharge; described below), and three mental health self-report measures were completed at the time of discharge (e.g., assessing perioperative dissociation, peritraumatic distress). Thirty days following discharge, participants completed eight self-report measures (e.g., to assess PTS, depressive/anxiety symptomatology, subjective cognitive concerns, subjective cognitive abilities), distributed by mail with a stamped and addressed envelope for return upon completion. For the purpose of the current study, only select measures from each stage were included (refer to Figure 2 for assessment timeline).

Primary Measures

Postoperative delirium. The Confusion Assessment Method-Severity measure (CAM-S; Inouye, Kosar et al., 2014) assessed the presence and severity of postoperative delirium each

day, beginning on postoperative day 0 (day of surgery) through postoperative day 5 (unless discharged prior to day 5). The CAM-S is a comprehensive and well-validated structured clinical interview for assessing delirium with high inter-rater reliability, construct validity, and predictive validity (Inouye, Kosar et al., 2014). Well-trained interviewers conducted the CAM-S assessments, which required approximately 15 minutes to complete. Training involved familiarization with the interview and scoring system, practicing clinical judgment of delirium status while watching video recordings of participants portraying various presentations of delirium severity, shadowing CAM-S assessments performed by an expert interviewer, and performing supervised CAM-S assessments until two cases of delirium were encountered and identified. In circumstances where delirium status or symptoms were difficult to assess, the research team reviewed these cases as a group to reach consensus. In cases where patients could not complete the CAM-S long-form (e.g., not enough time), the briefer CAM-S short-form (i.e., first four items of the CAM-S long-form) was administered. In addition, if the daily CAM-S assessment was missed, a chart review was performed and information was included as to whether the participant was delirious according to the CAM-ICU (Ely et al., 2001), administered daily by nursing staff as standard of care. The CAM-S long-form assesses the following 10 symptoms of delirium: acute onset/symptom fluctuation in mental status, inattention, disorganized thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbances, psychomotor agitation, psychomotor retardation, and sleep-wake cycle disturbances. Acute onset/symptom fluctuation (within the past 24-hours) is identified as either absent (score of 0) or present (score of 1), and the remaining nine symptoms are identified as absent (score of 0), mild (score of 1), or marked (score of 2). Summing the scores of all 10 items creates a total severity score, ranging from 0-19. I reported the peak severity score (i.e., the

highest severity score across all CAM-S assessments) in line with prior research (e.g., El-Gabalawy et al., 2017; Inouye, Kosar et al., 2014); in cases where only the short-form was completed, only those four items were included in the peak severity score. A diagnosis of postoperative delirium was based on the presence of acute onset/symptom fluctuation in mental status, inattention, and either disorganized thinking or altered level of consciousness, in line with prior research (e.g., Ely et al., 2001). Subsyndromal postoperative delirium was defined by having a severity score of 5 or greater, on at least one postoperative day, without meeting criteria for full delirium. This cut off is in accordance with prior research (e.g., El-Gabalawy et al., 2017) and has been associated with poorer outcomes (e.g., functional decline, cognitive impairment, risk of increased length of hospitalization, mortality within 90 days postoperatively) compared to lower severity scores (Inouye, Kosar et al., 2014). The internal consistency for the CAM-S long-form in the current study from postoperative day 0-postoperative day 5 ranged from α: .993-.998.

Perioperative dissociation. The Peritraumatic Dissociative Experiences Questionnaire (PDEQ; Marmar et al., 1997) assessed perioperative dissociation at discharge from hospital. The PDEQ is a reliable (internal consistency from prior research: α = .78-.85; Birmes et al., 2001; Birmes et al., 2005; Olde et al., 2008) and valid (Birmes et al., 2005; Marmar et al., 1997) self-report assessment of dissociation symptoms, which includes 10 items rated on a 5-point scale (1 = *not true at all*, to 5 = *extremely true*). Summing the scores from the 10 items creates a total score (ranging from 10-50), with a score above 15 indicating clinically significant dissociation (Brunet, 2009; Mattos et al., 2016). For the purpose of this study, the dichotomous scoring (i.e., ≤15 vs. >15) was included descriptively and individual items and the continuous scoring were used for primary analyses. The instructions from the original format of the PDEQ were modified

for the purpose of this study in order to ensure participants rated their symptoms specifically related to their surgery ("*Please complete the items below by circling the number that best describes the experiences you had during your surgery and/or the days following your surgery when you were in hospital. If an item does not apply to your experience, please circle 'not true at all'."*). The internal consistency for the PDEQ total score at discharge in the current study was α = .899.

Posttraumatic stress. The Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5; Weathers et al., 2013) assessed past-month PTS preoperatively and at 30-day follow-up. The PCL-5 is a 20-item self-report measure that assesses PTS in accordance with DSM-5 criteria. Each item is rated on a 5-point scale, ranging from 0 [*not at all*] to 4 [*extremely*]. Summing the scores from each of the 20 items creates a total symptom severity score, ranging from 0-80. A cut off score of 33 has been suggested for clinically significant PTS (e.g., Bovin et al., 2016; Weathers at al., 2013). Alternatively, items can be separated into PTSD symptom clusters of re-experiencing (i.e., cluster B; items 1-5; e.g., "repeated, disturbing, and unwanted memories of the stressful experience"), avoidance (i.e., cluster C; items 6-7; e.g., "avoiding memories, thoughts, or feelings related to the stressful experience"), negative alterations in mood and cognition (i.e., cluster D; items 8-14; e.g., "trouble remembering important parts of the stressful experience"), and hyperarousal (i.e., cluster E; items 15-20; "irritable behavior, angry outbursts, or acting aggressively"). Using this method, summing the scores on the appropriate items for each cluster creates a cluster severity score. Further, each item rated as 2 [*moderately*] or higher is considered endorsed. Endorsement of at least one re-experiencing symptom, one avoidance symptom, two negative alterations in mood and cognition symptoms, and two hyperarousal symptoms suggests a probable PTSD diagnosis. For the purposes of this study, I examined the

continuous total and individual cluster symptom severity scores for primary analyses. Prior research on illness- and medical-treatment-related PTSD suggests subthreshold levels of PTS are more common than full threshold PTSD in this population (Tedstone & Tarrier, 2003); this suggests a dimensional or continuous examination of PTS may be most appropriate for the current study. For descriptive purposes, I also reported the frequency and proportion of individuals meeting the cut off score for a probable PTSD diagnosis. The preoperative PCL-5 score was examined as a covariate, in order to determine that the PTS captured postoperatively was independent from elevated pre-existing PTS, and the 30-day follow-up PCL-5 score was included as a primary outcome. The PCL-5 has demonstrated excellent reliability (internal consistency: α = .90-.95) and validity (Ashbaugh, Houle-Johnson, Herbert, El-Hage, & Brunet, 2016; Blevins, Weathers, Davis, Witte, & Domino, 2015; Bovin et al., 2016; Sveen, Bondjers, & Willebrand, 2016), and has a specificity of .95, and sensitivity of .85 (Ashbaugh et al., 2016). The internal consistency for the PCL-5 total score at 30-day follow-up in the current study was α = .917 (see Appendix A for primary measures). Of note, the original format of the PCL-5 was modified for the 30-day follow up; following the written directions, two questions were included: "*Was your surgery your most stressful experience? (circle one) YES/NO"* and "*If you responded "no", the most stressful event you experienced was: _____ (event) on _____ (date)*". Of those who completed the PCL-5 at 30-day follow-up, 63.8% indicated their surgery was their most stressful event.

Covariates

Sociodemographics. Age was assessed continuously and sex was assessed dichotomously (i.e., male, female). These sociodemographics have been associated with PTSD either in the context of surgery specifically, or in the general population (Davydow et al., 2008;

Goldstein at al., 2016; Gries et al., 2013; Patel et al., 2016; Liberzon et al., 2006). Due to high rates of attrition in the current study, a large proportion of missing data, and therefore reduced statistical power associated with the lower total sample size than anticipated (described below), I was required to limit the number of covariates included in the regression models. As a result I chose to exclude race/ethnicity and education as covariates for regressions; although research has found associations between these sociodemographic characteristics and PTSD, the evidence is less consistent for these characteristics compared to age and sex (e.g., Giannon-Pastor, Eiroa-Orosa, Fidel Kinori, Arguello, & Casas, 2016; Grekin & O'Hara, 2014; Karam et al., 2014; Tang, Deng, Gilk, Dong, & Zhang, 2017).

Depression and anxiety. The 4-item Patient Health Questionnaire for Depression and Anxiety (PHQ-4; Kroenke, Spitzer, William, & Lowe, 2009) assessed depressive and anxiety symptomatology using a two-week timeframe, and was administered preoperatively, at discharge (with a modified timeframe of "since surgery"), and at 30-day follow-up. The PHQ-4 is comprised of the first two items of the PHQ-8 (known as the PHQ-2, which assess the two core criteria for depressive disorders) in addition to the first two items of the Generalized Anxiety Disorder-7 Scale (GAD-7; known as the GAD-2, which assess the two core criteria for GAD). Items are rated on a 4-point scale ranging from 0 [*not at all*] to 3 [*nearly every day*]. Summing the scores from each of the four items creates a total severity score, ranging from 0-12. Cut off scores (e.g., 6 = significant symptom severity, 9 = positive screen of a depressive/anxiety disorder; Lowe et al., 2010) have been established for the total score, as well as depression (items 1 and 2) and anxiety (items 3 and 4) subscales (Kroenke et al., 2009; Lowe et al., 2010). However, for the purpose of this study, the PHQ-4 was assessed continuously; continuous measurement maintains greater measure-specific variability in the data, which helps conserve

statistical power (Royston, Altman, & Sauerbrei, 2006). In addition, as with PTS, it is likely that subthreshold manifestations of depression and anxiety are more common among this population compared to full threshold levels, making continuous measurement more appropriate. The PHQ-4 has demonstrated acceptable internal consistency and good construct validity (Lowe et al., 2010). The preoperative PHQ-4 score was examined as a covariate, as preoperative depressive and anxiety disorders are risk factors for postoperative PTSD (e.g., Deisseroth & Hart, 2012; Jeantieu et al., 2014). The internal consistency for the PHQ-4 total score at preoperative assessment in the current study was $\alpha = .795$.

Analytic Strategy

Before conducting the primary analyses I examined the skew and distribution of the primary continuously assessed variables (i.e., perioperative dissociation, postoperative delirium severity, PTS). Next, I examined the proportion of missing data and whether or not these data were missing completely at random. I also examined statistical assumptions for primary analyses including sampling adequacy, linearity, multicollinearity, multivariate normality, and homoscedasticity (described in greater detail in the results).

After testing assumptions for primary analyses I assessed the means and standard deviations for all primary measures (i.e., CAM-S, PDEQ at discharge, PCL-5 at 30-day follow-up), along with the prevalence estimates and cell sizes of those exceeding designated cut off scores. I ran these descriptive statistics both among the entire sample ($N = 492$) and among those who completed all primary measures only ($n = 181$). In addition, as a sensitivity analysis, I examined whether there were differences in mean scores on primary measures according to type of surgery (i.e., cardiac versus non-cardiac) and among those who completed all primary measures versus those who did not. I also conducted chi-square analyses and analyses of

variance (ANOVAs) to determine whether differences emerged in sociodemographic characteristics and mental health symptoms according to study follow-up components completed.

In line with aim 1 (i.e., to identify the symptom overlap and common components between perioperative dissociation and postoperative delirium), I conducted a principal components analysis (PCA) with an oblique (direct oblimin) rotation to examine overlap at an item-specific level. PCA is a dimension reduction technique that can identify underlying constructs that exist within a set of measures or individual variables (Field, 2013). PCA was chosen as the extraction method as opposed to principal axis factoring (i.e., traditional factor analysis) in order to include total item variance (i.e., common variance, unique variance, and residual variance) in the analysis, as opposed to common variance only; considering the exploratory nature of this analysis and the hypothesis that some items may not exhibit overlap with other items, it seemed appropriate to maintain unique and residual item variance to estimate the components. An oblique rotation was selected to enable the possibility of emergent components that are correlated (Costello & Osborne, 2005). Before running the PCA, I examined the correlation matrix of the 10 items from each measure in order to scan for items that should be not be included in the PCA (i.e., items with particularly small correlations, items with perfect correlations). The PCA reduced the items on the PDEQ and CAM-S long-form (or short-form, in cases where the long-form was not completed) into latent components according to the amount of total variance explained by groups of inter-correlated items. I determined the optimum number of components by examining the derived eigenvalues and scree plot (retaining components prior to a noticeable drop in eigenvalues), as well as the percentage of variance explained by each component.

Next, in accordance with aim 2 (i.e., to examine the association between perioperative dissociation and postoperative delirium components with PTS), I conducted multiple linear regressions to examine the associations between perioperative dissociation and postoperative delirium (independent variables) with postoperative PTS (dependent variable). Derived principal components were intended as the independent variables; however, as described below based on results of aim 1, CAM-S and PDEQ total scores were used as independent variables instead. In addition to examining total PTS as a dependent variable, I also examined individual PTS symptom clusters as separate dependent variables (i.e., re-experiencing, avoidance, negative alterations in mood and cognition, hyperarousal). I conducted four models for these regressions including unadjusted models examining both delirium and dissociation as independent predictors of PTS, a second model adjusting for sociodemographics (i.e., age, sex), a third model additionally adjusting for preoperative mental health symptoms (i.e., preoperative depressive/anxiety symptomatology, preoperative PTS), and a final model that also included perioperative dissociation and postoperative delirium concurrently. I conducted a power analysis with G*Power (Faul, Erdfelder, Buchner, & Lang, 2009) in line with the most stringent model of the proposed regression analyses (indicating 6 proposed predictors; age, sex, preoperative depressive/anxiety symptomatology, preoperative PTS, perioperative dissociation, postoperative delirium), which determined that in order to attain 0.95 power and a medium effect size, with an alpha of .05, I would need 146 participants. Analyses were conducted using SPSS software (version 25; IBM Corp., 2017).

Study 1 Results

Data Screening

Univariate normality. All primary variables (i.e., peak CAM-S, PDEQ at discharge, PCL-5 at 30-day follow-up) were assessed for univariate normality. As indicated by an absolute skew value < 2 (West, Finch, & Curran, 1995), peak CAM-S scores did not significantly depart from a normal distribution (skew = 0.80, *SE* = 0.12). PDEQ at discharge (skew = 3.03, *SE* = 0.15) and PCL-5 at 30-day follow-up (skew = 3.23, *SE* = 0.15) were non-normally distributed and positively skewed. To correct for departures from normality, PDEQ variables (item-level data required for PCA) were transformed using log transformations (Keene, 1995). A square root transformation was used for the PCL-5, as the range of scores included zeroes (Osbourne, 2002). Transformed variables were only utilized for primary analyses (i.e., PCA and regression analyses; descriptive statistics were based on the original variables).

Missing data. Among the entire sample, 12.0% (*n* = 59) of those who underwent surgery had no CAM-S data, 49.0% (*n* = 241) had no PDEQ data at discharge, and 46.7% (*n* = 230) had no PCL-5 data at 30-day follow-up. Among those who were administered the CAM-S, 17.3% of participants had some missing CAM-S data on at least one postoperative day. As these data were not missing completely at random (Little's MCAR: $p < .001$), imputation methods were not used. Instead, CAM-S assessments with missing items were still included when computing peak CAM-S scores. Among those who were administered the PDEQ at discharge, 0.4% had missing data, and among those who were administered the PCL-5 at 30-day follow-up, 5.4% had missing data. Case deletion (Schafer, 1999) was used to handle missing data for the PDEQ and PCL-5.

As shown in Table 1, participants significantly differed in age according to study modules completed, $F(3, 378) = 3.24$, $p = .022$ (baseline only $M_{age} = 71.61$; baseline & discharge $M_{age} = 69.00$; baseline & 30-day $M_{age} = 71.84$; all study components $M_{age} = 69.78$). Groups also

differed in race according the study modules completed, χ^2 (3) = 22.61, p < .001; those who completed all study modules and those who completed baseline & discharge were primarily White (56.9% and 55.7%, respectively), whereas those who completed baseline only and baseline & 30-day follow-up primarily endorsed "other" race (67.9% and 64.6%, respectively). Groups also differed in the prevalence of subsyndromal or threshold postoperative delirium on at least one postoperative day, χ^2 (3) = 11.22, p = .011, and in the average peak CAM-S score, F(3, 432) = 3.03, p = .029; both the prevalence of postoperative delirium and the average peak CAM-S score were highest among participants who did not complete discharge or 30-day follow-up study components (i.e., baseline only; 54.9%, M = 5.07 versus 34.2%-50.8%, M = 4.07-4.98).

Sample Characteristics

At the time of data extraction and analysis the sample included 492 participants (ENGAGES site: Kingston: n = 81, 16.5%, Health Sciences Centre: n = 61, 12.4%, Saint Boniface Hospital: n = 262, 53.3%, Montreal: n = 88, 17.9%; type of surgery: cardiac: n = 376, 76.4%, non-cardiac: n = 116, 23.6%). Participants were 70 years old on average, primarily male (60.6%) and married (61.2%) with a high school education or higher (56.3%); 40% were White and 47.0% indicated "other" race. Of these participants, only 181 (36.8%) completed all primary measures (i.e., CAM-S, PDEQ at discharge, PCL-5 at 30-day follow-up; see Figure 3). Participants within the subsample of total completers also were 70 years old on average, primarily male (66.3%) and married (68.0%) with a high school degree or higher (64.7%); 53.6% were White and 40.9% endorsed "other" race. See Table 2 for additional sample characteristics.

Not included in Table 2, there were no significant mean differences across primary measures according to type of surgery (i.e., cardiac versus non-cardiac) among those who

completed all primary measures; CAM-S: $F(1, 180) = 0.02$, $p = .894$; PDEQ at discharge: $F(1, 180) = 0.85$, $p = .357$; PCL-5 at 30-day follow-up: $F(1,173) = 3.36$, $p = .069$.

Principal Components Analysis

Testing assumptions. The 10 CAM-S items from the day during which participants had their peak CAM-S score and the 10 PDEQ discharge items were included in a PCA with an oblique (direct oblimin) rotation. The Kaiser-Meyer-Olkin statistic (= .852) suggested the sample was of satisfactory size for the analysis. A correlation matrix was computed to determine the suitability of the 20 items included in the PCA; Bartlett's test revealed that the data did not resemble an identity matrix (χ^2 (190) = 1,623.36, $p < .001$), however there were a large number of relatively small correlations ($r < .30$), particularly for CAM-S items 7, 8, and 10 (see Table 3); this may be an initial indicator of limited overlap between items. However, I proceeded with the analysis as planned, as Bartlett's test did not indicate correlations were problematic. The lack of correlations > .80 alongside a determinant value of .001 suggested no issues of multicollinearity between items.

PCA results. Missing data on individual CAM-S and PDEQ items were treated with pairwise deletion in order to include participant data from individuals with missing data on some of the CAM-S or PDEQ items. Table 4 displays initial item communalities and communalities after extraction. In line with the initial small correlations, CAM-S items 7, 8, and 10 demonstrated low communalities (< .10) after extraction. After examining the magnitude of the initial eigenvalues and the percentage of variance explained by each component it was determined that two components should be retained (see Table 5). As shown in Tables 6 and 7, all PDEQ items loaded onto the Dissociation Factor (i.e., component 1) and all CAM-S items, except items 7, 8, and 10, loaded onto the Delirium Factor (i.e., component 2). CAM-S items 7,

8, and 10 did not adequately load onto either component. Results of the PCA did not support overlap between CAM-S and PDEQ items; therefore, hypotheses 1A-1C were not supported, however, hypothesis 1D (prediction of at least two condition-specific components) was supported. In light of these results, CAM-S and PDEQ total scores were utilized in regression analyses as opposed to component scores.

Associations Between Delirium and Dissociation with Posttraumatic Stress

Testing assumptions. Mahalanobis distances were computed based on the most stringent model of the linear regressions and compared to a chi-square distribution with the corresponding degrees of freedom to determine whether there was a violation of multivariate normality (Wicklin, 2012). Probability values were > .001, indicating the data likely emerged from a multivariate normal distribution. Overview of scatterplots revealed no violations of the assumption of linearity. I also correlated the total PDEQ and CAM-S scores to determine whether there was evidence of multicollinearity ($r = .432$, $p < .001$). However, examination of the Variance Inflation Factors (VIF) and Tolerance values with all independent variables included revealed no issues of multicollinearity (VIF range: 1.07-1.33; Tolerance range: .76-.94); prior research suggests that VIF values of 10 or greater and Tolerance values less than .20 suggest issues with multicollinearity (Hair, Anderson, Tatham, & Black, 1995; Menard, 1995). Finally, the plotted regression standardized residuals did not reveal signs of heteroscedasticity.

Due to the lack of support for hypotheses 1A-1C, hypotheses 2A and 2B were not examined. Instead, regressions examined associations between the peak CAM-S (postoperative delirium) and total PDEQ (perioperative dissociation) scores with PTS at 30-day follow-up. In the unadjusted model, dissociation symptoms were significantly associated with increased total PTS (unstandardized regression coefficient (b) = 0.05, 95% confidence interval (CI) [0.01-0.08],

p = .013), re-experiencing symptoms (b = 0.04, 95% CI [0.02-0.06], p < .001), negative alterations in mood and cognition symptoms (b = 0.03, 95% CI [0.00-0.05], p = .023), and hyperarousal symptoms (b = 0.03, 95% CI [0.01-0.05], p = .004) at 30-day follow-up. After controlling for age, sex, preoperative depressive/anxiety symptomatology, preoperative PTS, and entering delirium severity and dissociation symptoms concurrently, delirium severity was significantly associated with increased total PTS (b = 0.14, 95% CI [0.01-0.28], p = .037), re-experiencing symptoms (b = 0.10, 95% CI [0.02-0.18], p = .016), and negative alterations in mood and cognition symptoms (b = 0.10, 95% CI [0.01-0.19], p = .037) at 30-day follow-up. Model 2 is not described in-text due to strong consistency with model 1, and similarly, model 3 is not described in-text due to strong consistency with model 4. In support of hypothesis 2C, across all PTS symptom clusters, strongest associations emerged between dissociation and delirium with re-experiencing symptoms (indicated by the largest standardized regression coefficient (β) values: β = .26 for dissociation in model 1 (f^2 = .07 [small to medium effect size]); β = .27 for delirium in model 3 (f^2 = .08 [small to medium effect size]); see Table 8).

Study 1 Discussion

To my knowledge, this represents the first study to examine the relationship between delirium and dissociation symptoms, the association between perioperative dissociation and postoperative PTS using a validated assessment of dissociation, and the association between severity of postoperative delirium and postoperative PTS. Results suggest there is limited statistical overlap between items from the CAM-S and the PDEQ among this sample; subsequently, delirium and dissociation were examined independently as predictors of postoperative PTS. Results further revealed that at the bivariate level, perioperative dissociation

was associated with increased postoperative PTS, whereas in the most stringent regression model, delirium severity emerged as the only significant predictor of postoperative PTS.

Sample Characteristics

A considerable proportion of study participants (> 60%) did not complete all primary measures of the current study (i.e., CAM-S, PDEQ at discharge, PCL-5 at 30-day follow-up). Interestingly, participants who did not complete the 30-day follow-up measures had higher prevalence estimates of subsyndromal or threshold postoperative delirium during their hospital stay compared to those who completed the 30-day follow-up (i.e., 50.8-54.9% versus 34.2-39.2%); similarly, these participants had higher postoperative delirium symptom severity (i.e., M_{range} = 4.98-5.07 versus M_{range} = 4.07-4.28). It is possible that a proportion of individuals who had clinically significant postoperative delirium symptoms (and/or other postoperative morbidity) were unable to continue their participation in the study due to their health status. This is in line with prior research, which has shown that poor health status is associated with increased attrition rates in a randomized controlled trial (Applebaum et al., 2012). In addition, postoperative delirium is associated with long-term declines in cognitive functioning (e.g., Bulic et al., 2015; Girard et al., 2010; Pandharipande et al., 2013). This may have impaired individuals' abilities to complete self-reported follow-up measures, and may have impacted the reliability of postoperative measures that were completed. The high rates of attrition and the impaired health status of individuals who did not complete all study phases may be associated with underestimations of emergent associations in the current study; thus compromising the validity of the findings.

Delirium and Dissociation Symptoms

As indicated, results of the PCA suggest there is insufficient statistical overlap between items of the CAM-S and PDEQ to warrant mixed-measure components (i.e., components where items from both measures have high loadings). A two-component solution was selected as the optimum fit wherein 7/10 CAM-S items loaded onto one component and 10/10 PDEQ items loaded onto the second component; the remaining three CAM-S items (i.e., perceptual disturbances, psychomotor agitation, altered sleep-wake cycle) did not load highly onto either component. Statistically, this suggests that there is not a meaningful amount of inter-scale shared variance. This finding does not support the initial hypothesis that components characterized by combinations of delirium and dissociation symptoms would emerge. This hypothesis stemmed from the various similarities and common characteristics between delirium and dissociation. However, total scores of the CAM-S and PDEQ were significantly correlated, suggesting that although individual items across scales do not substantially overlap, the underlying constructs of either scale appear related.

Results of the PCA may suggest that despite conceptual overlap, dissociation and delirium are distinct and independent symptom presentations. Conversely, it is possible that the absence of statistical overlap stems from differences in how delirium and dissociation were assessed, as opposed to differences in symptom presentstion. The CAM-S is an administered structured clinical interview whereas the PDEQ is self-reported. Prior research has shown that self-report measures of psychopathology do not always have high concordance with clinical interviews (e.g., Cody, Jones, Woodward, Simmons, & Gayle Beck, 2017). In addition, the recent Nomenclature Consensus Working Group suggested that there are marked differences in the incidence of delirium according to the type of assessment method used (e.g., chart review, routine screening, clinical interview, mental status testing with an applied diagnostic algorithm;

Evered et al., 2018). Therefore it is possible that delirium and dissociation do share symptom overlap; however, this was not captured by the assessment methods used in the current study. Similarly, the lack of statistical overlap between the CAM-S and PDEQ may be a result of characteristics of the measures themselves, or general poor convergent validity (or if considered distinct presentations, acceptable discriminant validity). The CAM-S is a targeted, relatively homogeneous and objective assessment of delirium, whereas the PDEQ is a more subjective and heterogeneous assessment measure; the items on the PDEQ are subject to increased interpretation, and prior research has shown that participants tend to over-report their symptoms when completing self-report measures of dissociation (Merckelbach, Boskovic, Pesy, Dalsklev, & Lynn, 2017). Depending on the individual's interpretation, the PDEQ items may capture a combination of depressive, anxiety, and cognitive dysfunction symptoms, as opposed to dissociation specifically; this may reflect limited face validity of the PDEQ. In fact, the PHQ-4, a measure of anxiety and depressive symptomatology, was also administered at discharge; post-hoc analyses revealed significant small to moderate correlations between each of the four PHQ-4 items and each of the 10 PDEQ items (r range: .15-.49, $p < .05$), suggesting overlap between the PDEQ and general anxiety/depressive symptomatology.

It is also possible limited statistical overlap emerged due to increased measurement error or inaccurate responding, stemming from the presence of clinically significant delirium and dissociation symptoms. Although patients are unlikely discharged with clinically significant postoperative delirium, residual delirious symptoms and current/residual dissociative symptoms at discharge may influence participant responding. Effects of perioperative medications and sleep disturbances during recovery may also influence participant self-report at discharge from hospital. Delirium and dissociation symptoms are often associated with confusion, disorganized

thinking, impairments in memory and awareness, perceptual disturbances, and fluctuations in consciousness (American Psychiatric Association, 2013; Briere et al., 2005; Davydow et al., 2008; DiMartini et al., 2007; Ehlers & Clark, 2000; Halligan, Michael, Clark, & Ehlers, 2003; Marra et al., 2017; McKinnon et al., 2016; Wade et al., 2015); therefore, it is possible that individuals with these symptoms may be unable to accurately respond to self-report measures, such as the PDEQ. The CAM-S may have more accurately captured participants' symptom presentations, as it was administered by trained personnel. Further investigation is warranted in order to examine these possibilities.

Associations Between Delirium and Dissociation with Posttraumatic Stress

Results of the first two models of multiple linear regressions (i.e., model 1 = unadjusted, model 2 = adjusted for age and sex) revealed that perioperative dissociation symptoms were significantly associated with increased postoperative PTS; re-experiencing, negative alterations in mood and cognition, and hyperarousal symptoms in particular, with small to medium effect sizes. This finding is consistent with previous research that has shown associations between dissociation symptoms and increased severity of PTS outside of perioperative contexts (e.g., Blevins et al., 2014; Tsai et al., 2015; Waelde, Silvern, & Fairbank, 2005; Wolf et al., 2012). Prior research has also demonstrated associations between dissociative symptoms and PTSD re-experiencing symptoms, flashbacks in particular, both among veteran (Wolf et al., 2012) and general population-based (Stein et al., 2013) samples. Perhaps this association captures the dissociative quality of flashbacks and the associated disruption to normal consciousness, fragmented awareness, and disorientation (Brewin, 2015; Ford, 2018; van der Kolk & van der Hart, 1989; van der Hart, van Ochten, van Son, Steele, & Lensvelt-Mulders, 2008). Ford (2018) suggested that one of the hallmarks of PTSD is the involuntary dissociative experience and

extreme hypervigiliance that occurs when re-experiencing the traumatic event; the hypothesized co-occurrence of dissociation and hypervigilance may explain the emergent association between dissociation and PTS hyperarousal symptoms in the current study. In further support, prior research found that hyperarousal was a significant predictor of peritraumatic dissociation in a sample of novice skydivers (Sterlini & Bryant, 2002), and that both intrusive symptoms and hypervigilance were significantly correlated with dissociative symptoms in a sample of cancer patients (Civlotti et al., 2015).

Further, dissociation was also associated with negative alterations in mood and cognition. As indicated, items from the PDEQ were significantly correlated with items from the PHQ-4, a measure of depressive and anxiety symptomatology. It is possible that items from the PDEQ capture transdiagnostic negative mood-related symptoms, which may explain the emergent association with PCL-5 negative alterations in mood and cognition symptoms. In addition, one of the symptoms within this PTS cluster is *the inability to remember important aspects of the trauma*, which may be caused by dissociative amnesia (American Psychiatric Association, 2013); the inherent dissociative nature of this symptom may be driving this emergent association. In addition, prior research has identified various negative correlates of dissociative experiences including numbing, depressed mood, and negative self-perception (e.g., Bennett, Modrowski, Kerig, & Chaplo, 2015; Gusic et al., 2018; McCanlies, Sarkisian, Andrew, Burchfiel, & Violanti, 2017; Tsai et al., 2015), all of which may explain the association between dissociation and negative alterations in mood and cognition symptoms in the current study.

Although initial regression models revealed associations between dissociation and PTS, after controlling for baseline mental health symptoms dissociation was no longer associated with PTS. This may suggest that perioperative dissociation is driven by poor baseline mental health

status. Relatedly, the PDEQ items may be capturing the presence of psychological vulnerability, or transdiagnostic depressive, anxiety, and cognitive dysfunction symptoms. In fact, prior research has shown that pre-existing psychopathology is a significant predictor of peritraumatic dissociation (Choi & Seng, 2016; Fullerton et al., 2000; Gomez-Perez, Lopez-Martinez, & Asmundson, 2013). In addition, the loss of significant associations between dissociation and PTS upon inclusion of baseline mental health symptoms as covariates may suggest that preoperative mental health status is a stronger predictor of postoperative PTS compared to perioperative symptomatology. In support, prior research suggests that having pre-existing psychopathology or a mental health condition is a significant predictor of postoperative PTS (e.g., Deisseroth & Hart, 2012; Hart, Perry, Hiratzka, Kane, & Deisseroth, 2013; Jeantieu et al., 2014; Whitlock et al., 2015). In addition, in a study conducted by Diesseroth and Hart (2012), having a preoperative mental health condition emerged as the strongest predictor of postoperative PTS in a model that also included sociodemographic characteristics, history of previous surgery, and perioperative factors such as blood loss, surgical complications, and prolonged intubation. Alternatively, the loss of significance upon controlling for baseline mental health status may suggest the presence of a confounding relationship between baseline mental health status, perioperative dissociation, and postoperative PTS. This is an important avenue for future research.

In contrast to dissociation, severity of delirium only emerged as a significant predictor of PTS, including total PTS, re-experiencing, and negative alterations in mood and cognition symptoms, after controlling for baseline mental health symptoms; emergent effect sizes ranged from small to medium. The increase in predictive ability (demonstrated by larger β values and emergence of statistical significance) of severity of delirium on PTS upon adjustment for

baseline mental health symptoms may be indicative of a suppression effect (Thompson & Levine, 1997), which may suggest the presence of a confounding association (MacKinnon, Krull, & Lockwood, 2000) or moderated relationship. These associations are consistent with previous research, which has demonstrated that postoperative delirium is associated with postoperative PTS (Bashar et al., 2017; Davydow et al., 2008; DiMartini et al., 2007; Drews et al., 2015; Jackson et al., 2015; Warlan, Howland, & Connelly, 2016). The fact that significant associations emerged between delirium and PTS after controlling for sociodemographics, preoperative mental health symptoms, and perioperative dissociation suggests that delirium is an independent predictor of postoperative PTS, which is also consistent with prior research (Drews et al., 2015; Morrissey & Collier, 2016). Researchers have suggested that frightening hallucinations and delusions that may occur during a delirious state, and subsequent re-experiencing of these frightening symptoms, may play an important role in the relationship between postoperative delirium and PTS (Davydow et al., 2008; DiMartini et al., 2007; Wade et al., 2015); this may explain the emergent association with PTS re-experiencing symptoms in the current study. Of note, upon adjusting for dissociative symptoms, the magnitude of association between delirium and re-experiencing symptoms decreased (i.e., β model 3 = 0.27 versus β model 4 = 0.21). This may support that dissociative symptoms mediate the relationship between delirium severity and re-experiencing symptoms (MacKinnon et al., 2000), suggesting that dissociation in the context of delirium may be an indicator of greater symptom severity of PTS (re-experiencing in particular); further investigation is warranted to examine this possibility.

Severity of postoperative delirium was also significantly associated with increased PTS negative alterations in mood and cognition symptoms. This may reflect an association found in previous research between postoperative delirium and postoperative depressive symptoms

(Nguyen et al., 2018; Pulido, 2018). Further, it is possible that some of the PTS negative cognition symptoms (e.g., *inability to remember important aspects of the trauma, distorted cognitions about the trauma, exaggerated negative beliefs*) may stem from core symptoms of delirium. For example, delirium has a noticeable impact on cognitive functioning, including memory (Bulic et al., 2015; Girard et al., 2010; Inouye, Robinson et al., 2015; Pandharipande et al., 2013). Delusions, perceptual distortions, and disorganized thoughts are also experienced during a delirious state (American Psychiatric Association, 2013; Arora et al., 2017; Inouye, 2006; Inouye, Robinson et al., 2015), which may impact trauma-related beliefs and thoughts, and subsequently, an individual's understanding of his or her perioperative experiences. However, to my knowledge, this possibility has yet to be investigated.

Limitations

Although the results of study 1 are compelling, they must be considered alongside several limitations. First, although perioperative dissociation was temporally assessed after the completion of delirium assessments, the PDEQ required patients to report on dissociative symptoms that occurred either during surgery or throughout the postoperative hospital stay. Therefore, temporal and causal assumptions regarding dissociation and delirium cannot be made. Second, with the exception of postoperative delirium, mental health symptoms (e.g., perioperative dissociation, PTS) were assessed by self-report, which may be susceptible to response biases, including recall bias. This is of particular relevance to individuals who had elevated symptoms of dissociation and delirium, which may be associated with impairments in memory, attention, and awareness (American Psychiatric Association, 2013; Inouye, 2006; McKinnon et al., 2016; Pandharipande et al., 2013). Third, as indicated, a substantial proportion of participants did not complete all follow-up components of the study, and those who did not

complete the 30-day follow-up had elevated estimates and symptom severity of postoperative delirium; this suggests the current sample is biased, and results may not reflect the true severity of the examined associations. Relatedly, the limited proportion of follow-up data, and the loss of participant follow-up for those with the highest severity of delirium likely resulted in reduced variation across dissociation and PTS scores. Another sample characteristic that may have influenced results is participant age. The sample was comprised of older adults, who are known to have lower prevalence estimates of PTSD (e.g., Reynolds, Pietrzak, Mackenzie, Chou, & Sareen, 2016), but higher estimates of postoperative delirium (e.g., Inouye et al., 2015); results may not generalize to younger and middle-age adult samples. Finally, as a result of the high rates of attrition, analytic power was compromised; subsequently, relevant covariates (e.g., preoperative cognitive functioning, preoperative substance misuse, history of delirium, education, race/ethnicity) were omitted. The current analyses will be re-run among the entire ENGAGES-CANADA sample once the trial is complete.

Implications

In contrast to the hypothesized and conceptual similarities between perioperative dissociation and postoperative delirium, results did not support statistical overlap. Although dissociation and delirium may be distinct and independent, their lack of statistical overlap in the current study may stem from assessment-related factors, as opposed to true symptom presentation differences, as described above. Perhaps additional investigation using a clinical interview to assess dissociation (e.g., Structured Clinical Interview for DSM Dissociative Disorders [SCID-D]; Bremner, Steinberg, Southwick, Johnson, & Charney, 1993) may provide additional insights into the similarities and differences between perioperative dissociation and postoperative delirium. Nonetheless, both perioperative dissociation and postoperative delirium

were associated with increased postoperative PTS. These results highlight the importance of postoperative assessment of mental health in order to enable the opportunity for early intervention to reduce risk or prevent the occurrence of additional mental health sequelae. For example, patients with elevated symptoms of perioperative dissociation and postoperative delirium may benefit from brief exposure-based interventions (Rothbaum et al., 2008; Rothbaum et al., 2012) or an ICU diary intervention (Garrouste-Orgeas et al., 2012; Jones et al., 2010) to mitigate risk of postoperative PTS and other postoperative mental health sequelae. In addition, a recent review outlined psychological (e.g., cognitive-behavioural therapy, meaning-making, mindfulness), pharmacological (e.g., hydrocortisone administration), rehabilitative (e.g., exercise, occupational therapy, speech/language therapy), and other medical interventions (e.g., increased monitoring of physical symptoms including sensory defects) for the prevention of medical-related PTSD (Birk et al., 2019); these interventions may be particularly advantageous for individuals who experience perioperative mental health sequelae (e.g., perioperative dissociation, postoperative delirium) and may be at increased risk for postoperative PTS. Finally, results may support the utility of preoperative assessment of mental health to identify those who may be at increased risk for adverse mental health outcomes. For example, risk prediction models for postoperative delirium that include preoperative assessment of mental state, cognitive functioning, and substance use have been developed, but require additional evaluation to determine their effectiveness (van Meenen, van Meenen, de Rooji, & ter Riet, 2014).

Study 2 Method

Overview & Participants

Study 2 aimed to examine how individuals experience and describe delirious and dissociative symptoms related to their surgery, and explore the impact (e.g., psychological, interpersonal, functional) that these symptoms have on individuals, using qualitative methodology. Cardiac surgery participants from study 1 who met specific mental health symptom inclusion criteria (described below) were invited to participate in this follow up study. Study 2 built on the objectives of study 1 in order to gain a richer understanding of perioperative dissociation and postoperative delirium symptoms. More specifically, while study 1 aimed to identify whether common components existed between delirium and dissociation, study 2 aimed to examined the perceptions and experiences of individuals who exhibited clinically significant levels of these symptoms, without being limited to the terminology and symptom descriptions (i.e., items) included in the PDEQ and CAM-S. Study 1 also examined PTS specifically as a mental health outcome associated with delirium and dissociation, while study 2 aimed to investigate how individuals were impacted by these symptoms more broadly (e.g., psychologically, functionally) in order to understand the full spectrum of mental health sequelae. Overall, study 2 aimed to extend the quantitative findings of study 1, through gaining a rich and in-depth understanding of participants' descriptions of their perioperative mental health experiences.

I submitted an amendment to the original ethics for the ENGAGES-CANADA study through the Research Ethics Board at the University of Manitoba Bannatyne campus. My target was to recruit between 10-15 participants for study 2. In addition to the inclusion and exclusion criteria for study 1, my plan was to recruit participants for study 2 if they had a PDEQ score above 15 at discharge from hospital (if the PDEQ score was missing at discharge, I planned to utilize the PDEQ score at 30-day follow-up) and a CAM-S score of 5 or greater on at least one

postoperative day before discharge (i.e., subsyndromal postoperative delirium). Exclusion criteria omitted individuals unable to provide informed consent independently (i.e., were nonresponsive when I tried to obtain consent), in addition to institutionalized or deceased participants. Following one month of unsuccessful recruitment (absence of participants meeting inclusion criteria), I modified the criteria such that participants only needed to score above 15 on the PDEQ at discharge (or 30-day follow-up in the case of missing discharge data) *or* score 5 or greater on the CAM-S on a least one postoperative day, instead of meeting both criteria. Participants were also still eligible if they met both inclusion criteria (refer to Figure 4 for recruitment targets). It was my hope that by changing the recruitment criteria, a larger sample of individuals would be eligible to participate.

Research Strategy

I utilized qualitative methods informed by constructivist grounded theory (Charmaz, 2006; 2014) to understand how participants experienced dissociative and delirious symptoms and how they were impacted by these symptoms. Constructivist grounded theory is a flexible yet structured method used to better-understand concepts or processes, or to develop theoretical frameworks that are grounded in data; this method provides strategies to guide the process of data collection and analysis (described below), which can be applied flexibly (e.g., phases of analysis will not always occur in a linear manner) according to what best fits the study in progress. This research strategy allowed me to begin data collection and analysis with a broad perspective (appropriate for the nature of the research question and the limited understanding of this topic in the extant literature), and as concurrent data collection and analysis continued, my approach became more focused in order to refine my developing coding framework. This method permits continual shifts in focus and the adoption of new perspectives as additional data

are introduced and analyzed, which allowed for a richer understanding of the participants' experiences. Constructivist grounded theory stems from an interpretive approach where the phenomenon being studied is seen as a construction of experience, created by both the researcher and research participants (Charmaz, 2006). This aspect of constructivist grounded theory was important for this study and its target population. Co-construction by the participants enabled an understanding of the subjective essence of their experiences of dissociation and delirium, while co-construction by the researcher allowed for consideration of these experiences in the context of the confusion, memory impairment, alterations in awareness, and other cognitive and psychological impacts these symptoms may have. Based on the grounded theory method, the preliminary theoretical framework was grounded in the unique experiences of participants, who endorsed symptoms of delirium and/or dissociation. Drawing on the constructivist approach, I acknowledge the co-construction of the emerging theoretical framework. Namely, that the framework was a result of my interaction with the participant, the questions I asked, the prompts I followed up with, and their responses on the specific day and time that I spoke with them, as well as my prior life experiences and perspectives, and the impact this had on the themes that I saw and identified as emergent from interview transcripts.

Key components of grounded theory include simultaneous data collection and analysis, identifying codes and categories (also referred to as themes and subthemes) from collected data, making comparisons between and within data throughout stages of analysis, continuous development and refinement of a theoretical model as data collection and analysis progress, memo-writing to outline details of codes and categories developed, documentation of fieldnotes to highlight important observations about participants, diagramming to visually integrate developed categories into a preliminary conceptual model, and sampling of participants targeted

toward enriching the model (Charmaz, 2006). Concurrent and iterative data collection and analysis keep the researcher closely involved in the data. Throughout the analytic process, data are assigned codes (i.e., labels that define a section of data), and codes are categorized according to conceptual significance. Typically, this approach is targeted toward the construction of a theory that is grounded in the collected data. The analytic process is described in greater detail below.

Data Collection Procedure

Recruitment. As part of the ENGAGES-CANADA study, participants were given the option to consent to being contacted in the future for further research study involvement, beginning in March 2018. I began recruitment using purposive sampling in order to target participants who surpassed both the cut off score on the CAM-S (i.e., ≥ 5 on at least one day postoperatively) in addition to the PDEQ (i.e., >15). This method of sampling was chosen to allow me to collect rich data from participants about how they experienced their delirious and dissociative symptoms. Once concurrent data collection and analysis were underway, I intended to implement theoretical sampling in order to further refine the emergent analytic codes and categories. However, as indicated, due to recruitment difficulties, inclusion criteria were modified (i.e., participants only had to meet *either* the CAM-S *or* the PDEQ criteria) and purposive sampling continued.

As part of the recruitment process, the ENGAGES-CANADA research coordinator at Saint Boniface Hospital gathered participant names and contact information for those who met inclusion criteria and consented to being contacted about additional follow-up research. I contacted eligible, consenting participants by telephone in order to briefly explain the purpose of my study and determine whether or not they were interested in participation. If participants

expressed an interest in participating I scheduled an interview and provided participants with a telephone number in order to reach me if they desired additional information about the study. In light of the limited number of participants meeting inclusion criteria, I attempted to recruit all eligible participants and did not implement theoretical sampling. According to the initial recruitment strategy, I planned to discontinue recruitment once theoretical sufficiency was achieved (i.e., data suggests emergent categories are sufficiently described; Dey, 1999). Theoretical saturation (i.e., collection of new data no longer adds to the explanation of codes, categories, and their relationships; Glaser & Strauss, 1967) is commonly used as a signal to cease data collection, however some have suggested it is conceptually unobtainable (Dey, 1999), and thus theoretical sufficiency is a more suitable and realistic guideline to signal cessation of recruitment. However, in light of unexpected challenges, recruitment did not progress as anticipated. In consultation with my committee, recruitment was stopped in March 2019, following no additional eligible participants since December 2018.

Interviews were scheduled between one month and six months following the participant's discharge from hospital, depending on convenience and patient recovery. This time frame was determined with the hope of permitting sufficient recovery from surgery while also allowing the interview to take place when detailed recollection of the surgical experience was still accessible to memory. Prior to being interviewed, participants provided verbal consent (formal written consent was not required as this study was framed as an additional component of ENGAGES-CANADA, and participants had already consented to participate in the ENGAGES-CANADA main study). As part of the consent process I let each interviewee know that they were not required to answer each question and if they felt uncomfortable at any point during the interview,

we could proceed to the next question. Interviewees were also informed that they could withdraw their participation at any point while the study is ongoing.

Individual interviews. I conducted individual, semi-structured interviews with participants. Although participants were provided the option of having in-person interviews (either in the participant's home, at the University of Manitoba Fort Garry campus, or at the University of Manitoba Bannatyne campus, depending on which location was most convenient for each participant), all participants requested to have their interviews conducted over-the-phone due to scheduling convenience and personal preference. The target duration for interviews was 30-60 minutes; although 30 minutes is a relatively short duration for a qualitative interview, some participants were reluctant to commit to a 60-minute interview after having completed numerous questionnaires as part of ENGAGES-CANADA, while still recovering from major surgery. Interviews were audio-recorded and transcribed verbatim and both the transcribed documents and audio recordings were stored on a password-protected computer in a secure location. I changed any identifying information gathered during interviews in order to protect the confidentiality of participants.

Before beginning the interview and after obtaining consent, I administered a brief background questionnaire to each participant (e.g., age, sex, marital status, perceived mental and physical health; see Appendix B). Administering this questionnaire not only provided background information about each participant, but it also provided an opportunity to assess the participant's mental status/level of awareness at the time of the interview (i.e., if they were unable to complete the questionnaire that may suggest a potential impairment in awareness and could signal that the subsequent interview should be delayed; although this did not apply to any recruited participants). The interview began with an open-ended question about the participant's

experience of undergoing cardiac surgery ("I understand that you underwent cardiac surgery at Saint Boniface hospital in (X month, X year). Can you tell me what you remember about having the surgery?"). I then asked the participant questions related to their experiences during and after the actual procedure, what recovery in-hospital was like, and whether they experienced anything abnormal or were told by others that they had unusual experiences, to attempt to explore participants' recollection and experiences related to delirium and dissociation. In order to gain insight regarding how these symptoms impacted the participant, I asked an open-ended question about their experience of recovering at home ("Can you tell me what you remember about recovering from surgery, once you were back at home?"). I probed for additional details about how long the described symptoms lasted, how they were experienced, and how they impacted daily living (e.g., ability to carry out daily routines, impact on relationships). Throughout the interview, I also used general probes (e.g., "can you tell me more about that", "can you provide me with an example of what you mean by that") in order to gain additional details about participants' unique experiences (see Appendix C). If at any point it appeared that the interviewee was no longer capable of proceeding with the interview (e.g., no longer coherent, appeared significantly distressed), I planned to ask if it was alright that we finish the interview at that point and whether they wanted to arrange a second interview session at a later time; however, this situation did not occur during any interviews. Following the completion of each interview I documented memos and fieldnotes (see below for descriptions) and mailed each participant a $10 grocery store gift card in appreciation of their time and participation in this study.

Data Analysis

Coding. I engaged in three phases of coding: initial coding, focused coding, and theoretical coding (Charmaz, 2006, 2014). During initial coding, I examined, defined, and assigned labels to individual lines or segments of the transcribed interviews (i.e., line-by-line coding). I remained open-minded, made comparisons between codes and segments of data, and remained close to the data. I also included *in vivo* codes (i.e., codes that consist of the interviewee's own words) and used action-words (i.e., verbs ending in "ing") as codes in order to preserve the essence of interviewee's experiences. Focused coding involved examination and categorization of initial codes and identification of sub-codes (i.e., labels assigned to smaller sections of data related to an identified code), both within and across interviews. This phase of coding allowed for integration and analysis of larger segments of data. Finally, theoretical coding involved identification of relationships between focused codes, and integration of codes into a theoretical model through diagramming. During this final stage of coding the preliminary grounded theory became refined and cohesive.

Memo-writing. As outlined by Charmaz (2006; 2014), memo-writing is an important analytic process that takes place throughout the concurrent data collection and analysis process. Memos are analytic notes written about data, codes, theoretical categories, interview protocol, and ideas/thoughts about the data collection and analysis processes more generally. This process is crucial for documenting important comparisons and connections noted between codes and other data, and helps guide protocol modifications and direct subsequent recruitment techniques (i.e., changing from purposive to theoretical sampling). Memo-writing also helps ensure the research stays grounded in and connected to the data.

Fieldnotes. Following each interview, I documented detailed fieldnotes, highlighting important interview observations. This included reflections about participants' response styles

and affect, as well as any changes in these characteristics that occurred throughout the interview. I also paid attention to whether symptoms of dissociation and delirium (e.g., confusion, disorientation, fluctuations in awareness) were present throughout the interview (e.g., through monitoring of thought content and process). If I found that the participant's level of awareness or state of consciousness was severely impaired I planned to end the interview; however this did not occur during any interviews. The fieldnotes were incorporated into analysis, which aided in capturing participants' experiences and behaviours.

Rigor

In order to increase the trustworthiness, or rigor, of my data and interpretations I employed several techniques commonly used in qualitative research (e.g., Guba 1981; Krefting, 1991; Lincoln & Guba, 1985). To increase credibility (i.e., accuracy in descriptions and interpretations of the phenomenon being studied) and dependability (i.e., consistency of the interpretation of the data) I compiled an audit trail (i.e., detailed record) to describe any changes made to the study methodology, outline the details and schedule for the study, and track my ideas, decisions, and thoughts as I was engaged in the research process (i.e., Lincoln & Guba, 1985). I also employed negotiated validity, a process that involves discussing aspects of the research process (e.g., emergent codes/categories, questions, ideas) with research colleagues in order to gain additional insight that may inform the interpretation of the findings. I also had transcripts independently coded by multiple researchers, including myself. The team of coders met throughout the research process to discuss and compare emergent codes, categories, and thoughts about the data. When the nature of our coding differed, we discussed our perspectives in further detail until we reached consensus. Finally, I employed triangulation of methods (Knafl & Breitmayer, 1989), an approach used to compare findings resulting from different forms of

data (in this case, quantitative and qualitative data). I compared quantitative findings from study 1 with qualitative findings from study 2 to explore their convergence and divergence. I will expand on triangulation in the final chapter of this thesis (General Discussion).

Study 2 Results

Sample Characteristics

A total of five participants who met inclusion criteria participated in study 2; four participants met the CAM-S inclusion criterion only and one participant met both the CAM-S and PDEQ inclusion criteria. Participants underwent their cardiac surgery procedure between August and December 2018 at Saint Boniface Hospital in Winnipeg, Manitoba. Participants were on average 70 years old and the majority were married (80.0%). All participants were male and requested to have their interview conducted over the phone. Participants generally rated their current mental health as either *good* (40.0%) or *excellent* (40.0%) and the most common physical health rating was *very good* (40%). See Table 9 for additional sample characteristics.

Interview Process

Interviews lasted between 20-60 minutes in duration; participants who had shorter interviews endorsed limited recall of details from the perioperative period or provided minimal details in their descriptions, even in response to probing questions. Across interviews, various questions appeared irrelevant to participants (e.g., "Was there anything that felt abnormal or different than usual [after surgery and while recovering in-hospital]?", "Some people describe having a difficult time piecing together what has happened to them after a major surgery, did you find yourself feeling this way?"), either due to limited participant recall or evidenced by participants' responses (e.g., "No, not at all", "Not really"); in such cases, corresponding follow-up questions were omitted. While a few participants engaged in periods of storytelling, others

appeared relatively closed off in comparison. As indicated, detailed information was not offered voluntarily by some participants and sometimes was difficult to obtain using probes.

Theoretical Framework of Participants' Perioperative Mental Health Experiences

Although the objectives of this study were to examine how individuals describe and experience symptoms of dissociation and delirium and the impact of these symptoms, this information did not emerge as primary components of the coding framework. Figure 5 outlines the emergent content and characteristics of participants' descriptions of their perioperative experiences; communication 'volume' (i.e., silence, whisper, voice) resembles the extent to which various topics were discussed. Participants' *perioperative silence* captures the absence of discussion of mental health symptoms and experiences. All participants exhibited clinically elevated (i.e., subsyndromal or threshold) symptoms of delirium or dissociation during the surgical period, however participants did not describe these symptoms as related to their mental health, or did not describe them at all. Although mental health was not directly discussed, some participants described experiencing disorientation, confusion, and other mental health-related symptoms and experiences indirectly (e.g., endorsed feeling confused, but did not discuss this as relevant to mental health). These descriptions were described using vague language and limited detail; as such, these descriptions are characterized as the *perioperative whisper*. Some elements related to physical health (e.g., severity of illness) are also characterized within the *perioperative whisper*; participants sometimes used minimizing language when discussing their physical health, which may be a protective strategy against negative mental health (e.g., stress, anxiety). In contrast to mental health experiences, most physical health-related experiences and experiences related to being a patient and undergoing surgery were discussed clearly and readily;

these experiences are captured by participants' *perioperative voice*. The primary emergent components of the theoretical framework are described in detail below.

Perioperative silence. As indicated, participants did not openly discuss perioperative mental health symptoms and experiences. Participants also did not demonstrate awareness that they experienced symptoms of delirium or dissociation (i.e., the terms "delirium" and "dissociation" were not mentioned by any participants). When probed about perioperative mental health experiences participants generally provided short responses that lacked detail, or that implied the question was inapplicable to their experiences. For example, when asked about whether anything abnormal or different than usual occurred during recovery, participants responded: "*Uhh, actually, not really.*" [P2]; "*No, no.*" [P3]; "*Hmm...Not really, no. Nope. Not really.*" [P5]; only one participant described experiencing a negative emotional impact related to unusual experiences during recovery (see descriptions below for P4). Participants provided similar responses when asked if they had trouble piecing together or making sense of their experiences around the time of surgery or during recovery, which may occur as a result of delirious or dissociative symptoms: "*Uh...I don't think so. I think...you know obviously, when you're out – you're out.*" [P1]; "*Actually no*." [P2]. In addition to the lack of detail and short responses, *perioperative silence* may also be captured by the relatively short duration of some interviews. Specifically, four of the five interviews lasted less than 40 minutes; two of which lasted less than 30 minutes.

Perioperative whisper. Although mental health was not the main focus of any of the interviews, some participants did describe mental health symptoms or experiences including: disorientation and confusion ("*I found one thing, that my days were all mixed up when I...when all this was happening, you know. Maybe it was a day or two, and I couldn't remember what*

date it was…" [P3]; "*I don't even remember where I was, whether I was up in the ICU or down in the…step down…I think I was in the step down when I started remembering things…on the ward, yeah.*" [P5]), warped perception of time ("*But I can't say how long that took; I have really no idea at this point*" [P1]), dream-like experiences ("*It was such an absurd idea in the first place. When she walked in the room, and I knew it was over, you know, I knew it was over; it was just a dream. It was sort of like a dream while I was awake was what it was, cause I didn't sleep*" [P4]), and perceptual disturbances ("*I remember waking up and seeing everything through like a little TV screen, type of situation*" [P4]). These descriptions are characterized as a *whisper* due to the ways in which they were communicated; mainly, in ways that detracted focus, importance, or emotional engagement.

For example, descriptions of mental health symptoms and experiences were often vague and lacked detail; in response to being asked about his experiences while in hospital, one participant responded, "*oh, they were good*" [P3]. In such circumstances, additional probing was required, although this did not always yield greater detail. Participants also sometimes used non-specific language, or appeared to struggle to articulate their message clearly (e.g., "*I guess it was...it did something to me.*" [P4]). One participant also expressed having a difficult time describing his experiences to his loved ones: "*And then the next day I tried to explain it to my wife; I couldn't even explain it. I was just really kind of zonked out*" [P4].

Another common characteristic of participants' descriptions was the use of minimizing language. Sometimes participants discussed mental health experiences while describing a reaction that seemed milder than expected. For example, after describing a distressing dream, instead of expressing emotions triggered by the dream, the participant indicated, "*it sort of bothered me*" [P4] (i.e., may be considered a more mild reaction). After additional probing he

later revealed that he felt "*really worried*" and that the dream had been "*really scary*", although this was not offered upon initially discussing the impact of the dream. Although the participant may have been trying to distance himself from these emotions initially, he alternatively may not have considered the emotional impact of this dream until later in the interview; being asked about this experience may have initiated a meaning-making process, which later revealed the negative emotional impact of the dream. Another participant communicated with a minimizing style through the use of humour: "*I really haven't had any trouble…well you know, unless you have to cough {laughs}. That…that was something else…*" [P3]. Other participants normalized relatively atypical experiences, including the day of surgery ("*So you know, getting ready was just kind of like a daily wakeup event; there was nothing special about it…everything seemed to go really normally, and I wasn't particularly upset*" [P1]) and experiencing a perceptual distortion ("*There was nothing really special to put my finger on about it…that was all it was. It's just suddenly it was like somebody turned the TV on*" [P4]), which may also be described as a minimizing style. In addition, some participants minimized their discomfort or suffering during recovery, or implied that unusual experiences were justified, because it was expected during the recovery process. For example, one participant noted: "*Everybody that I talked to said, well it just takes time, so I've been putting up with it. I just put up with it really. I just knew, you know, this wasn't going to be...it's just gonna be what it's gonna be.*" [P5]. Another participant indicated, "*Uh, that's no problem...part of the recovery*." [P2], when asked about the 'odd' behaviour that he described. As outlined above, though the content being discussed with minimizing language is not solely focused on mental health experiences, the use of minimizing language in these examples (e.g., related to surgery or physical recovery) may be a strategy that is protective against poor mental health (e.g., stress, anxiety).

In addition to using vague and minimizing language to describe mental health experiences during their interviews, some participants' indicated that mental health symptoms and experiences were not discussed directly with the health professionals while in hospital. For example, a family member told one participant that he had exhibited odd behaviour while recovering in hospital. When asked if the nurses or other medical professionals discussed this behaviour with him, he indicated: "*Actually no, 'cause they don't talk about what I did too much, they tell me you gotta eat and get better. The nurses tell you [you're] doing okay. That's all they keep telling me – you doing okay…no, maybe I was an idiot, who like I say, I don't know. But they don't tell me. They don't tell me nothing, that I was bad or anything*" [P2]. Another participant, who endorsed dissociative symptoms, was asked whether any of the healthcare professionals at the hospital discussed these symptoms with him or helped explain them to him. He explained: "*Not really, they didn't dwell on it…you know, they didn't really dwell on it. There was somebody there doing a research study and she asked about it a bit…they might have done stuff behind the scenes that I didn't see, or talked about it, but…yeah*" [P4]; of note, the research study being referred to was ENGAGES-CANADA, where trained personnel assessed postoperative delirium daily and participants self-reported on symptoms at the time of discharge.

Another reason why mental health symptoms and experiences were not discussed explicitly and directly may be because some participants attributed their abnormal experiences to the effects of the anesthesia and other perioperative medications. For example, one participant described perceptual distortions he experienced following a previous surgery: "*...like when I was on morphine, like about three days later you start to see things because you're coming out of morphine*" [P3]. Another participant who was asked why he thought he had experienced gaps in his memory during the perioperative period expressed, "*well, probably because of the*

anesthetic...I would think." [P5]. Finally, the one participant who described dissociative experiences explained, "*It all had to be because of the --- of the medication that they give you during the operation. Like yeah, I think so*" [P4].

Perioperative voice. In contrast to descriptions of mental health experiences, participants described patient (e.g., onset of illness), physical health (e.g., pain, other physical symptoms), and surgery-related (e.g., preoperative preparations, regaining mobility after surgery) experiences clearly and directly. For example, most participants described a change in their physical health prior to needing surgery: "*But when the original cardiac arrest took place, and they hauled me down to the hospital eventually...*" [P1], "*The day before I went back to work in the afternoon and I wasn't feeling good in the morning and when I got back to work I…up around my neck on one side I got such a real burning*" [P3], "*I was just happy to be going under because I was out of breath. I wasn't feeling good*" [P4]. One participant also described the severity of his state of physical health prior to surgery: "*...five doctors standing around in the hallway, probably discussing whether or not this guy had a chance at survival. I'm sure that's what they were wondering about at the time*" [P1]. Participants also described the day of surgery, including preoperative preparations ("*I remember getting ready, I had a shower and somebody came with some sort of electric razor and cut off any hair on my chest. I remember that. And I think he should have cut the hair off my arms where they were jamming needles and putting tape on but they didn't*" [P1]), being transported to the operating room ("*I just remember being wheeled into the operating room and it looked like there was a massive amount of equipment hanging around*" [P5]), and the process of anesthetic induction ("*but after they put that thing in my mouth, to breathe in, don't remember anything*" [P2]).

Participants also readily described physical symptoms and related experiences from the recovery process. For example, most participants discussed being in pain or feeling discomfort postoperatively: "*And then at night when I sleep, I know I get pain in the chest cause I'm a light sleeper and it hurts the chest so I go back on my back and it hurts my back too*" [P2], "*My chest was sorer than I thought it would be*" [P4], "*I don't remember much about it other than when I woke up I was quite sore mostly*" [P5]. Participants also noted other physical symptoms they experienced during recovery including water retention ("*We got the uh, water retention problem accomplished at one point, but then it recurred*" [P1]), swelling ("*I'm still getting a little problem with the one foot that I got the cut. It's swelling a little bit, but that's not a big problem*" [P2]), and tight skin ("*Most of the scabs cleared off now, well except for a couple spots down my leg, that part there well when you go walking, you'll feel a lot of pulling*"). All participants also described sleep difficulties or low energy during the recovery period: "*I remember being tired and such*" [P1], "*I walk, but I can't sleep…*" [P2], "*Well you just, one thing comes up after another. Boom boom boom and you can't go to sleep*" [P3], "*Yeah, I would, yeah 'cause, you know, I just felt kind of like all my energy kind of just got zonked out*" [P4], "*Well, it kept me awake at night…*" [P5]. In addition, the one participant who recalled and expressed negative mental health experiences also noted a negative impact on his physical functioning: "*I think it kind of set me back. I wasn't as good as I was the day before. Like I was doing pretty well and that set me back, like it really did…I don't know…days, you know. It just probably did delay getting better by days sort of thing…*" [P4].

Participants also discussed the process of recovering from surgery ("*Just hoping that I recover properly and manage to continue living for a while yet*" [P5]). In particular, most participants talked about regaining mobility after surgery: "*It took quite a while, I'm sure we*

were there for a good length of time. I don't race around, but I get the exercise of walking around and that's part of the general, I guess developmental part of recovering" [P1], "*The nurse was good with me, he let me do it my own way. I start walking at 3 o'clock in the morning and stuff*" [P2], "*They had you walking, well the first day it was just a couple of short walks but after that you kept extending your walking and that*" [P3]. Some participants also described receiving regular check-ups, both while in hospital ("*I remember the fact that there were so many people coming to check my blood pressure, check everything*" [P1]) and after returning home ("*But like I go back in November for my check-ups*" [P3]). As demonstrated by the descriptions above, participants also openly discussed the role of the health professionals in their physical recovery from surgery, however, they do not describe care received related to their mental health throughout recovery.

These descriptions of patient, physical health, and surgery-related experiences are characterized as the *perioperative voice* because of how they were communicated. These topics were readily discussed by all participants, without hesitation; some participants engaged in 'story-telling' related to these topics without the use of probing questions. In addition, these descriptions were clear; they were comprised of direct language and more detailed information relative to descriptions of mental health experiences.

Study 2 Discussion

This study explored older adult surgical patients' experiences and descriptions of perioperative mental health symptoms, delirium and dissociation in particular, and how participants are impacted by these symptoms. Results revealed that participants generally did not describe their mental health experiences during the perioperative period; however, when they did, descriptions were characterized by vague and minimizing language, and generally were not

explicitly linked to mental health. Instead, participant descriptions largely included content related to physical health experiences in the perioperative period. This study represents the first qualitative investigation of perioperative dissociation and adds to a growing body of literature that describes individuals' experiences of delirium. This study is an important contribution to the perioperative mental health literature and has notable implications for perioperative patient care.

In line with the inclusion criteria, participants experienced elevated symptoms of delirium and/or dissociation during the perioperative period. However, not a single participant explicitly mentioned the terms "delirium" or "dissociation", and the majority of participants did not characterize their perioperative mental health in a negative light. Further to this, participants rarely made explicit links between their reported experiences and their mental health. When participants did discuss mental health experiences, this was done in an indirect way characterized by vagueness, minimizing language, and gaps in communication between the patient and healthcare professionals.

There are various possible reasons to account for the relative *silence* surrounding perioperative mental health descriptions. For example, due to the nature of symptoms of dissociation and delirium (e.g., fragmented memory, alterations in awareness, confusion; American Psychiatric Association, 2013; Inouye, Westendorp et al., 2014; van der Kolk & Fisler, 1995) and elements of postoperative care patients may have been exposed to (e.g., administration of sedatives; Shinotsuka & Serafim, 2014), patients may have limited recall of these symptoms; thus, self-report of mental health symptoms and experiences may be inconsistent with symptom elevations from the CAM-S, which was administered by trained personnel. Prior research has shown that patients with delirium may exhibit reduced recall of factual experiences compared to

those without delirium (Roberts et al., 2007). However, overall the literature is relatively inconsistent regarding the proportion of patients who recall their experiences of delirium, specifically (Partridge, Martin, Harari, & Dhesi, 2013); some studies report the majority of patients do not recall their experiences during a delirious state, particularly those with elevated preoperative cognitive dysfunction (Duppils & Wikblad, 2007), whereas others have found high rates of delirium recall (Andersson, Hallberg, Norberg, & Edberg, 2002).

In comparison to delirium, qualitative research pertaining to the experience of perioperative dissociation is non-existent, to my knowledge, so it is unclear how these symptoms may impact perioperative recall. Interestingly, the one participant who had elevated symptoms of perioperative dissociation reported vivid recall of "unusual" perioperative experiences (i.e., dissociative experiences) and described experiencing a negative emotional impact; he indicated this experience was disturbing and scary and that he felt worried as a consequence of his perceived loss of control over his mind. In addition, the participant felt that the experience of these symptoms also impacted him physically, and set back his postoperative recovery. This reported experience is in line with previous research that has shown recall of unusual experiences (e.g., perceptual distortions, delusional memories, vivid dreams) following treatment in the ICU is associated with poor mental health, including distress, anxiety, and PTS (Jones et al., 2001; Jones et al., 2007; Kiekkas et al., 2010). Considering the established association between poor perioperative mental health and poor postoperative physical health outcomes (Cremeans-Smith, Green, & Delahanty, 2011; Hanusch, O'Connor, Ions, Scott, & Gregg, 2014), it is unsurprising that this participant also noticed an impact on his physical recovery.

Another possible explanation for the *silence* of perioperative mental health may be that participants were reluctant to share their experiences with others. Prior research suggests that

patients who experience perceptual distortions or other unusual symptoms that may occur during a delirious state may be reluctant to discuss these experiences with healthcare professionals (O'Malley, Leonard, Meagher, & O'Keefe, 2008; Tate et al., 2013; Van Rompaey et al., 2016); this may also extend to the interviewer in the current study. A recent qualitative study by Van Rompaey and colleagues (2016) found that communication with patients who had delirium was difficult; these patients exhibited limited self-expression and some denied having experienced symptoms of delirium. These authors also found that patients attributed the cause of their symptoms to the anesthetic they were administered or to other administered medications, which is also consistent with the current study. Other researchers found that patients who had delirium were less likely than those who did not to initiate communication with hospital staff regarding symptoms experienced postoperatively (Tate et al., 2013). This gap in communication between patients and healthcare professionals was also evident in the current study. The sociodemographic characteristics of participants in the current study, age and sex in particular, may also have influenced the silence of perioperative mental health and gaps in communication about mental health with health professionals. The current sample was comprised solely of older adult males. Prior research has demonstrated that males tend to have less positive attitudes toward mental health-related help-seeking compared to females (Mackenzie, Gekoski, & Knox, 2006). Research has also shown that older adults have lower rates of mental health service utilization compared to younger adults (DiNapoli et al., 2016), which may extend to a reduced willingness to discuss mental health.

It is also possible that the lack of communication surrounding symptoms of delirium and dissociation is a consequence of under-recognition and under-diagnosis, which have been found in previous research on delirium (O'Mahony, Murthy, Akunne, Young, & Guideline

Development Group, 2011; Lawlor & Bush, 2014). Lawlor and Bush (2014) suggest that poor recognition of delirium by health professionals may be due to its clinical presentation or inadequate communication between health professionals. In light of occasional poor patient recall of delirious experiences and low recognition by health professionals there is general consensus that increased education and communication about delirium for both patients and health professionals would be beneficial (Abraha et al., 2016; Eeles, McGrow, Teodorczuk, & Caplan, 2017; Eghbali-Babadi, Shokrollahi, & Mehrabi, 2017; National Institute for Health and Clinical Excellence, 2010; Partridge et al., 2013). In fact, a panel of experts in delirium rated education and training to increase knowledge and awareness of delirium as one of the most important interventions for delirium (Eelse et al., 2017). The National Institute for Health and Clinical Excellence (NICE) has also published guidelines for the prevention, diagnosis, and management of delirium. These guidelines highlight the importance of information provision to those at risk of delirium including descriptions of delirious experiences, explanation that delirium is both common and often temporary, and encouragement for patients to share their delirious experiences with healthcare professionals (NICE, 2010). Health professionals are also encouraged to proactively ask patients questions about delirium symptoms in light of patients' occasional reluctance to initiate communication about these symptoms (Partridge et al., 2013). In support, a recent study of a cardiac surgical sample showed that communication with patients about these symptoms in the acute postoperative period might actually reduce the incidence of postoperative delirium (Eghbali-Babadi et al., 2017). Regardless of why participants in the current study rarely described experiences of delirium and dissociation, it appears information provision and education about these symptoms would be beneficial.

As indicated, perioperative mental health experiences were occasionally described in the form of a *whisper*; descriptions were often vague and included minimizing language. On occasion, participants also used this communication style when discussing their physical health or illness severity. This style of communication has been found in previous medical populations (e.g., diabetes, cancer, neurosurgery; Goebel, Mederer, & Mehdorn, 2018; Huang et al., 2016; Sehlen et al., 2003) and has been described as a verbal defense mechanism aimed at reduction of anxiety-provoking thoughts and feelings (Della Silva & Malan, 2004; Schlesinger, 1994). Some research suggests that these types of avoidant coping styles may be adaptive; Goebel and colleagues (2018) found that avoidant coping styles prior to neurosurgery were associated with reduced depressive symptoms and greater mental health-related quality of life during preoperative assessment. However, these same coping styles may have negative long-term consequences. For example, Sehlen and colleagues (2003) found that among a sample of cancer patients, 'minimizing importance' coping strategies (e.g., minimizing the severity of having cancer) prior to the commencement of radiotherapy were associated with increased psychological distress and reduced quality of life two years following treatment. Further investigation is warranted to better understand the health-related outcomes associated with these coping and communication styles.

In contrast to the limited descriptions pertaining to mental health, physical health was the focus of participant descriptions of their perioperative experiences. This finding is consistent with prior qualitative research which found that physical wellbeing was the primary focus of content from cardiac surgical patients' charts in comparison to psychological wellbeing (Karlsson, Lidell, & Johansson, 2013); perhaps a primary focus on physical health is shared by patients and healthcare providers. In particular, participants noted their decline in physical

health and the severity of their physical status prior to surgery, the experience of pain, other physical symptoms (e.g., water retention, swelling, skin tightness), sleep difficulties, and low energy following surgery, as well as the process of regaining mobility and having their physical health status monitored regularly during recovery. These themes are consistent with those that have emerged in other surgical samples (e.g., Chang & Tsia, 2017; Gelhorn et al., 2018; Sibbern et al., 2017). For example, a recent qualitative study of illness descriptions in a cardiac surgical sample highlighted the experience of sudden and serious symptoms (e.g., pain, breathing difficulty, passing out), uncertainty of survival, physical discomfort (e.g., pain, weakness), and sleep difficulties as common emergent themes (Chang & Tsai, 2017). Further investigation is warranted to understand whether a primary focus on physical health is related to certain patient (e.g., sex, age, type of physical illness) or surgery-related (e.g., type of surgery) characteristics, or is common across individuals and samples.

Limitations

Although this study represents an important contribution to the perioperative mental health literature, results must be considered alongside some limitations. First, the sample was relatively homogeneous (all participants were older adults, male, married/common law, and underwent cardiac surgery at Saint Boniface Hospital). Although results are not intended to generalize to all cardiac surgical patients, it is important to consider the influence of the sample characteristics on the emergent theoretical model (e.g., may have directly contributed to the silence of perioperative mental health). Second, the initial recruitment strategy required modifications due to the lack of participants who met the initial inclusion criteria; thus, I was unable to investigate experiences of individuals who had co-occurring dissociation and delirium symptoms (only a single participant met both inclusion criteria). After applying less stringent

inclusion criteria, recruitment challenges persisted (though were attenuated) due to a relatively small proportion of individuals who were eligible to participate. Although this reflects positive postoperative mental health outcomes for participants in ENGAGES-CANADA, challenges with recruitment resulted in a smaller sample size than anticipated, which may have resulted in a less comprehensive theoretical framework. Finally, although all participants were offered the option of in-person interviews, all participants selected to have their interviews conducted over-the-phone; this style of interview inhibited my ability to observe participants' non-verbal cues. In addition, my ability to connect with participants during interviews may have been limited with this interview method; this may have influenced the degree to which participants were willing to share openly. Nonetheless, the current study produced a detailed theoretical framework, which has important implications for perioperative patient care.

Implications

Overall, results of this study highlight the general lack of communication about and awareness of mental health experiences during the cardiac perioperative period. These results have important implications with respect to the management of perioperative mental health. First and foremost, participants in this study generally did not appear aware of the relevance of mental health in commonly experienced symptoms in the perioperative period (e.g., confusion, disorientation, fragmented memory). In addition, there appeared to be a gap in communication related to perioperative mental health experiences between participants and healthcare professionals. These findings highlight the importance of implementing NICE's guidelines surrounding provision of information on mental health experiences to patients (NICE, 2010) and recommendations for the use of educational interventions to increase knowledge and awareness of perioperative mental health experiences for both patients and health professionals (Abraha et

al., 2016; Eeles et al., 2017); such interventions have been associated with improvements in mental health during the perioperative period (e.g., Eghbali-Badabi et al., 2017; Partridge et al., 2013). With limited awareness of and communication about perioperative mental health experiences, these symptoms may end up going unnoticed, and ultimately may persist in the absence of proper intervention; this is problematic, especially in the context of delirium, given the well-established adverse associated outcomes (e.g., greater length of hospital stay, increased risk of postoperative complications, functional decline, cognitive impairment, post-discharge institutionalization, mortality; Bulic et al., 2015; Girard et al., 2010; Inouye, Kosar et al., 2014; Pandharipande et al., 2013; Raats et al., 2015; Rudolph et al., 2010; Witlox et al., 2010). In addition to increased information, education, and communication, further attention dedicated to assessment and early intervention is warranted to mitigate risk of long-term consequences of these perioperative mental health experiences.

General Discussion

This thesis represents an in-depth examination of perioperative dissociation and postoperative delirium in a non-emergent surgical sample of older adults, using quantitative and qualitative methodologies. Using quantitative methods, study 1 examined symptom-level overlap between perioperative dissociation and postoperative delirium, and associations between these symptom presentations with PTS. Results revealed limited statistical overlap between individual symptoms of dissociation and delirium, but independent associations for both conditions with postoperative PTS. These associations differed according to the covariates included in regression models. Using qualitative methods informed by constructivist grounded theory, study 2 explored how participants describe and experience symptoms of dissociation and delirium, and how they are impacted by these symptoms. Results highlighted the limited

communication regarding perioperative mental health experiences; instead of discussing their mental health, participants generally focused on physical health-related experiences throughout the perioperative period. Across both studies, results document the existence of mental health sequelae in the perioperative period as well as notable similarities and differences between perioperative dissociation and postoperative delirium.

Triangulation of Quantitative and Qualitative Data

Participants from both studies endorsed mental health symptoms in the perioperative period. With respect to study 1, over 16% of participants experienced postoperative delirium (this increases to nearly 40% if including subsyndromal delirium) and over 18% had clinically significant perioperative dissociation at discharge from hospital; in total nearly 45% of participants had either subsyndromal (or threshold) postoperative delirium or clinically significant perioperative dissociation, or both. Interestingly, nearly 80% of those with clinically significant dissociation also had subsyndromal or threshold postoperative delirium, however less than 40% of those with subsyndromal or threshold postoperative delirium had clinically significant dissociation. In addition, all participants from study 2 experienced subsyndromal delirium on at least one postoperative day and one participant also experienced clinically significant perioperative dissociation symptoms. No participants screened for study 2 had clinically significant dissociation in the absence of subsyndromal or threshold postoperative delirium, supporting that 'pure' dissociation is relatively uncommon. Overall, this thesis suggests the experience of mental health symptoms in the perioperative period is not uncommon.

Are Dissociation and Delirium Overlapping or Distinct? Although this thesis does not provide a definitive answer regarding whether dissociation and delirium are overlapping or distinct symptom presentations, triangulation of data across studies may provide helpful insights.

In line with conceptually overlapping features outlined in previous literature (American Psychiatric Association, 2013; Briere et al., 2005; DiMartini et al., 2007; Inouye, Westendorp et al., 2014; McKinnon et al., 2016), total scores for dissociation and delirium from study 1 were significantly correlated. In addition, cross-tabulations demonstrated elevated rates of subsyndromal or threshold postoperative delirium among individuals with clinically significant dissociation. Study 2 also provides support for similarities between dissociation and delirium; in this study, none of the participants recognized the relevance of either symptom presentation to their mental health. Instead, these participants conceptualized that their symptoms (or "unusual experiences") arose as a result of the anesthetic or other perioperative medications. Nonetheless, study 2 participants described common elements of dissociative and/or delirious experiences including confusion, disorientation, fragmented memory, and a warped perception of time. Overall, quantitative and qualitative data across both studies suggest that some similarities exist between perioperative dissociation and postoperative delirium.

Despite these similarities, this thesis also outlines important differences between perioperative dissociation and postoperative delirium. Most notably, results from study 1 revealed insufficient statistical overlap between dissociation and delirium at the symptom-level; as discussed previously, this may reflect true distinctions between symptoms or discrepancies stemming from differences in how these symptoms were assessed. As indicated, although nearly 80% of those with clinically significant dissociation endorsed subsyndromal or threshold postoperative delirium, only approximately one-third of those with delirium endorsed clinically significant dissociation; the reduced prevalence of dissociation among those with delirium may also have contributed to the PCA results from study 1. Had this analysis been run among the subset of those with delirium who had co-occurring dissociation, results may have supported

symptom-level overlap. Interestingly, participant descriptions of their mental health experiences from study 2 also demonstrated differences between perioperative dissociation and postoperative delirium. In particular, the one participant in study 2 who experienced clinically significant perioperative dissociation was the only individual who reported vivid recall of unusual perioperative experiences (e.g., dream-like state, inability to speak, frightening dream, perceptual disturbances). This may suggest that dissociation and delirium are associated with varying degrees of recall. Perhaps subjective endorsement of clinically significant dissociation is an indicator of recall of delirium, or recall of adverse perioperative mental health experiences in general. Implications of recall on adverse mental health outcomes are elaborated below.

Are Dissociation and Delirium Associated with Adverse Mental Health Outcomes?

Triangulation of quantitative and qualitative data suggests that dissociation and delirium can be associated with adverse mental health outcomes, under certain circumstances. Results from study 1 outlined significant associations between both dissociation and delirium with postoperative PTS. Dissociation was only associated with PTS in unadjusted models and models adjusted for sociodemographics, whereas delirium was only associated with PTS in models adjusting for preoperative mental health symptoms and perioperative dissociation; a more detailed description of hypotheses to explain these differential associations are outlined below (see "Working Conceptual Model of Perioperative Mental Health"). In study 2, the majority of participants (i.e., who had subsyndromal delirium without clinically significant dissociation) did not endorse adverse mental health outcomes. However, as indicated, the one individual who experienced co-occurring subsyndromal postoperative delirium and clinically significant dissociation was the only participant who described a negative impact (e.g., fear, worry) related

to these symptoms; in addition to adverse mental health impacts, he also expressed that he felt these symptoms caused him a setback in his physical recovery from surgery.

The differential associations between dissociation and delirium with PTS and other adverse mental health outcomes may stem from variations in recall and/or symptom severity. For example, individuals from study 2 with delirium may have had severe symptoms that were not recalled (e.g., due to associated cognitive impairment or fluctuations in awareness) or symptoms that were particularly mild such that participants did not perceive subjective changes in their mental health or cognitive functioning; in either case, it is less likely that symptoms would be associated with adverse mental health outcomes. On the other hand, the participant who experienced dissociation may have had moderate symptoms, such that he experienced recall and the associated subjective distress. Of note, designated severity ratings based on the CAM-S have not yet been established, so it is unclear what constitutes a 'mild', 'moderate', or 'severe' score, and whether these hypotheses are supported; participants in study 2 with delirium only had peak scores ranging from 6-12, and the participant with co-occurring dissociation had a peak CAM-S score of 5. See below for an elaboration on these hypotheses in the Working Conceptual Model of Perioperative Mental Health.

Overall, results of this thesis convey important implications for management of perioperative mental health symptoms and experiences. As evidenced by study 2 results, individuals appear to have limited awareness of mental health symptoms that may be experienced throughout the perioperative period. This may have negative implications in the context of recall of unusual perioperative experiences (e.g., strange dreams, perceptual disturbances), in line with previous research that supports a relationship between recall of postoperative hallucinations and delusions with PTS (DiMartini et al., 2007; Marra et al., 2017;

Wade et al., 2015). Both patients and healthcare professionals would benefit from increased education regarding these symptoms, how they may be experienced, and how they may impact patients. This is particularly important in light of the *silence* of perioperative mental health outlined in study 2 and the well-established negative health outcomes associated with postoperative delirium (Bulic et al., 2015; Girard et al., 2010; Inouye, Kosar et al., 2014; Pandharipande et al., 2013; Raats et al., 2015; Rudolph et al., 2010; Witlox et al., 2010). With increased education regarding these symptoms, patients and health professionals may be more likely to discuss these symptoms and other unusual perioperative experiences more often, which may facilitate proper symptom identification and treatment. Stemming from the elevated prevalence estimates of dissociation and delirium in study 1 and their associations with PTS, results highlight the importance of integrating routine mental health screening into perioperative patient care. Although the importance of delirium screening is well recognized, screening for other mental health symptoms (e.g., preoperative PTS or depressive/anxiety symptomatology, perioperative dissociation) in a surgical setting is not considered standard of care. Preoperative screening could help identify individuals at risk for perioperative dissociation and postoperative delirium, and postoperative screening may detect early manifestations of these symptom presentations. However, in a perioperative context, mental health screening at multiple stages may not be feasible. Perhaps implementing a perioperative dissociation screen in the acute postoperative period or at discharge from hospital may be particularly beneficial; such screening may capture pre-existing mental health vulnerabilities in addition to subjective recall of delirious and dissociative experiences, both of which would help identify individuals at-risk for additional adverse postoperative mental health sequelae. Identification of clinically significant dissociation, particularly among those with postoperative delirium, could highlight individuals who may

benefit most from early interventions (e.g., brief exposure-based interventions, other cognitive behavioural interventions, ICU diary intervention [see study 1 discussion]; Birk et al., 2019; Garrouste-Orgeas et al., 2012; Jones et al., 2010; Rothbaum et al., 2008; Rotubaum et al., 2012). Such interventions could be administered prior to discharge from hospital, or at the time of postoperative physical health follow-up appointments, and may mitigate the risk of postoperative PTS. Additional investigation is warranted to further examine appropriate assessment tools and determine suitable intervention strategies for surgical patient populations that are feasible to implement in a hospital setting.

Working Conceptual Model of Perioperative Mental Health

Based on the results from studies 1 and 2, I modified the diathesis-stress models for postoperative delirium and PTS (described in the introduction) into a working conceptual model of perioperative mental health. Figure 6 highlights components implicated in the diathesis-stress model that are particularly relevant to findings from this thesis. Of note, additional relevant factors (e.g., age, perioperative medication, social support) are not included in this model, due to either limited empirical support from study 1 or 2 or not being assessed in these studies, but nonetheless may be implicated in perioperative mental health.

As shown in Figure 6, the interaction between poor baseline mental health (i.e., one of many diatheses) and the physiological and psychological stress associated with surgery and elements of postoperative care (e.g., intensive care) catalyze the expression of postoperative delirium and perioperative dissociation. In turn, these symptom presentations may be conceptualized as additional stressors, which ultimately catalyze the expression of postoperative PTS. A Venn diagram in the figure represents the conceptual and symptom severity overlap between postoperative delirium and perioperative dissociation. This overlap is supported by a

significant correlation between total scores and overlapping prevalence estimates of subsyndromal or threshold postoperative delirium with clinically significant perioperative dissociation. The proportion of overlap in the figure mirrors the overlap in prevalence demonstrated by cross-tabulations; most individuals with clinically significant dissociation endorsed subsyndromal or threshold postoperative delirium, however only a small subset of those with postoperative delirium endorsed clinically significant perioperative dissociation.

As indicated by the most prominent arrow pointing toward postoperative PTS, individuals with postoperative delirium who also endorse clinically significant perioperative dissociation appear to have the greatest risk of postoperative PTS. This hypothesis is supported by changes in the associations between postoperative delirium and PTS upon inclusion of perioperative dissociation as a covariate in study 1. For re-experiencing symptoms, inclusion of dissociation resulted in a reduction in predictive ability of delirium on PTS. However, for negative mood and cognition symptoms, controlling for dissociation resulted in an increase in predictive ability of delirium. These changing associations suggest that perioperative dissociation is somehow implicated in the association between postoperative delirium and PTS, perhaps as a mediator, moderator, or confounding factor; this is an important avenue to explore in future investigations. Although none of the participants from study 2 endorsed symptoms of postoperative PTS, the one participant who experienced both subsyndromal postoperative delirium and clinically significant perioperative dissociation was the only participant who endorsed symptoms indicative of subjective distress (e.g., worry, fear). Overall, results of both studies suggest that clinically significant perioperative dissociation may be an indicator of poor mental health outcomes among those with postoperative delirium, PTS in particular based on study 1 results.

In line with prior research, the model also displays associations between postoperative delirium and perioperative dissociation with PTS, independent of one another (i.e. indicated by white and grey arrows). In study 1, postoperative delirium was significantly associated with postoperative PTS after controlling for baseline mental health symptoms, both prior to and after adjusting for perioperative dissociation. Further, with respect to the relationship between delirium and total PTS, the magnitude of association remained nearly unchanged after additionally adjusting for perioperative dissociation. These results support an association between delirium and PTS, independent of perioperative dissociation, which is supported by previous research (Drews et al., 2015; Morrissey & Collier, 2016). Studies suggest that frightening hallucinations and delusion experienced while delirious may increase the risk of PTS (Davydow et al., 2008; DiMartini et al., 2007; Wade et al., 2015); although speculative, it is possible these experiences may occur in the absence of endorsement of clinically significant dissociation. This may be relevant to the sub-sample of over 60% of those with subsyndromal or threshold delirium who did not endorse clinically significant dissociation.

Results from study 1 also revealed associations between perioperative dissociation and PTS, prior to controlling for baseline mental health symptoms and postoperative delirium. Figure 6 includes an indirect pathway from poor baseline mental health symptoms to postoperative PTS through perioperative dissociation (i.e., grey arrows). This resembles the hypothesized pathway of association from study 1. After adjusting for baseline mental health symptoms, perioperative dissociation was no longer significantly associated with PTS. This may suggest that poor baseline mental health is either a stronger predictor of postoperative PTS, or is driving or confounding the association between perioperative dissociation and PTS. For example, those with pre-existing PTS symptoms may be more vulnerable to perioperative

dissociation, which then increases the risk of postoperative PTS. Another possibility is that individuals with a preoperative mental health history are more aware of or sensitive to mental health symptoms, and thus more likely to endorse self-reported symptoms, including dissociation. It may also be that the PTS being captured in these associations reflects pre-existing symptoms, as opposed to new onset symptoms related to surgery; these symptoms may worsen in the context of increased stress associated with surgery, or worsen overtime due to factors that were not measured in the current study (e.g., interpersonal stressors). As such, Figure 6 also includes a direct path between poor baseline mental health and PTS to reflect the possibility of an independent association between these factors (i.e., bottom arrow).

Finally, Figure 6 also includes "other influential factors" that may help elucidate the differential associations between postoperative delirium and perioperative dissociation with postoperative PTS; these factors are also relevant to the communication style (e.g., silence, whisper [from study 2 framework]) utilized by individuals who experience these symptoms. For example, participants from study 2 who experienced subsyndromal postoperative delirium only did not endorse symptoms of PTS, or any adverse mental health symptoms in the perioperative period. Rather, descriptions by these participants were characterized as part of the *silence* of perioperative mental health, outlined in the study 2 framework. The "other influential factors" included in Figure 6 may help explain the silence exhibited by these participants. For example, in the absence of recall, participants likely would not endorse subjective distress or adverse mental health symptoms. This might occur in the context of mild symptom severity, wherein symptoms do not have a noticeable impact on mental functioning, or in the context of severe symptoms, such that the individual exhibits no awareness or recall. Under these circumstances,

silence may be advantageous and perhaps protective against adverse mental health outcomes. This hypothesis is an important avenue for future investigations.

In contrast, perhaps the one study 2 participant who endorsed explicit recall of his symptoms and subjective distress experienced moderate symptom severity; in support, he was noticeably impacted by his symptoms, but not to the point of losing awareness or recall ability. If endorsement of self-reported clinically significant dissociation is indeed an indicator of recall of perioperative mental health symptoms (including delirium), perhaps *silence* in this context would be associated with adverse outcomes (e.g., PTS); this may be particularly relevant if an individual experiences fragmented memories of mental health experiences, which may increase the risk of PTS (Briere et al., 2005; Ehlers & Clark, 2000; Peltonen et al., 2017). Under such circumstances, the individual would likely benefit from communication, education, and/or psychological intervention related to his or her mental health symptoms and experiences.

Conclusion

This thesis investigated mental health sequelae in the perioperative period, including perioperative dissociation, postoperative delirium, and postoperative PTS. Although results shed light on the nature of the associations between these factors, additional investigation is warranted to better understand the causality and temporality of these relationships and their underlying mechanisms. Nonetheless, results highlight the importance of public awareness of these symptoms and improvements in perioperative management of these symptoms. In light of the unique and adverse mental health correlates associated with perioperative dissociation in the context of postoperative delirium, perioperative screening for dissociation may prove beneficial for identifying individuals at risk for additional adverse mental health sequelae, including PTS.

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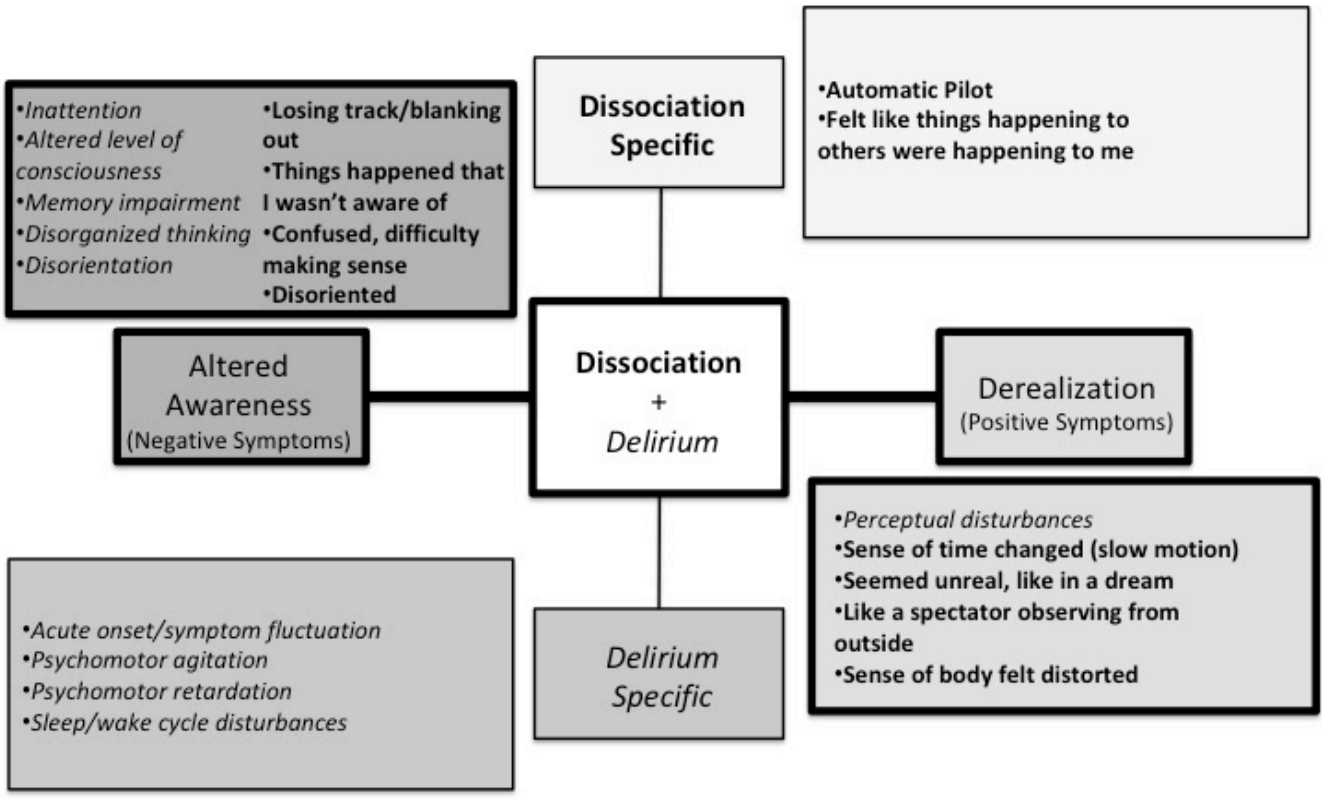

Figure 1. Hypothesized common components of dissociation and delirium; Bold items represent dissociation; Italicized items represent delirium.

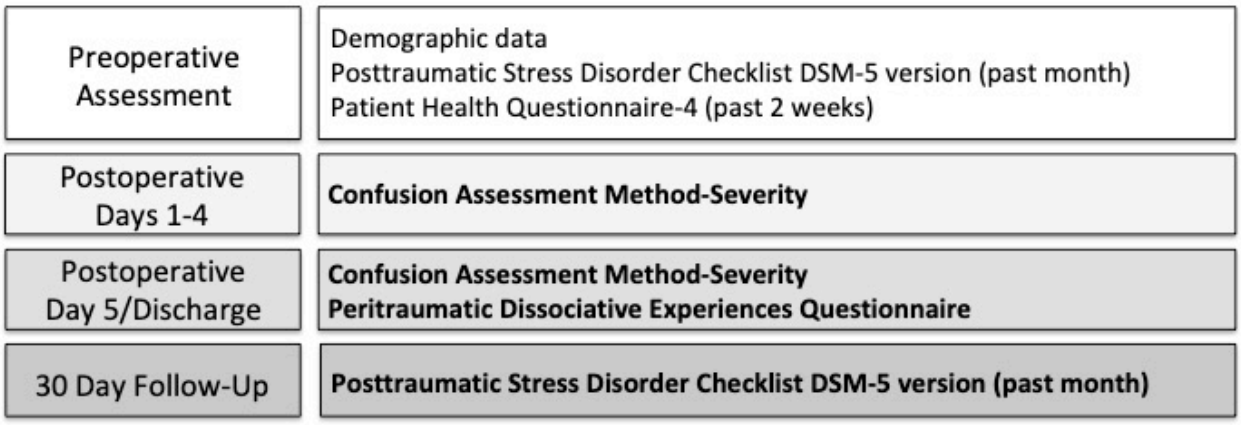

Figure 2. ENGAGES assessment timeline; Bolded measures were utilized as primary measures in analyses. Non-bolded measures were examined as covariates in analyses.

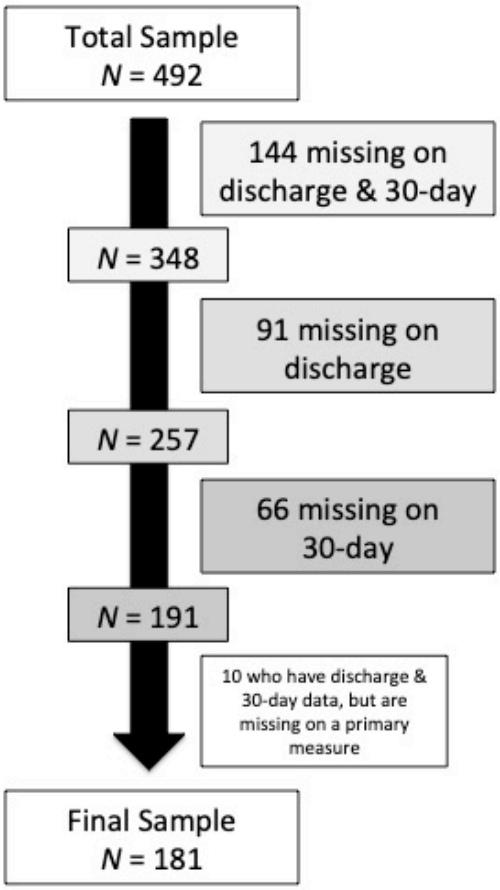

Figure 3. Study 1 participation flow chart

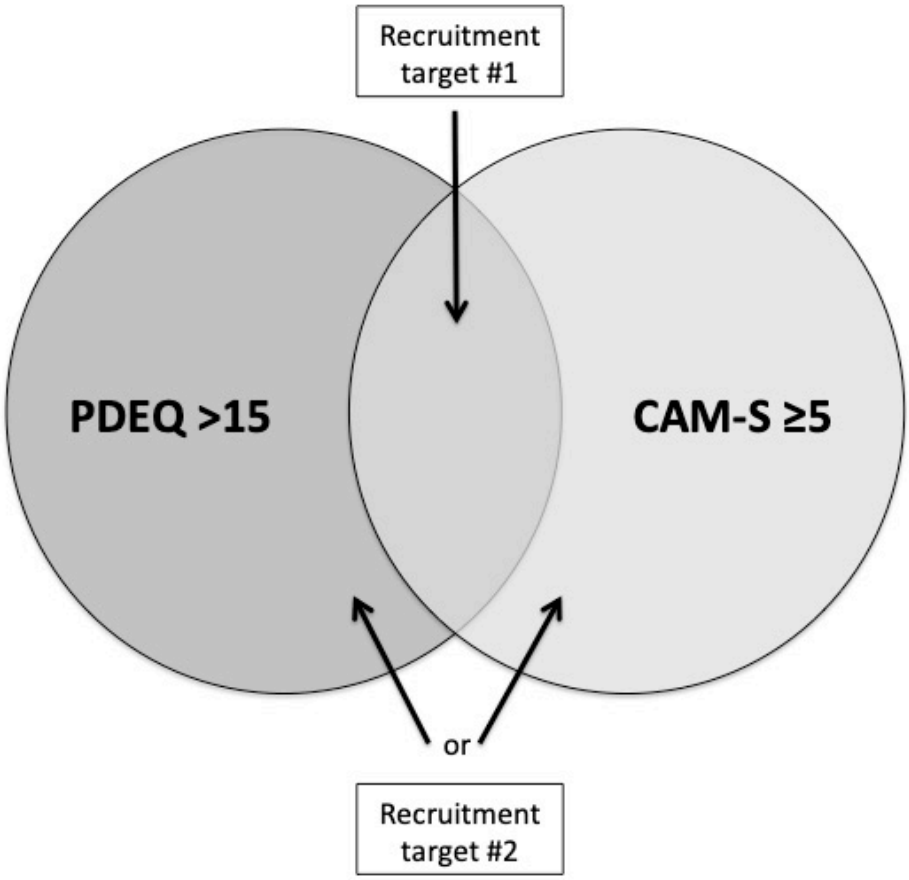

Figure 4. Recruitment targets for study 2 qualitative interviews

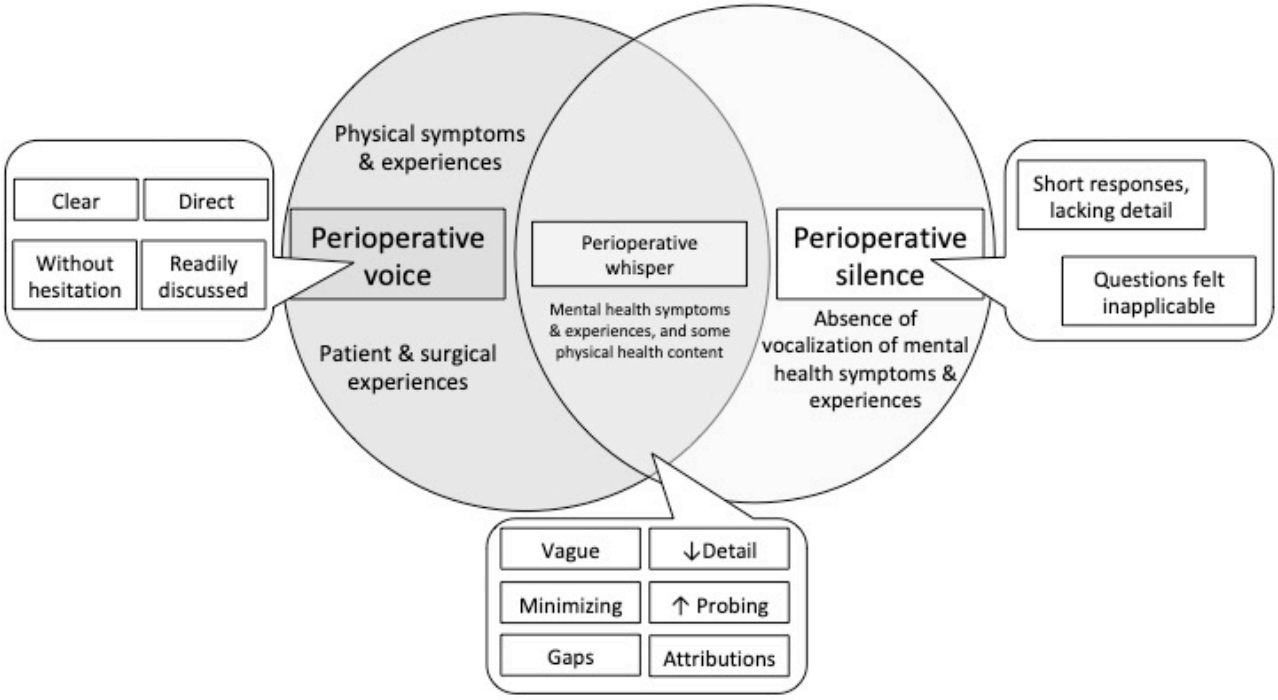

Figure 5. Study 2 theoretical model.

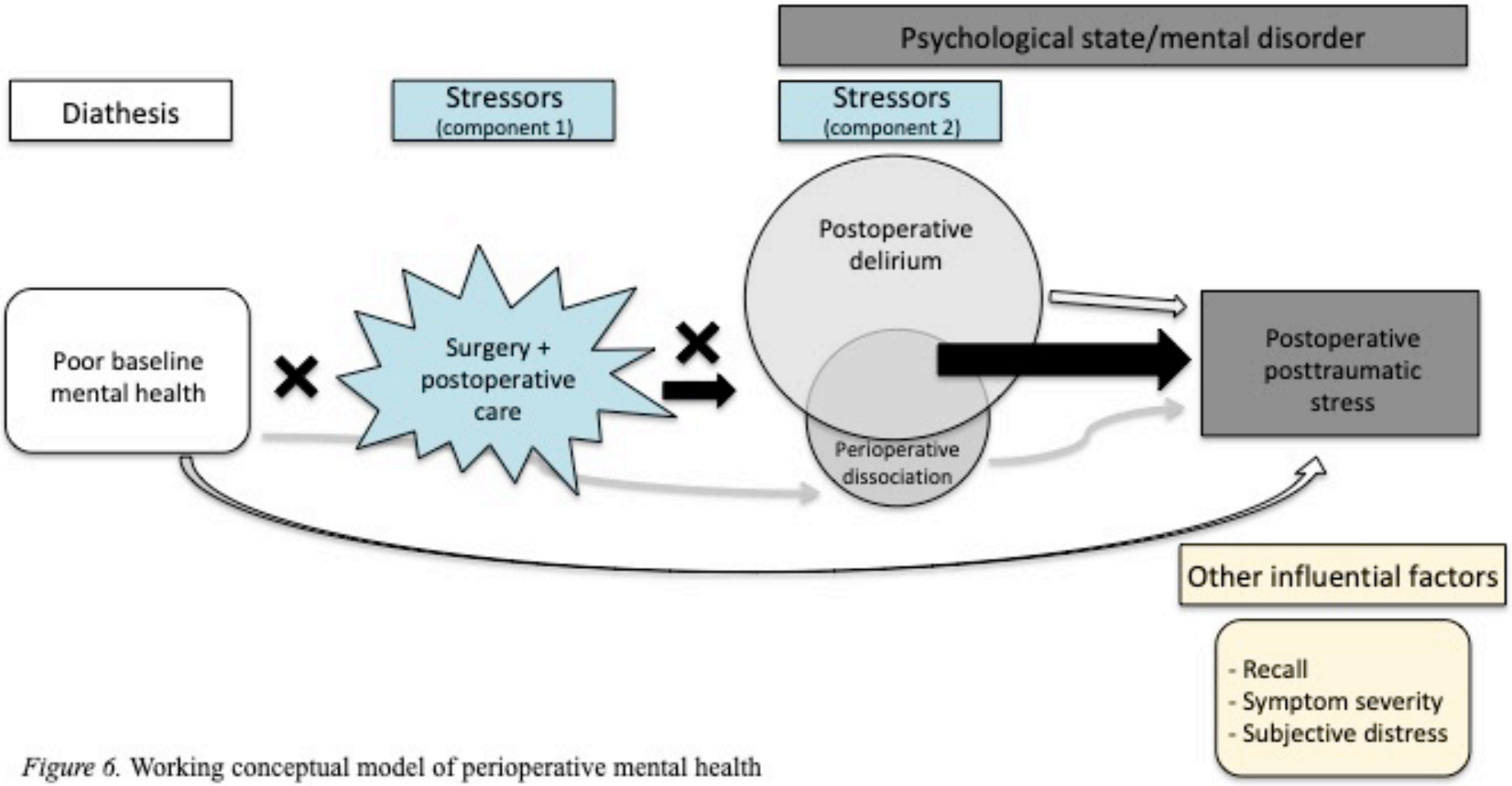

Figure 6. Working conceptual model of perioperative mental health

Table 1
Comparison of sample characteristics according to additional modules completed

	Baseline Only	Baseline & Discharge	Baseline & 30-Day	All Study Components	
n(%)	144 (29.3)	66 (13.2)	91 (18.5)	186 (37.8)	Chi-Square/ ANOVA
Sociodemographic Characteristics					
Age[a]	71.61 (6.9)	69.00 (6.05)	71.84 (7.87)	69.78 (6.44)	3.24[b]*
Sex					0.86
Male	76 (74.5)	40 (76.9)	59 (76.6)	121 (72.0)	
Female	26 (25.5)	12 (23.1)	28 (23.4)	47 (28.0)	
Race					22.61***
White	34 (32.1)	34 (55.7)	29 (35.4)	99 (56.9)	
Other	72 (67.9)	27 (44.3)	53 (64.6)	75 (43.1)	
Education					9.23
Less than high school	30 (30.6)	11 (21.2)	26 (34.7)	43 (26.5)	
High school or equivalent	23 (23.5)	21 (40.4)	26 (34.7)	47 (29.0)	
Some college or higher	45 (45.9)	20 (38.5)	23 (30.7)	72 (44.4)	
Marital Status					7.22
Single	11 (10.6)	4 (7.1)	8 (10.5)	17 (10.1)	
Married	69 (66.3)	46 (82.1)	59 (77.6)	126 (75.0)	
Widowed/separated/divorced	24 (23.1)	6 (10.7)	9 (11.8)	25 (14.9)	
Mental Health					
Postoperative Delirium					
POD on at least one day	18 (21.7)	16 (25.4)	10 (13.2)	30 (16.5)	4.50
Subsyndromal /threshold POD on at least one day	62 (54.9)	32 (50.8)	26 (34.2)	71 (39.2)	11.22*
Highest [peak] POD symptom severity[a]	5.07 (3.01)	4.98 (3.04)	4.07 (2.55)	4.28 (2.81)	3.03[b]*
Perioperative Dissociation					
Clinically significant dissociation	--	13 (20.0)	--	35 (18.8)	0.04
Dissociative symptom severity[a]	--	12.88 (4.09)	--	13.86 (6.87)	-1.38[b]
Postoperative Posttraumatic Stress					
Posttraumatic stress symptom severity[a]	--	--	6.42 (6.62)	6.30 (8.87)	0.11[b]

Note. [a]Values represent *M*(*SD*); [b]Values represent t-statistics; *$p < .05$, ***$p < .001$

Table 2

Sample characteristics of major elective surgery patients (study 1)

	Total Sample	Completed Primary Measures
n(%)	492 (100.0)	181 (36.8)
ENGAGES site		
Kingston	81 (16.5)	29 (16.0)
Health Sciences Centre	61 (12.4)	38 (21.0)
Saint Boniface Hospital	262 (53.3)	74 (40.9)
Montreal	88 (17.9)	40 (22.1)
Type of surgery		
Cardiac	376 (76.4)	118 (65.2)
Non-cardiac	116 (23.6)	63 (34.8)
Sociodemographic Characteristics		
Age[a]	70.47 (6.84)	69.76 (6.42)
Sex		
Male	298 (60.6)	120 (66.3)
Female	103 (20.9)	45 (24.9)
Race		
White	197 (40.0)	97 (53.6)
Other	231 (47.0)	74 (40.9)
Education		
Less than high school	111 (22.6)	42 (23.2)
High school or equivalent	117 (23.8)	45 (24.9)
Some college or higher	160 (32.5)	72 (39.8)
Marital Status		
Single	40 (8.1)	17 (9.4)
Married	301 (61.2)	123 (68.0)
Widowed/separated/divorced	64 (13.0)	25 (13.8)
Mental Health		
Postoperative Delirium		
POD on postoperative day 0	25 (5.1)	8 (4.4)
POD on postoperative day 1	31 (6.3)	14 (7.7)
POD on postoperative day 2	24 (4.9)	11 (6.1)
POD on postoperative day 3	15 (3.0)	5 (2.8)
POD on postoperative day 4	7 (1.4)	3 (1.7)
POD on postoperative day 5	7 (1.4)	1 (0.6)
POD on at least one day	74 (15.0)	30 (16.6)
Subsyndromal/threshold POD on at least one day	191 (38.8)	71 (39.2)
Highest [peak] POD symptom severity[a]	4.55 (2.87)	4.28 (2.81)
Perioperative Dissociation		
Clinically significant dissociation at discharge	48 (9.8)	33 (18.2)
Dissociative symptom severity[a]	13.61 (6.28)	13.84 (6.90)
Posttraumatic Stress		
Clinically significant posttraumatic stress	3 (0.6)	3 (1.7)
Posttraumatic stress symptom severity[a]	6.34 (8.20)	6.21 (8.93)
Re-experiencing[a]	1.34 (2.60)	1.39 (2.80)
Avoidance[a]	0.36 (0.94)	0.39 (1.06)
Negative alterations in mood and cognition[a]	2.29 (3.34)	2.29 (3.60)
Hyperarousal[a]	2.57 (2.85)	2.49 (2.98)

Note. [a]Values represent *M*(*SD*); POD = postoperative delirium.

Table 3
Correlation matrix of CAM-S and PDEQ items

	CAM-S Items										PDEQ Items									
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1. Acute onset/fluctuating course	1.00	.42*	.22*	.21*	.25*	.23*	.29*	.13*	.18*	.07	.20*	.11*	.07	.19*	.13*	.08	.07	.14*	.15*	.21*
2. Inattention		1.00	.30*	.33*	.31*	.34*	-.06	.10	.32*	-.04	.22*	.16*	.18*	.18*	.24*	.18*	.14*	.23*	.26*	.21*
3. Disorganized thinking			1.00	.32*	.52*	.26*	.03	.20*	.41*	.06	.27*	.23*	.10	.24*	.29*	.31*	.16*	.21*	.34*	.21*
4. Altered level of consciousness				1.00	.23*	.13	-.01	-.02	.51*	.11*	.20*	.11	.25*	.17*	.18*	.07	.12*	.11*	.23*	.14*
5. Disorientation					1.00	.22*	.11	.15*	.29*	-.07	.25*	.09	.03	.11*	.09	.21*	.06	.19*	.34*	.32*
6. Memory impairment						1.00	-.02	.09	.11*	-.03	.19*	.12*	.07	.06	.13*	.11	-.03	.08	.13*	.17*
7. Perceptual disturbances							1.00	-.00	.11	.09	.11*	.12*	.01	.08	.00	-.04	.05	.11*	.09	.15*
8. Psychomotor agitation								1.00	-.06	-.06	.14*	.15*	.03	.19*	.20*	.24*	.12*	.14*	.15*	.15*
9. Psychomotor retardation									1.00	.07	.22*	.13*	.21*	.17*	.24*	.08	.09	.14*	.36*	.15*
10. Altered sleep-wake cycle										1.00	.15*	.19*	.15*	.16*	.09	.06	.03	.10	.09	.18*
11. Blanking out, spacing out, losing track											1.00	.61*	.33*	.55*	.57*	.43*	.32*	.47*	.57*	.54*
12. Automatic pilot; doing things I did not decide to do												1.00	.35*	.54*	.49*	.39*	.40*	.45*	.56*	.46*
13. Sense of time changed													1.00	.41*	.44*	.31*	.41*	.36*	.36*	.31*
14. Seemed unreal or dream-like														1.00	.69*	.54*	.40*	.52*	.58*	.53*
15. Felt like a spectator watching what was happening to me															1.00	.61*	.32*	.41*	.47*	.38*
16. Distorted sense of body																1.00	.40*	.46*	.47*	.39*
17. Things happening to others seemed like they were happening to me																	1.00	.48*	.36*	.39*
18. A lot of things happened that I was not aware of																		1.00	.49*	.45*
19. Confused; had difficulty making sense of what was happening																			1.00	.62*
20. Disoriented; uncertain about where I was/the time																				1.00

Note. CAM-S = Confusion Assessment Method-Severity (items 1-10); PDEQ = Peritraumatic Dissociative Experiences Questionnaire (items 11-20)

*$p < .05$

Table 4

Communalities

	Initial	Extraction
CAM-S Items		
Acute onset/fluctuating course	1.000	.311
Inattention	1.000	.450
Disorganized thinking	1.000	.496
Altered level of consciousness	1.000	.365
Disorientation	1.000	.463
Memory impairment	1.000	.240
Perceptual disturbances	1.000	.023
Psychomotor agitation	1.000	.067
Psychomotor retardation	1.000	.426
Altered sleep-wake cycle	1.000	.046
PDEQ Items		
Blanking out, spacing out, losing track	1.000	.578
Automatic pilot; doing things I did not decide to do	1.000	.558
Sense of time changed	1.000	.332
Seemed unreal or dream-like	1.000	.668
Felt like a spectator watching what was happening to me	1.000	.578
Distorted sense of body	1.000	.496
Things happening to others seemed like they were happening to me	1.000	.394
A lot of things happened that I was not aware of	1.000	.498
Confused; had difficulty making sense of what was happening	1.000	.616
Disoriented; uncertain about where I was/the time	1.000	.503

Note. Extraction method: principal component analysis

Table 5
Total variance explained by principal components

	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings
Component	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total
1	**5.95**	**29.75**	**29.75**	**5.95**	**29.75**	**29.75**	**5.56**
2	**2.16**	**10.79**	**40.54**	**2.16**	**10.79**	**40.54**	**3.61**
3	1.37	6.87	47.40				
4	1.29	6.46	53.87				
5	1.05	5.24	59.10				

Note. Extraction method: principal component analysis; when components are correlated, sums of squared loadings cannot be added to obtain a total variance.

Table 6
Pattern Matrix

	Component	
	1 Dissociation Factor	2 Delirium Factor
CAM-S Items		
Acute onset/fluctuating course		.564
Inattention		.663
Disorganized thinking		.667
Altered level of consciousness		.608
Disorientation		.690
Memory impairment		.506
Perceptual disturbances		
Psychomotor agitation		
Psychomotor retardation		.651
Altered sleep-wake cycle		
PDEQ Items		
Blanking out, spacing out, losing track	.701	
Automatic pilot; doing things I did not decide to do	.760	
Sense of time changed	.580	
Seemed unreal or dream-like	.825	
Felt like a spectator watching what was happening to me	.745	
Distorted sense of body	.707	
Things happening to others seemed like they were happening to me	.656	
A lot of things happened that I was not aware of	.703	
Confused; had difficulty making sense of what was happening	.672	
Disoriented; uncertain about where I was/the time	.650	

Note. Extraction method: principal component analysis; Rotation method: Oblimin with Kaiser Normalization; Coefficients < .300 resemble factors loadings of insufficient strength, and were therefore suppressed.

Table 7
Structure Matrix

	Component	
	1 Dissociation Factor	2 Delirium Factor
CAM-S Items		
Acute onset/fluctuating course		.557
Inattention		.671
Disorganized thinking	.316	.699
Altered level of consciousness		.604
Disorientation		.557
Memory impairment		.487
Perceptual disturbances		
Psychomotor agitation		
Psychomotor retardation		.652
Altered sleep-wake cycle		
PDEQ Items		
Blanking out, spacing out, losing track	.748	.375
Automatic pilot; doing things I did not decide to do	.746	
Sense of time changed	.576	
Seemed unreal or dream-like	.817	
Felt like a spectator watching what was happening to me	.759	
Distorted sense of body	.704	
Things happening to others seemed like they were happening to me	.618	
A lot of things happened that I was not aware of	.706	
Confused; had difficulty making sense of what was happening	.752	.462
Disoriented; uncertain about where I was/the time	.697	.357

Note. Extraction method: principal component analysis; Rotation method: Oblimin with Kaiser Normalization; Coefficients < .300 resemble factors loadings of insufficient strength, and were therefore suppressed.

Table 8

Associations between delirium and dissociation symptoms with posttraumatic stress

	Total Posttraumatic Stress (30 day)							
	Model 1		Model 2		Model 3		Model 4	
	b (95% CI)	*β*	*b* (95% CI)	*β*	*b* (95% CI)	*β*	*b* (95% CI)	*β*
Delirium	0.05 (-0.02-0.12)	0.09	0.07 (-0.01-0.15)	0.13	0.13 (0.03-0.23)*	0.21	0.14 (0.01-0.28)*	0.21
Dissociation	0.05 (0.01-0.08)*	0.19	0.04 (0.00-0.08)*	0.17	0.02 (-0.03-0.07)	0.07	-0.00 (-0.06-0.05)	-0.01
	Re-experiencing Symptoms (30 day)							
Delirium	0.04 (-0.00-0.08)	0.12	0.05 (-0.00-0.09)	0.13	0.10 (0.04-0.16)**	0.27	0.10 (0.02-0.18)*	0.23
Dissociation	0.04 (0.02-0.06)***	0.26	0.03 (0.01-0.05)*	0.21	0.03 (-0.00-0.06)	0.16	0.01 (-0.02-0.04)	0.07
	Avoidance Symptoms (30 day)							
Delirium	0.02 (-0.01-0.05)	0.08	0.02 (-0.01-0.05)	0.09	0.02 (-0.02-0.06)	0.02	0.04 (-0.01-0.09)	0.16
Dissociation	0.01 (-0.00-0.02)	0.10	0.01 (-0.01-0.02)	0.08	-0.00 (-0.02-0.02)	-0.03	-0.01 (-0.03-0.01)	-0.08
	Negative Alterations in Mood and Cognition Symptoms (30 day)							
Delirium	0.01 (-0.04-0.06)	0.03	0.02 (-0.03-0.08)	0.06	0.06 (-0.02-0.13)	0.13	0.10 (0.01-0.19)*	0.21
Dissociation	0.03 (0.00-0.05)*	0.17	0.03 (-0.00-0.05)	0.15	0.00 (-0.03-0.04)	0.02	-0.01 (-0.05-0.03)	-0.06
	Hyperarousal Symptoms (30 day)							
Delirium	0.03 (-0.01-0.08)	0.09	0.04 (-0.01-0.09)	0.12	0.07 (0.01-0.13)*	0.19	0.06 (-0.02-0.14)	0.15
Dissociation	0.03 (0.01-0.05)**	0.21	0.02 (0.00-0.05)*	0.17	0.02 (-0.02-0.05)	0.10	0.01 (-0.03-0.04)	0.05

Note. Values represent unstandardized regression coefficients and 95% confidence intervals; *β* = standardized coefficients, for the purpose of comparing effect sizes; Model 1 = unadjusted; Model 2 = adjusted for age and sex; Model 3 = adjusted for age, sex, preoperative depressive/anxiety symptomatology, and preoperative posttraumatic stress; Model 4 = adjusted for age, sex, preoperative depressive/anxiety symptomatology, preoperative posttraumatic stress, and either delirium or dissociation symptoms.

*$p < .05$, **$p < .01$, ***$p < .001$

Table 9
Sample characteristics (study 2)

Sample Characteristics	*n*(%)
Age[a]	70.40 (6.58)
Sex	
Male	5 (100.0)
Female	0 (0.0)
Marital Status	
Single	0 (0.0)
Common Law	1 (20.0)
Married	4 (80.0)
Widowed	0 (0.0)
Separated	0 (0.0)
Divorced	0 (0.0)
Mental Health	
Poor	0 (0.0)
Fair	0 (0.0)
Good	2 (40.0)
Very Good	1 (20.0)
Excellent	2 (40.0)
Physical Health	
Poor	1 (20.0)
Fair	1 (20.0)
Good	0 (0.0)
Very Good	2 (40.0)
Excellent	1 (20.0)
Hospital where cardiac surgery took place	
Saint Boniface General Hospital	5 (100.0)
Format of interview	
Over the phone	5 (100.0)
In person	0 (0.0)
Screen-In Criteria	
CAM-S ≥ 5 (POD 0-5)	4 (80.0)
PDEQ > 15 (POD 5)	0 (0.0)
Both	1 (20.0)
Peak CAM-S (POD 0-5) [range]	7.60 [5.00-12.00]
PDEQ (POD 5) [range][b]	16.00 [16.00-16.00]

Note. [a]Value represents *M*(*SD*); [b]*n* = 1; POD = postoperative day.

Appendix A

Primary Measures

CAM-S LONG FORM DELIRIUM SEVERITY SCORING WORKSHEET

Feature	Question	Severity Score
1. ACUTE ONSET & FLUCTUATING COURSE	Is there evidence of an acute change in mental status from the patient's baseline? Did the patient's behavior fluctuate at any point during the interview for any of the 10 features?	No: 0 Yes: 1
2. INATTENTION	Did the patient have difficulty focusing attention, for example being easily distractible, or having difficulty keeping track of what was being said?	No: 0 Yes (mild): 1 Yes (marked): 2
3. DISORGANIZED THINKING	Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow or of ideas, unpredictable switching from subject to subject?	No: 0 Yes (mild): 1 Yes (marked): 2
4. ALTERED LEVEL OF CONSCIOUSNESS	Overall, how would you rate the patient's level of consciousness? - Alert (normal) - Vigilant - Lethargic - Stupor - Coma - Uncertain	Normal: 0 Mild: vigilant or lethargic: 1 Marked: stupor or coma: 2
5. DISORIENTATION	Was the patient disoriented at any time during the interview, such as thinking he/she was somewhere other than the hospital, using the wrong bed, or misjudging the time of day?	No: 0 Yes (mild): 1 Yes (marked): 2
6. MEMORY IMPAIRMENT	Did the patient demonstrate any memory problems during the interview, such as inability to remember events in the hospital or difficulty remembering instructions?	No: 0 Yes (mild): 1 Yes (marked): 2
7. PERCEPTUAL DISTURBANCES	Did the patient have any evidence of perceptual disturbances, for example, hallucinations, illusions, or misinterpretations (such as thinking something was moving when it was not)?	No: 0 Yes (mild): 1 Yes (marked): 2
8. PSYCHOMOTOR AGITATION	At any time during the interview, did the patient have an unusually increased level of motor activity, such as restlessness, picking at bedclothes, tapping fingers, or making frequent sudden changes of position?	No: 0 Yes (mild): 1 Yes (marked): 2
9. PSYCHOMOTOR RETARDATION	At any time during the interview, did the patient have an unusually decreased level of motor activity, such as sluggishness, staring into space, staying in one position for a long time, or moving very slowly?	No: 0 Yes (mild): 1 Yes (marked): 2
10. ALTERED SLEEP-WAKE CYCLE	Did the patient have evidence of disturbance of the sleep-wake cycle, such as excessive daytime sleepiness with insomnia at night?	No: 0 Yes (mild): 1 Yes (marked): 2
Long Form SEVERITY SCORE:	Add the scores in rows 1-10. Range is 0-19.	LF Severity Score Total (0-19) ☐
Short Form SEVERITY SCORE:	Add the scores in rows 1-4. Range is 0-7.	SF Severity Score Total (0-7) ☐
Scoring the CAM-S: Rate each symptom of delirium listed in the CAM instrument as absent (0), mild (1), marked (2). Acute onset or fluctuation is rated as absent (0) or present (1). Summarize these scores into a composite.		

 Reference: Inouye SK et al. The CAM-S: Development and Validation of a New Scoring System for Delirium Severity in 2 Cohorts. Ann Intern Med. 2014; 160:526-533.

Patient Enrollment ID: _____
POD: _____

CAM or CAM-ICU Overall Score			
Feature:		**Yes** (IF UNCERTAIN LEAVE BLANK)	**No**
I.	a)Acute Onset **CAM Scoring:** Check 'Yes' if 1.a. is scored as 1 **CAM-ICU Scoring:** Check 'Yes' if patient is different than his/her mental status.		
I.	b)Fluctuating Course **CAM Scoring:** Check 'Yes' if 2.b, 3.b, 4.b., 9.b., or 10.b. is scored as 1 **CAM-ICU Scoring:** Check 'Yes' if patient had any fluctuation in mental status; e.g. evidenced by fluctuation on a sedation scale?		
II.	Inattention **CAM Scoring:** Check 'Yes' if 2.a. is scored as 1, 2, or 3 **CAM-ICU Scoring:** Check 'Yes' if patient had more than 2 errors on inattention task.		
III.	Disorganized thinking **CAM Scoring:** Check 'Yes' if 3.a. is scored as 1, 2, or 3 **CAM-ICU Scoring:** Check 'Yes' if patient had more than one error on complex command and disorganized thinking questions.		
IV.	Altered Level of Consciousness **CAM Scoring:** Check 'Yes' if 4.a. is scored as 1, 2, or 3 **CAM-ICU Scoring:** Check 'Yes' if RASS is other than 0.		

☐ POSITIVE
☐ NEGATIVE
☐ UNCERTAIN

POSITIVE for delirium if at least one 'Yes' checked in each box.

PDEQ Discharge

Patient enrollment ID:_____ Date:_____

Instructions: Please complete the items below by circling the number that best describes the experiences you had during your surgery and/or the days following your surgery when you were in hospital. If an item does not apply to your experience, please circle "not at all true".

	Not at all true	*Slightly true*	*Somewhat true*	*Very true*	*Extremely true*
1. I had moments of losing track of what was going on. I "blanked out" or "spaced out" or in some way felt that I was not part of what was going on.	1	2	3	4	5
2. I found that I was on "automatic pilot". I ended up doing things that I later realized I hadn't actively decided to do.	1	2	3	4	5
3. My sense of time changed. Things seemed to be happening in slow motion.	1	2	3	4	5
4. What was happening seemed unreal to me, like I was in a dream, or watching a movie or play.	1	2	3	4	5
5. I felt as though I were a spectator watching what was happening to me, as if I were floating above the scene or observing it as an outsider.	1	2	3	4	5
6. There were moments when my sense of my own body seemed distorted or changed. I felt disconnected from my own body, or it was unusually large or small.	1	2	3	4	5
7. I felt as though things that were actually happening to others were happening to me – like I was in danger when I really wasn't.	1	2	3	4	5
8. I was surprised to find out afterwards that a lot of things happened at the time that I was not aware of, especially things I ordinarily would have noticed.	1	2	3	4	5
9. I felt confused; That is, there were moments when I had difficulty making sense of what was happening.	1	2	3	4	5
10. I felt disoriented; that is, there were moments when I felt uncertain about where I was or what time it was.	1	2	3	4	5

INVESTIGATOR NAME:_____

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PATIENT ID: _____ DATE: _____

PCL-5 Pre-Operative

Instructions: This questionnaire asks about problems you may have had after a very stressful experience involving *actual or threatened death, serious injury, or sexual violence*. It could be something that happened to you directly, something you witnessed, or something you learned happened to a close family member or close friend. Some examples are a *serious accident; fire; disaster such as a hurricane, tornado, or earthquake; physical or sexual attack or abuse; war; homicide; or suicide.*

First, please answer a few questions about your *worst event*, which for this questionnaire means the event that currently bothers you the most. This could be one of the examples above or some other very stressful experience. Also, it could be a single event (for example, a car crash) or multiple similar events (for example, multiple stressful events in a war-zone or repeated sexual abuse).

Briefly identify the worst event (if you feel comfortable doing so): _____

How long ago did it happen? _____ (please estimate if you are not sure)

Did it involve actual or threatened death, serious injury, or sexual violence?

_____Yes

_____No

How did you experience it?

_____ It happened to me directly

_____ I witnessed it

_____ I learned about it happening to a close family member or close friend

_____ I was repeatedly exposed to details about it as part of my job (for example, paramedic, police, military, or other first responder)

_____ Other, please describe _____

If the event involved the death of a close family member or close friend, was it due to some kind of accident or violence, or was it due to natural causes?

_____Accident or violence

_____Natural causes

_____Not applicable (the event did not involve the death of a close family member or close friend)

Second, keeping this worst event in mind, read each of the problems on the next page and then circle one of the numbers to the right to indicate how much you have been bothered by that problem in the past month.

PATIENT ID: _____ DATE: _____

In the past month, how much were you bothered by:	*Not at all*	*A little bit*	*Moderately*	*Quite a bit*	*Extremely*
1. Repeated, disturbing, and unwanted memories of the stressful experience?	0	1	2	3	4
2. Repeated, disturbing dreams of the stressful experience?	0	1	2	3	4
3. Suddenly feeling or acting as if the stressful experience were actually happening again *(as if you were actually back there reliving it)*?	0	1	2	3	4
4. Feeling very upset when something reminded you of the stressful experience?	0	1	2	3	4
5. Having strong physical reactions when something reminded you of the stressful experience *(for example, heart pounding, trouble breathing, sweating)*?	0	1	2	3	4
6. Avoiding memories, thoughts, or feelings related to the stressful experience?	0	1	2	3	4
7. Avoiding external reminders of the stressful experience *(for example, people, places, conversations, activities, objects, or situations)*?	0	1	2	3	4
8. Trouble remembering important parts of the stressful experience?	0	1	2	3	4
9. Having strong negative beliefs about yourself, other people, or the world *(for example, having thoughts such as: I am bad, there is something seriously wrong with me, no one can be trusted, the world is completely dangerous)*?	0	1	2	3	4
10. Blaming yourself or someone else for the stressful experience or what happened after it?	0	1	2	3	4
11. Having strong negative feelings such as fear, horror, anger, guilt, or shame?	0	1	2	3	4
12. Loss of interest in activities that you used to enjoy?	0	1	2	3	4
13. Feeling distant or cut off from other people?	0	1	2	3	4
14. Trouble experiencing positive feelings *(for example, being unable to feel happiness or have loving feelings for people close to you)*?	0	1	2	3	4
15. Irritable behavior, angry outbursts, or acting aggressively?	0	1	2	3	4
16. Taking too many risks or doing things that could cause you harm?	0	1	2	3	4
17. Being "superalert" or watchful or on guard?	0	1	2	3	4
18. Feeling jumpy or easily startled?	0	1	2	3	4
19. Having difficulty concentrating?	0	1	2	3	4
20. Trouble falling or staying asleep?	0	1	2	3	4

PCL-5 (8/14/2013) Weathers, Litz, Keane, Palmieri, Marx, & Schnurr -- National Center for PTSD

INVESTIGATOR NAME: _____

Version 1.0 5 January 2016

Appendix B

Questionnaire

Name: _____

Today's date: _____

Location of interview: _____

Hospital where cardiac surgery took place: _____

Age: _____

Sex: _____

Marital status:

( ) Single ( ) Common law ( ) Married ( ) Widowed ( ) Separated ( ) Divorced

In general, how would you say your mental health is (how are you feeling emotionally)?

1( ) poor 2( ) fair 3( ) good 4( ) very good 5( ) excellent

In general, how would you say your physical health is (how are you feeling physically)?

1( ) poor 2( ) fair 3( ) good 4( ) very good 5( ) excellent

Appendix C

Interview Protocol

Thank you for agreeing to participate in this interview.

During the interview, I will be asking you a number of questions related to your experiences during and after your surgery. If I ask you a question that you do not feel comfortable answering, please feel free to let me know, and we will move on to the next question. Do you have any questions for me before we start the interview? I will be turning the audio-recorder on now.

1) I understand that you underwent cardiac surgery at Saint Boniface hospital in (month and year). Can you tell me what you remember about having the surgery?

a. Can you recall anything about the surgery itself?

2) Can you tell me a bit more about your specific experiences shortly after surgery and while recovering in-hospital?

a. What are some things you remember after waking up after surgery?

b. What was your recovery like?

c. Was there anything that felt abnormal or different than usual?

d. Some people describe having a difficult time piecing together what has happened to them after a major surgery, did you find yourself feeling this way?

i. Can you tell me a bit more about that?

ii. Why do you think you might have felt this way?

e. Did your family or medical team tell you about any experiences that you had during surgery or the recovery period?

i. Did that surprise you?

ii. How did that make you feel?

3) Can you tell me what you remember about recovering from surgery, once you were back at home?

a. What was this like?

b. You mentioned x [dissociation or delirium] symptoms earlier in our interview. Did you experience these at home?

i. What was this like for you?

ii. Did those symptoms make it challenging to go about your normal daily routine?

d. How long after surgery did these symptoms continue?

e. How did this make you think and feel?

f. How did this affect you? What about your relationships?

g. Do you think about your experiences from during/after surgery often?

i. Are there any specific parts that are difficult to remember clearly?

Thanks again for your time today.

4) Is there anything else that you would like to share before we end the interview?

Probes: (used throughout)
- Can you tell me more about that?
- Can you provide me with an example of what you mean by that?

If the interview needs to be stopped early (e.g., interviewee is no longer coherent or is significantly distressed):

- Would you like to stop the interview at this point?

(if yes)

- Thank you again for your time today. If you would like to schedule a second interview to finish up our conversation please contact me by phone (I will remind them of that phone number) and we can get that set up.