Published in final edited form as:

J Clin Nurs. 2019 June ; 28(11-12): 2351–2360. doi:10.1111/jocn.14776.

The Life Course Health Development Model: A Theoretical Research Framework for Pediatric Delirium

Laura Beth Kalvas, BSN, RN, PCCN

T32 Pre-Doctoral Fellow, The Ohio State University College of Nursing

Abstract

Aims and Objectives: The purpose of this article is to create a framework for future research through application and critique of the Life Course Health Development Model to the phenomenon of pediatric delirium.

Background: Delirium in the pediatric intensive care unit is associated with increased duration of mechanical ventilation, length of stay, and mortality. Nurses are uniquely positioned at the bedside to identify, prevent, and treat delirium. An understanding of the potential long-term consequences of pediatric delirium is necessary to provide impetus for nursing research and practice change. The Life Course Health Development Model is a valuable tool when considering the multiple mechanisms and processes through which the experience of delirium could affect a child's life trajectory.

Design: Critical review of the literature through application and critique of the Life Course Health Development Model in the context of pediatric delirium. Gaps in the current understanding of pediatric delirium, as well as future directions for research and practice, are discussed.

Methods: The seven core principles of the model are considered in the context of pediatric delirium. Each of the principles has the potential to further understanding of pediatric delirium and identify areas for future inquiry. This discussion leads to a critique of the ability of the model to lead future research and practice change.

Conclusions: The Life Course Health Development Model depicts a process in which the acute and severe stress of critical illness leads to maladaptive neurologic changes that contribute to the development of delirium and impair a child's life trajectory.

Relevance to Clinical Practice: By emphasizing the potential lifelong consequences for critically ill children who experience delirium, this application of the Life Course Health Development Model will stimulate discussion, research, and practice change among pediatric clinicians and researchers.

Keywords

delirium; pediatric intensive care unit; critical care nursing; biobehavioral model

Aims

The Life Course Health Development (LCHD) Model is a valuable tool when considering the multiple mechanisms and processes through which the experience of pediatric delirium during critical illness could affect a child's long-term cognitive and functional outcomes. The purpose of this critical review is to create a framework for future research through application and critique of the LCHD Model to the phenomenon of pediatric delirium. By emphasizing the potential lifelong consequences for critically ill children who experience delirium, this author hopes to stimulate discussion, research, and practice change among pediatric researchers and clinicians.

Background

Delirium is defined as a disturbance in attention and awareness with a change in cognition (memory deficit, disorientation, or perceptual disturbance) that develops over a short period of time and fluctuates throughout the day (American Psychiatric Association, 2013). Although previously considered harmless, delirium is now recognized as a serious complication of critical illness associated with poor outcomes. Delirium affects up to 87% of adult ICU patients (Cavallazzi, Saad, & Marik, 2012) and is known to be independently associated with increased length of stay (Ely et al., 2001a), mortality (Shehabi et al., 2010), and long-term cognitive impairment (Girard et al., 2010).

Nurses are uniquely positioned to detect, prevent, and treat delirium (Balas et al., 2012; Costa et al., 2018). Through prolonged contact with the patient, bedside nurses are best able to identify the fluctuating nature of delirium. Nurse-driven interventions such as goal-directed sedation protocols (Girard et al., 2008), early mobility (Schweickert et al., 2009), sleep promotion (Flannery, Oyler, & Weinhouse, 2016), and increased family presence at the bedside (Rosa et al., 2017) decrease the incidence and duration of delirium in adult populations (Balas et al., 2014; Barnes-Daly, Phillips, & Ely, 2017). Additionally, nurses are ideally situated to facilitate communication and coordination of care between the medical team, respiratory therapy, and physical therapy, which is important for the successful implementation of delirium prevention and treatment protocols (Balas et al., 2013).

Despite the current focus on prevention and treatment of delirium in adult populations, there is a scarcity of information regarding delirium in pediatric populations. Pediatric delirium has been found to affect only 25% of children in pediatric intensive care units (PICU) around the world (Traube, Silver, Reeder, et al., 2017). Whether this reflects a true difference in the clinical presentation of delirium between critically ill children and adults or is due instead to under-recognition remains to be seen. Children less than 5 years of age appear to be especially at risk for delirium, as are children who are developmentally delayed, have a high severity of illness, are mechanically ventilated, or receive benzodiazepines (Holly, Porter, Echevarria, Dreker, & Ruzehaji, 2018; Mody et al., 2018; Silver et al., 2015; Smith et al., 2017; Traube, Silver, Gerber, et al., 2017). While efforts have been made to implement sedation protocols (Curley et al., 2015), sleep promotion (Kawai et al., 2017), early mobility (Betters et al., 2017), and increased family presence (Harrison, 2010) in pediatric intensive care, it remains unknown if there is a resulting decrease in the incidence

or duration of delirium. Long-term effects of pediatric delirium are unknown, but children with delirium have an increased duration of mechanical ventilation, PICU length of stay, and risk for mortality (Silver et al., 2015; Smith et al., 2017; Traube, Silver, Gerber, et al., 2017).

It was not until compelling evidence of the devastating effects delirium has on patient outcomes was publicized that treatment and prevention efforts in adult populations began. In much the same way, buy-in from pediatric clinicians and researchers will not come until the long-term effects of pediatric delirium are better understood. It is clear further research is needed in the area of pediatric delirium; what is less clear is where the work should begin. A theoretical research framework is needed to guide the study of the long-ranging effects of delirium over the life course of a child.

The Life Course Health Development Model

The LCHD Model (Maternal and Child Health Life Course Research Network, 2014; Figure 1) reflects a shift of emphasis in clinical practice from reactive treatment in the late stages of disease to strategies that are focused on optimizing health in early life before disease begins (Halfon, Larson, Lu, Tullis, & Russ, 2014). The model assumes that health development begins before conception and continues throughout the lifespan, continuously interacting with and adapting to environmental influences. Through this lifelong adaptation, health development is the process of building and maintaining optimal functional capacity and disease resistance (Halfon & Hochstein, 2002). The model focuses on four basic principles: the multiple contexts of health development, the processes of health development, the mechanisms that account for variation in health trajectories, and the integration of multiple time frames in health development.

Contexts of health development include the macro- and micro-context. The macro-context represents the dynamic environment of a child, including the social influences of family and community, and the overarching environment created by community structure and policy (left side of Figure 1). The micro-context, by contrast, contains the specific, individual processes and mechanisms that shape health development. These include behavioral, developmental, and biological pathways (middle of Figure 1). Health is defined as an individual's capacity, or ability, to successfully adapt to his or her environment through these pathways (Halfon et al., 2014). The macro-context influences the micro-context through the processes of biological and behavioral embedding, with the effects accumulating over time. The interaction of the macro- and micro-context is reflected in health development trajectories over the lifespan (right side of Figure 1; Halfon & Hochstein, 2002). Stressful exposures lead to a dip in the trajectory, while positive environmental exposures boost a trajectory to higher levels of health. These dips and boosts continue throughout the life span, accumulating in the health status of an individual at each phase of his or her health development.

Design

This critical review of the literature undertakes an application and critique of the LCHD Model in the context of pediatric delirium. Current gaps in the understanding of pediatric delirium are identified and promising evidence from similar populations is reviewed.

Through use of the LCHD Model as a theoretical research framework, future directions for research and practice are discussed.

Method

Application of the LCHD Model is undertaken through consideration of the seven core principles of the model (bottom of Figure 1) in the context of pediatric delirium. Each of the core principles has the potential to further understanding of pediatric delirium, identify areas for future inquiry, and emphasize the long-term effects of early life stressors, such as critical illness and delirium. Special attention is given to how the macro- and micro-contexts of a child might affect his or her long-term outcomes after experiencing delirium. This discussion leads to a critique of the ability of the LCHD Model to lead future research and practice change in the area of pediatric delirium.

Model Application

Principle one: Health as an emergent property.—Within the LCHD Model, health is conceptualized as the evolutionary ability of an individual to adapt to the demands of his or her environment (Halfon et al., 2014). Theories on the pathogenesis of delirium, however, suggest that the condition represents end-organ damage of the brain as a result of multiple insults (Silver, Kearney, Kutko, & Bartell, 2010). Therefore, in the LCHD Model delirium is conceptualized as the result of an acute dysfunction of the brain's adaptive abilities due to the multiple insults of critical illness and the current environment.

Principle two: Continuous development of health.—There are four phases of health development throughout the lifespan (Halfon et al., 2014). Children in the acquisition phase of development (right side of Figure 1), a period spanning early childhood through early adulthood, are at an increased risk for delirium (Silver et al., 2015; Traube, Silver, Gerber, et al., 2017; Traube, Silver, Reeder, et al., 2017). During this time, children are acquiring differing capacities for health development. Capacity is the ability to successfully adapt to future changes in the macro-context and is important for the maintenance of health across the lifespan. Capacity for health is developed through a continuous interaction between the macro-and micro-contexts (Halfon et al., 2014). The macro-context represents the environment of a child, while the micro-context contains the specific, individual mechanisms (i.e., capacities) that interact with the environment to shape health. Disruptions during the acquisition phase of development, such as critical illness and delirium, have the potential to damage the developing micro-context of a child and thus hinder the optimization of capacity. Therefore, while delirium may be a transient childhood exposure, the resulting damage to the child's adaptive capacity may have long-reaching effects on his or her health trajectory.

Principle three: Health development is a complex, non-linear process.—

Biochemical, psychological, and environmental factors interact in complex relationships to affect the continuous process of health development (Halfon et al., 2014). Critical care clinicians and researchers are more frequently concerned with biochemical processes, and have only recently begun to consider the influence of the macro-context (i.e., environmental

factors) and micro-context (e.g., psychological factors) on the individual life trajectories of critically ill children. Yet socially disadvantaged children are at an increased risk for adverse health outcomes, with early life adversity increasing biological stress and risk for cardio-metabolic disease (Theall, Shirtcliff, Dismukes, Wallace, & Drury, 2017; Wickrama, O'Neal, Lee, & Wickrama, 2015).

It is possible that the poor life course of disadvantaged children also reflects increased risk for the development of delirium during critical illness. Children awakening from anesthesia postoperatively are more likely to experience emergence delirium (i.e., transient agitation) if they have pre-existing emotional or behavioral problems, or have highly anxious or absent caregivers (Kain et al., 2004, 2007). These children may have a reduced health capacity due to stressful macro-context exposures that hinders the ability of their micro-context to adapt and therefore leaves them vulnerable to delirium. Researchers should evaluate how environmental and psychological factors, in addition to biochemical factors, influence risk for pediatric delirium.

Further, few have considered the role institutional resources play in the ability to identify, prevent, and treat pediatric delirium, although healthcare facilities in more disadvantaged neighborhoods tend to have fewer resources (White, Haas, & Williams, 2012). Implementation of delirium prevention measures in adult populations requires considerable time and effort to effectively change outcomes (Balas et al., 2013; Boehm et al., 2017; Carrothers et al., 2013). The social determinants of health, which include the influence of family, community structure, and policy on the macro-context, should be considered when working with critically ill children at risk for delirium.

Principle four: Health development is highly sensitive.—Early childhood is a sensitive period of development during which environmental interaction shapes individual differences in vulnerability or resilience to future adversity (Davidson & McEwen, 2012), which are important for the development of health capacity. Latent effects (right side of Figure 1) are experiences during early life that result in biological or behavioral embedding (Halfon et al., 2014), or permanent alterations to a child's micro-context, and may reflect the process through which pediatric delirium results in poor long-term functional and cognitive outcomes. Given that young age is an identified risk factor for pediatric delirium (Silver et al., 2015; Traube, Silver, Gerber, et al., 2017; Traube, Silver, Reeder, et al., 2017), it is possible that the experience of delirium during a sensitive time of development may result in maladaptive changes in a child's micro-context that contribute to a long-term dip in health trajectory.

Survivors of pediatric critical illness are known to have long-term cognitive impairment. Compared to healthy controls, children 5 months post-PICU have been found to have deficits in spatial working memory, rapid visual information processing, verbal learning, and memorization of word pairs (Elison, Shears, Nadel, Sahakian, & Garralda, 2008). It remains unknown whether children who experience delirium have worse cognitive and developmental outcomes than other survivors of pediatric critical illness. Survivors of adult critical illness demonstrate high rates of cognitive impairment in multiple domains at 3- and 12-months post-ICU (Pandharipande et al., 2013). However, critically ill adults who

experienced delirium demonstrate significantly more impairment in global cognition and executive function, with severity of impairment significantly associated with increased duration of delirium (Girard et al., 2010; Pandharipande et al., 2013). It is possible that critically ill children who experience delirium also exhibit higher rates of cognitive impairment compared to critically ill children who do not experience delirium.

A supportive macro-context may act as a buffer against latent effects in children who experience delirium. Among adults recovering from stroke, both social ties and emotional support independently predict cognitive function at 6 months post-stroke (Glymour, Weuve, Fay, Glass, & Berkman, 2008). Results such as this suggest that social and emotional support may play a role in recovery from other types of brain injury, like delirium. These effects may be magnified in children, who are even more reliant on those around them for care and support.

Principle five: Evolution affects health development.—Health development is an evolutionary adaptive process that promotes resilience and plasticity in the face of stressful macro-contexts (Halfon et al., 2014). A child's micro-context consists of the developmental, behavioral, and biological adaptations that interact with the macro-context to promote health development (middle of Figure 1). The acute dysfunction of these adaptive abilities due to the multiple insults of critical illness may result in both delirium and long-term impairments in health capacity.

Developmental adaptation.: Plasticity is the brain's ability to adapt in response to environmental cues during early development. In young animal models, environmental stressors have been found to lead to reversible changes in neuroanatomy over the course of a few days (Bloss, Janssen, McEwen, & Morrison, 2010). In children, early life adversity and chronic stress have been found to decrease the size of the hippocampus and prefrontal cortex while increasing the size of the amygdala (Davidson & McEwen, 2012; Tottenham et al., 2010). These areas are important for emotional regulation, and abnormalities in these regions are associated with psychopathology such as anxiety and mood disorders (Tottenham et al., 2010). It is hypothesized that the increased plasticity of the young brain may lead to an increased ability to resist and recover from delirium (Silver et al., 2010), although no evidence exists to support this hypothesis. Instead, it is possible that the stress of pediatric delirium results in maladaptive structural changes in the highly malleable developing brain that leave children at increased risk for future cognitive and psychological morbidity.

In critically ill adult populations, increased duration of delirium is associated with both structural and functional brain changes on neuroimaging (Haggstrom, Welschinger, & Caplan, 2017; Nitchingham, Kumar, Shenkin, Ferguson, & Caplan, 2017), even among relatively young adults with no history of dementia. Furthermore, this damage is highly associated with worse cognitive performance at 3- and 12-months post-ICU, including impaired executive function and visual attention (Gunther et al., 2012; Morandi et al., 2012). Few have examined the brain changes associated with delirium in pediatric populations. Among a small sample of pediatric surgery patients emerging from anesthesia, those who experienced emergence delirium exhibited high levels of functional connectivity on

electroencephalogram (Martin et al., 2014). These increased activity levels may reflect high levels of immature, hyper-excitatory neural activity that does not correlate with normal function (Bos et al., 2017). While these preliminary findings suggest that the highly plastic young brain may be susceptible to maladaptive changes during delirium, more studies are needed to understand the structural and functional brain changes associated with pediatric delirium.

Behavioral adaptation.: Self-regulation is the conscious control of thoughts, feelings, and behaviors, and stems from the interaction of executive functions and emotional regulation (Moffitt et al., 2011; Montroy, Bowles, Skibbe, McClelland, & Morrison, 2016). Self-regulation develops rapidly during early childhood (Montroy et al., 2016), and self-regulation in the first decade of life has been found to predict physical health, substance use, finances, and criminal outcomes in adulthood (Moffitt et al., 2011). Stressful environmental exposures in childhood, such as low socioeconomic status, are thought to contribute to poor development of behavioral self-regulation (Montroy et al., 2016). Emotional regulation is an important component of self-regulation. Early chronic stress is associated with structural brain changes, including decreased size of the hippocampus and pre-frontal cortex and increased size of the amygdala (Davidson & McEwen, 2012; Tottenham et al., 2010), which may impair the development of emotional regulation and leave children at increased risk for future psychological morbidity.

Emotional regulation can also become impaired during sleep deprivation due to the sensitivity of the prefrontal cortex and amygdala to sleep loss (Gruber & Cassoff, 2014). Critically ill children demonstrate extreme sleep fragmentation (i.e., frequent brief arousals) and alterations in normal sleep architecture (i.e., disruption of cyclical pattern of sleep stages) during stay in the PICU (Al-Samsam & Cullen, 2005; Cureton-Lane & Fontaine, 1997; Kudchadkar et al., 2015; Kudchadkar, Aljohani, & Punjabi, 2014). The resulting sleep deprivation and sleep/wake cycle disturbances experienced by these children are hypothesized to play a role in the development of delirium (Kamdar, Needham, & Collop, 2012; Maldonado, 2013, 2017; Weinhouse et al., 2009). Sleep/wake cycle disturbance is commonly noted in children with delirium (Holly et al., 2018), and may explain the increased lability of affect and irritability (i.e., impaired emotional regulation) described in these children (Tukel, Trzepacz, & Tavaré, 2006).

In children, the stressful experience of delirium and associated sleep/wake cycle disturbance during a time of rapidly-developing self-regulation may result in long-term impairments in emotional regulation. Adult survivors of critical illness have been found to experience a host of poor cognitive and psychological outcomes associated with both sleep deprivation and delirium, such as impaired executive function, anxiety, depression, and post-traumatic stress disorder (PTSD; Kamdar et al., 2012). Little is understood about the cognitive or psychological outcomes of children who experience delirium, however probable PTSD symptoms have been reported in children at 6 weeks post-PICU, with increased risk for children who recall delusional memories, a potential sign of delirium (Colville, Kerry, & Pierce, 2008).

Biologic adaptation.: The biological adaptations listed in the LCHD Model represent normal physiologic processes, including the stress response, immune system, and metabolic processes, designed to protect the body from harm and appropriately respond to environmental stress. However, when the external stressor is unusually severe, such as during critical illness, these adaptations can begin to cause harm and potentially contribute to the development of delirium through multiple mechanisms (Maldonado, 2013, 2017).

Critical illness is an acute stressor in the macro-context that activates the hypothalamic-pituitary-adrenal (HPA) axis to produce glucocorticoids (Maldonado, 2017). This stress response is a biologic adaptation represented in the LCHD Model by the HPA axis, sympathetic nervous system, and allostatic load concepts. However, the stress response becomes maladaptive when abnormally high glucocorticoid levels cause a pro-inflammatory effect inside the brain, which may contribute to the neurocognitive outcomes seen in delirium and result in long-term cognitive impairments. This inflammatory and immune response, identified in the LCHD Model as a biological adaptation, is exacerbated by peripheral stimuli such as infection or trauma, which activate inflammatory mediators to cause further neuronal and synaptic dysfunction (Maldonado, 2017). In an international point prevalence study of 994 critically ill children, 42.2% of children who developed delirium in the PICU were admitted with an infectious or inflammatory disorder (Traube, Silver, Reeder, et al., 2017), suggesting a potential role for inflammation in pediatric delirium pathophysiology.

The hippocampus contains a large number of glucocorticoid receptors and therefore begins to dysfunction early in the stress response (McEwen, Nasca, & Gray, 2016). Until its maturation in early childhood, the hippocampus has a high level of plasticity (Ganzel & Morris, 2011), indicating that very young children may have increased vulnerability to the damaging effects of glucocorticoids. Damage to the hippocampus can have long-term implications for learning, memory, and emotional regulation (McEwen et al., 2016). Excessive exposure to neurotoxic glucocorticoids during critical illness may also result in an impaired ability to shut off the stress response, as the hippocampus plays a role in the regulation of the HPA axis. This altered stress response can lead to prolonged exposure to glucocorticoids, contributing to long-term cognitive impairment after PICU discharge.

Physiologic processes occurring during critical illness, such as tissue damage, infection, and hypoxia, lead to an increased oxygen demand and decreased oxygen availability (Maldonado, 2017). Hypoperfusion results in the build-up of reactive oxygen species and an altered cerebral oxidative metabolism, normally considered a biologic adaptation in the LCHD Model. This altered metabolism can cause irreversible tissue damage and the neurocognitive outcomes seen in delirium and long-term cognitive impairment.

These developmental, behavioral, and biological mechanisms make up the micro-context of a child and are critical to the successful adaptation to changes in the macro-context. While the pathophysiology of pediatric delirium remains unknown, the damage to these processes caused by critical illness represents multiple potential pathways to delirium and poor life course outcomes in critically ill children.

Principle six: Optimal health development promotes survival.—Optimal health development promotes survival, enhances well-being, and is protective against disease (Halfon et al., 2014). Long-term outcomes in the developmental and cognitive realms are particularly relevant in the context of the LCHD Model. It is currently unknown if the life trajectory of a child is affected by the occurrence of delirium during critical illness. Yet application of the LCHD Model to current understanding of delirium suggests that children who experience delirium during critical illness are at risk for a poor life trajectory through multiple mechanisms.

The adaptive responses that comprise a child's micro-context are the mechanisms through which children adjust to changes in their environment. However, these processes can become maladaptive in the face of severe stress. Critically ill children who experience delirium may be at increased risk for structural brain changes in areas such as the prefrontal cortex, hippocampus, and amygdala (Davidson & McEwen, 2012; Maldonado, 2017; Tottenham et al., 2010). The increased plasticity of the immature brain leaves children particularly vulnerable in the face of noxious stimuli such as glucocorticoids, inflammation, and oxidative stress. Damage to these areas leave children at long-term risk for cognitive and psychological morbidities, ranging from impairments in learning and memory to disorders of emotional regulation resulting in anxiety, depression, and PTSD (McEwen et al., 2016). Excessive stimulation of the stress and immune responses result in prolonged elevation of glucocorticoids, ensuring further exposure to neurotoxic stimuli. Damages to these areas leave survivors of pediatric critical illness with lifelong impairments that may hinder future successful adaptation to environmental stressors.

Principle seven: Health development derives from synchronized timing.—The LCHD Model emphasizes the importance of the timing of exposures and experiences in shaping the maturation of developing systems in children (Halfon et al., 2014). Pediatric delirium can be thought of as a perfect storm, combining multiple risk factors and environmental exposures with acute stress, all in a time of sensitive development. Disruptions during the acquisition phase of development leave children with an impaired capacity to adapt to future environmental stressors in a healthy way. The latent effects of damage during this period of development, the biological and behavioral embedding of an altered stress response and impaired emotional regulation (Halfon et al., 2014), can have long-ranging effects on the health trajectory of a child. Researchers who are able to elucidate the latent effects of delirium on critically ill children will provide impetus for future work in the prevention and treatment of delirium in pediatric populations.

Model Critique

The LCHD Model is a useful and comprehensive way in which to consider the long-term outcomes of delirium on the life trajectory of children. The model depicts a process in which the acute and severe stress of critical illness in the macro-context of a child results in maladaptive changes in the micro-context that contribute to pediatric delirium and impair a child's health capacity and long-term health trajectory. This interpretation of pediatric delirium is based on several assumptions. Focusing on the long-term outcomes of a critically ill child who experiences delirium assumes that the child survives his or her stay in the

PICU. While mortality rates in the PICU are relatively low (Pollack et al., 2015), delirium does significantly increase risk (Traube, Silver, Gerber, et al., 2017). It is also assumed that the child experiences critical illness and delirium as a one-time isolated event with latent effects throughout the life trajectory. This leaves little consideration for children with chronic conditions that necessitate frequent hospitalization and make up a large percentage of the PICU population (Edwards et al., 2012).

Lastly, using pediatric delirium as the context for interpretation of the LCHD Model to some extent neglects the effects of chronic and critical illness on the life trajectory. It is difficult to differentiate the negatives effects of delirium from the negative effects of critical illness. Congenital heart abnormalities, sepsis, and acute respiratory failure are common conditions in the PICU (Pollack et al., 2015; Traube, Silver, Reeder, et al., 2017) that can cause hypoxia and hypotension, resulting in poor cognitive and functional outcomes (Elison et al., 2008; Newburger et al., 2003). This has been a salient issue in delirium research with adult populations and will continue to be an issue in pediatric delirium research. High-quality studies with adequate power to control for covariates and confounders, such as severity of illness and use of respiratory support, will be necessary to detect the long-term impairments independently associated with pediatric delirium.

These inherent assumptions limit the generalizability of this framework for pediatric delirium research, as does the LCHD Model's inherent focus on long-term outcomes, which may conflict with the short-term focus of many clinicians caring for critically ill children. Potential generalizability is further limited by the lack of consideration within the LCHD Model for certain characteristics of children that are present at birth. The model does depict a period of generativity (right side of Figure 1) during health development, which includes environmental exposures of the mother during the preconceptual and prenatal periods (Halfon et al., 2014). However, this does not include pre-existing developmental delays and birth defects in children not due to maternal environmental exposures, such as inherited genetic defects. Children with developmental delay are at increased risk for delirium during critical illness (Silver et al., 2015; Traube, Silver, Gerber, et al., 2017) and likely have a lower capacity for health development compared to normally developing children.

Scientists have only just begun to consider genetic risk factors that may predispose to delirium or influence recovery from delirium in adult populations, such as the apolipoprotein E (APOE) $\epsilon 4$ allele. While little association has been found between the APOE genotype and delirium among adults (Adamis, Meagher, Williams, Mulligan, & McCarthy, 2016), studies in pediatric populations have found structural brain changes in healthy young children with the $\epsilon 4$ allele (Chang et al., 2016; Dean et al., 2014) that could predispose to delirium during critical illness. While the LCHD Model does consider the biological embedding that can occur through interaction between the macro- and micro-context, hinting at epigenetic changes, the genetic makeup of children should be clearly depicted within the model.

The LCHD Model also fails to list resilience as a developmental adaptation within the micro-context of a child. Resilience is the ability of the body to successful adapt to stress (Masten, 2014), and while the concept is described in the literature (Halfon et al., 2014), it is

not shown the model. Moderate amounts of environmental adversity may lead to stress inoculation, or a better ability to handle adversity in the future (Kim-Cohen & Turkewitz, 2012). However, severe stress, especially during sensitive periods of development, may decrease a child's ability to adapt. The severe stress of delirium may represent a pathway by which a child fails to develop a healthy level of resilience, decreasing his or her ability to adapt to future health challenges. As an important adaptive process, it should be included in future revisions of the model.

Conclusions

The LCHD Model provides a framework for understanding the ways in which delirium during pediatric critical illness can act as a stressor that alters brain structure and function during a period of sensitive development, resulting in a lifelong impact on a child's health trajectory. Each of the seven core principles of the model is applicable in the context of pediatric delirium. This application of the LCHD Model to pediatric delirium assumes that a generally healthy child who survives critical illness and delirium as an isolated one-time event may experience poor long-term cognitive and functional outcomes. While current research has failed to adequately consider how the interaction of the macro- and micro-context of a child may relate to the occurrence of delirium and long-term outcomes, the LCHD Model serves as an excellent road map for future studies. The LCHD Model gives consideration to the ways in which social, psychological, behavioral, and biological determinants shape the health trajectory of a child, and is especially relevant as clinicians and researchers begin to conceptualize the lasting effects of critical illness on children (Manning, Pinto, Rennick, Colville, & Curley, 2018; Watson et al., 2018). By emphasizing the potential long-term consequences of delirium on a child's health trajectory, the LCHD Model is a useful framework that provides impetus for future research and practice change in the care of critically ill children.

Relevance to Clinical Practice

Bedside nurses are central to the identification, prevention, and treatment of delirium (Balas et al., 2012; Costa et al., 2018). As a constant bedside presence, nurses are best able to identify the fluctuating mental status central to delirium diagnosis. Interventions such as goal-directed sedation protocols (Girard et al., 2008), early mobility (Schweickert et al., 2009), sleep promotion (Flannery et al., 2016), and increased family presence (Rosa et al., 2017) are nurse-driven components of care known to decrease the incidence and duration of delirium in adult populations (Balas et al., 2014; Barnes-Daly et al., 2017). Nurses are key to coordinated communication and care among the various teams responsible for the critically ill patient, including the medical team, respiratory therapy, and physical therapy (Balas et al., 2013). In fact, nurse involvement in delirium prevention activities significantly increases the odds of intervention implementation (Costa et al., 2018), highlighting the crucial role of the bedside nurse in delirium care.

Researchers and clinicians are beginning to recognize the importance of sedation protocols (Curley et al., 2015), sleep promotion (Kawai et al., 2017), early mobility (Betters et al., 2017), and increased family presence (Harrison, 2010) in pediatric intensive care, however

the impact of these interventions on the incidence and duration of delirium remains unknown. Attempts to facilitate widespread implementation of these interventions and increase the prevention and treatment of delirium in pediatric populations will not be successful without the leadership and collaboration of bedside nurses. Increasing the understanding of the long-term cognitive and functional outcomes of children who experience delirium will motivate the participation of bedside clinical staff in delirium prevention and treatment. The LCHD Model provides a framework for such research.

Future research should compare the cognitive and functional outcomes of critically ill children who do and do not develop delirium at multiple time points after discharge from the PICU. Increased understanding of the long-term impact of pediatric delirium will highlight the importance of further inquiry into the risk factors and pathophysiology of delirium. The mechanisms by which delirium causes neurologic damage could be elucidated using tools such as biomarkers of neurologic damage or further analysis of neuroimaging obtained during pediatric critical illness. A better understanding of these factors will lead to the development of targeted interventions for the prevention and treatment of pediatric delirium. Through advocating for the well-being of their patients, leading research efforts, and changing practice at the bedside, nurses have the opportunity to play a key role in improving the quality of life for survivors of pediatric critical illness.

Acknowledgments

Funding: Research reported in this publication was supported by the National Institute of Nursing Research of the National Institutes of Health under Award Number T32 NR014225 (Pickler & Melnyk, MPI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

- Adamis D, Meagher D, Williams J, Mulligan O, & McCarthy G. (2016). A systematic review and meta-analysis of the association between the apolipoprotein E genotype and delirium. *Psychiatric Genetics*, 26(2), 53–59. 10.1097/YPG.000000000000122 [PubMed: 26901792]
- Al-Samsam RH, & Cullen P. (2005). Sleep and adverse environmental factors in sedated mechanically ventilated pediatric intensive care patients. *Pediatric Critical Care Medicine*, 6(5), 562–7. [PubMed: 16148818]
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: American Psychiatric Association.
- Balas MC, Burke WJ, Gannon D, Cohen MZ, Colburn L, Bevil C, ... Vasilevskis EE (2013). Implementing the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle into everyday care: Opportunities, challenges, and lessons learned for implementing the ICU Pain, Agitation, and Delirium Guidelines. *Critical Care Medicine*, 41(9 Suppl 1), S116–27. 10.1097/CCM.0b013e3182a17064 [PubMed: 23989089]
- Balas MC, Vasilevskis EE, Burke WJ, Boehm L, Pun BT, Olsen KM, ... Ely EW (2012). Critical care nurses' role in implementing the "ABCDE bundle" into practice. *Critical Care Nurse*, 32(2), 35–8, 40–7; quiz 48. 10.4037/ccn2012229
- Balas MC, Vasilevskis EE, Olsen KM, Schmid KK, Shostrom V, Cohen MZ, ... Burke WJ (2014). Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. *Critical Care Medicine*, 42(5), 1024–36. 10.1097/CCM.0000000000000129 [PubMed: 24394627]

- Barnes-Daly MA, Phillips G, & Ely EW (2017). Improving hospital survival and reducing brain dysfunction at seven California community hospitals. *Critical Care Medicine*, 45(2), 171–178. 10.1097/CCM.0000000000002149 [PubMed: 27861180]
- Bettors KA, Hebbar KB, Farthing D, Griego B, Easley T, Turman H, ... deAlmeida ML (2017). Development and implementation of an early mobility program for mechanically ventilated pediatric patients. *Journal of Critical Care*, 41, 303–308. 10.1016/j.jcrc.2017.08.004 [PubMed: 28821360]
- Bloss EB, Janssen WG, McEwen BS, & Morrison JH (2010). Interactive effects of stress and aging on structural plasticity in the prefrontal cortex. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 30(19), 6726–31. 10.1523/JNEUROSCI.0759-10.2010 [PubMed: 20463234]
- Boehm LM, Dietrich MS, Vasilevskis EE, Wells N, Pandharipande P, Ely EW, & Mion LC (2017). Perceptions of workload burden and adherence to ABCDE bundle among intensive care providers. *American Journal of Critical Care: An Official Publication, American Association of Critical-Care Nurses*, 26(4), e38–e47. 10.4037/ajcc2017544
- Bos DJ, Oranje B, Achterberg M, Vlaskamp C, Ambrosino S, de Reus MA, ... Durston S. (2017). Structural and functional connectivity in children and adolescents with and without attention deficit/hyperactivity disorder. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*. 10.1111/jcpp.12712
- Carrothers KM, Barr J, Spurlock B, Ridgely MS, Damberg CL, & Ely EW (2013). Contextual issues influencing implementation and outcomes associated with an integrated approach to managing pain, agitation, and delirium in adult ICUs. *Critical Care Medicine*, 41(9 Suppl 1), S128–35. 10.1097/CCM.0b013e3182a2c2b1 [PubMed: 23989090]
- Cavallazzi R, Saad M, & Marik PE (2012). Delirium in the ICU: an overview. *Annals of Intensive Care*, 2(1), 49. 10.1186/2110-5820-2-49 [PubMed: 23270646]
- Chang L, Douet V, Bloss C, Lee K, Pritchett A, Jernigan TL, ... Pediatric Imaging, Neurocognition, and Genetics (PING) Study Consortium. (2016). Gray matter maturation and cognition in children with different APOE ε genotypes. *Neurology*, 87(6), 585–94. 10.1212/WNL.0000000000002939 [PubMed: 27412137]
- Colville G, Kerry S, & Pierce C. (2008). Children's factual and delusional memories of intensive care. *American Journal of Respiratory and Critical Care Medicine*, 177(9), 976–982. 10.1164/rccm.200706-857OC [PubMed: 18244955]
- Costa DK, Valley TS, Miller MA, Manojlovich M, Watson SR, McLellan P, ... Iwashyna TJ (2018). ICU team composition and its association with ABCDE implementation in a quality collaborative. *Journal of Critical Care*, 44, 1–6. 10.1016/j.jcrc.2017.09.180 [PubMed: 28978488]
- Cureton-Lane RA, & Fontaine DK (1997). Sleep in the pediatric ICU: an empirical investigation. *American Journal of Critical Care*, 6(1), 56–63. [PubMed: 9116788]
- Curley MAQ, Wypij D, Watson RS, Grant MJC, Asaro LA, Cheifetz IM, ... RESTORE Study Investigators and the Pediatric Acute Lung Injury and Sepsis Investigators Network, P. A. L. I. and S. I. (PALISI). (2015). Protocolized sedation vs usual care in pediatric patients mechanically ventilated for acute respiratory failure: a randomized clinical trial. *JAMA*, 313(4), 379–89. 10.1001/jama.2014.18399 [PubMed: 25602358]
- Davidson RJ, & McEwen BS (2012). Social influences on neuroplasticity: Stress and interventions to promote well-being. *Nature Neuroscience*, 15(5), 689–95. 10.1038/nn.3093 [PubMed: 22534579]
- Dean DC, Jerskey BA, Chen K, Protas H, Thiyyagura P, Roontiva A, ... Reiman EM (2014). Brain differences in infants at differential genetic risk for late-onset Alzheimer disease. *JAMA Neurology*, 71(1), 11. 10.1001/jamaneurol.2013.4544 [PubMed: 24276092]
- Edwards JD, Houtrow AJ, Vasilevskis EE, Rehm RS, Markovitz BP, Graham RJ, & Dudley RA (2012). Chronic conditions among children admitted to U.S. pediatric intensive care units: their prevalence and impact on risk for mortality and prolonged length of stay. *Critical Care Medicine*, 40(7), 2196–203. 10.1097/CCM.0b013e31824e68cf [PubMed: 22564961]
- Elison S, Shears D, Nadel S, Sahakian B, & Garraalda ME (2008). Neuropsychological function in children following admission to paediatric intensive care: a pilot investigation. *Intensive Care Medicine*, 34(7), 1289–93. 10.1007/s00134-008-1093-9 [PubMed: 18392607]

- Ely E, Gautam S, Margolin R, Francis J, May L, Speroff T, ... Inouye S. (2001). The impact of delirium in the intensive care unit on hospital length of stay. *Intensive Care Medicine*, 27(12), 1892–1900. 10.1007/s00134-001-1132-2 [PubMed: 11797025]
- Flannery AH, Oyler DR, & Weinhouse GL (2016). The impact of interventions to improve sleep on delirium in the ICU: a systematic review and research framework. *Critical Care Medicine*, 44(12), 2231–2240. 10.1097/CCM.0000000000001952 [PubMed: 27509391]
- Ganzel BL, & Morris PA (2011). Allostasis and the developing human brain: Explicit consideration of implicit models. *Development and Psychopathology*, 23(4), 955–74. 10.1017/S0954579411000447 [PubMed: 22018076]
- Girard TD, Jackson JC, Pandharipande PP, Pun BT, Thompson JL, Shintani AK, ... Wesley Ely E. (2010). Delirium as a predictor of long-term cognitive impairment in survivors of critical illness. *Critical Care Medicine*, 38(7), 1513–1520. 10.1097/CCM.0b013e3181e47be1 [PubMed: 20473145]
- Girard TD, Kress JP, Fuchs BD, Thomason JWW, Schweickert WD, Pun BT, ... Ely EW (2008). Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. *Lancet* (London, England), 371(9607), 126–34. 10.1016/S0140-6736(08)60105-1
- Glymour MM, Weuve J, Fay ME, Glass T, & Berkman LF (2008). Social ties and cognitive recovery after stroke: Does social integration promote cognitive resilience? *Neuroepidemiology*, 31(1), 10–20. 10.1159/000136646 [PubMed: 18535395]
- Gruber R, & Cassoff J. (2014). The interplay between sleep and emotion regulation: Conceptual framework empirical evidence and future directions. *Current Psychiatry Reports*, 16(11), 500 10.1007/s11920-014-0500-x [PubMed: 25200984]
- Gunther ML, Morandi A, Krauskopf E, Pandharipande P, Girard TD, Jackson JC, ... Ely EW (2012). The association between brain volumes, delirium duration, and cognitive outcomes in intensive care unit survivors: the VISIONS cohort magnetic resonance imaging study. *Critical Care Medicine*, 40(7), 222–32. 10.1097/CCM.0b013e318250acc0 [PubMed: 22710202]
- Haggstrom L, Welschinger R, & Caplan GA (2017). Functional neuroimaging offers insights into delirium pathophysiology: a systematic review. *Australasian Journal on Ageing*, 36(3), 186–192. 10.1111/ajag.12417 [PubMed: 28519903]
- Halfon N, & Hochstein M. (2002). Life course health development: an integrated framework for developing health, policy, and research. *The Milbank Quarterly*, 80(3), 433–79, iii. [PubMed: 12233246]
- Halfon N, Larson K, Lu M, Tullis E, & Russ S. (2014). Lifecourse health development: Past, present and future. *Maternal and Child Health Journal*, 18(2), 344–365. 10.1007/s10995-013-1346-2 [PubMed: 23975451]
- Harrison TM (2010). Family-centered pediatric nursing care: State of the science. *Journal of Pediatric Nursing*, 25(5), 335–43. 10.1016/j.pedn.2009.01.006 [PubMed: 20816555]
- Holly C, Porter S, Echevarria M, Dreker M, & Ruzehaji S. (2018). CE: Original research: Recognizing delirium in hospitalized children: a systematic review of the evidence on risk factors and characteristics. *American Journal of Nursing*, 118(4), 24–36. 10.1097/01.NAJ.0000532069.55339.f9
- Kain ZN, Caldwell-Andrews AA, Maranets I, McClain B, Gaal D, Mayes LC, ... Zhang H. (2004). Preoperative anxiety and emergence delirium and postoperative maladaptive behaviors. *Anesthesia & Analgesia*, 99(6), 1648–1654. 10.1213/01.ANE.0000136471.36680.97
- Kain ZN, Caldwell-Andrews AA, Mayes LC, Weinberg ME, Wang S-M, MacLaren JE, & Blount RL (2007). Family-centered preparation for surgery improves perioperative outcomes in children: a randomized controlled trial. *Anesthesiology*, 106(1), 65–74. [PubMed: 17197846]
- Kamdar BB, Needham DM, & Collop NA (2012). Sleep deprivation in critical illness: Its role in physical and psychological recovery. *Journal of Intensive Care Medicine*, 27(2), 97–111. 10.1177/0885066610394322 [PubMed: 21220271]
- Kawai Y, Weatherhead JR, Traube C, Owens TA, Shaw BE, Fraser EJ, ... Niedner MF (2017). Quality improvement initiative to reduce pediatric intensive care unit noise pollution with the use of a pediatric delirium bundle. *Journal of Intensive Care Medicine*. 10.1177/0885066617728030

- Kim-Cohen J, & Turkewitz R. (2012). Resilience and measured gene–environment interactions. *Development and Psychopathology*, 24(04), 1297–1306. 10.1017/S0954579412000715 [PubMed: 23062298]
- Kudchadkar SR, Aljohani OA, & Punjabi NM (2014). Sleep of critically ill children in the pediatric intensive care unit: a systematic review. *Sleep Medicine Reviews*, 18(2), 103–110. 10.1016/j.smrv.2013.02.002 [PubMed: 23702219]
- Kudchadkar SR, Yaster M, Punjabi AN, Quan SF, Goodwin JL, Easley RB, & Punjabi NM (2015). Temporal characteristics of the sleep EEG power spectrum in critically ill children. *Journal of Clinical Sleep Medicine*, 11(12), 1449–1454. 10.5664/jcsm.5286 [PubMed: 26194730]
- Maldonado JR (2013). Neuropathogenesis of delirium: Review of current etiologic theories and common pathways. *The American Journal of Geriatric Psychiatry*, 21(12), 1190–1222. 10.1016/j.jagp.2013.09.005 [PubMed: 24206937]
- Maldonado JR (2017). Delirium pathophysiology: an updated hypothesis of the etiology of acute brain failure. *International Journal of Geriatric Psychiatry*, 1–30. 10.1002/gps.4823
- Manning JC, Pinto NP, Rennick JE, Colville G, & Curley MAQ (2018). Conceptualizing post intensive care syndrome in children—the PICS-p framework. *Pediatric Critical Care Medicine*, 19(4), 298–300. 10.1097/PCC.0000000000001476 [PubMed: 29406379]
- Martin JC, Liley DTJ, Harvey AS, Kuhlmann L, Sleigh JW, & Davidson AJ (2014). Alterations in the functional connectivity of frontal lobe networks preceding emergence delirium in children. *Anesthesiology*, 121(4), 740–752. 10.1097/ALN.0000000000000376 [PubMed: 25057840]
- Masten AS (2014). Global perspectives on resilience in children and youth. *Child Development*, 85(1), 6–20. 10.1111/cdev.12205 [PubMed: 24341286]
- McEwen BS, Nasca C, & Gray JD (2016). Stress effects on neuronal structure: Hippocampus, amygdala, and prefrontal cortex. *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology*, 41(1), 3–23. 10.1038/npp.2015.171 [PubMed: 26076834]
- Mody K, Kaur S, Mauer EA, Gerber LM, Greenwald BM, Silver G, & Traube C. (2018). Benzodiazepines and development of delirium in critically ill children. *Critical Care Medicine*, Epub ahead of print. 10.1097/CCM.00000000000003194
- Moffitt TE, Arseneault L, Belsky D, Dickson N, Hancox RJ, Harrington H, ... Caspi A. (2011). A gradient of childhood self-control predicts health, wealth, and public safety. *Proceedings of the National Academy of Sciences*, 108(7), 2693–2698. 10.1073/pnas.1010076108
- Montroy JJ, Bowles RP, Skibbe LE, McClelland MM, & Morrison FJ (2016). The development of self-regulation across early childhood. *Developmental Psychology*, 52(11), 1744–1762. 10.1037/dev0000159 [PubMed: 27709999]
- Morandi A, Rogers BP, Gunther ML, Merkle K, Pandharipande P, Girard TD, ... Hopkins RO (2012). The relationship between delirium duration, white matter integrity, and cognitive impairment in intensive care unit survivors as determined by diffusion tensor imaging: The VISIONS prospective cohort magnetic resonance imaging study. *Critical Care Medicine*, 40(7), 2182–9. 10.1097/CCM.0b013e318250acdc [PubMed: 22584766]
- Newburger JW, Wypij D, Bellinger DC, du Plessis AJ, Kuban KCK, Rappaport LA, ... Wernovsky G. (2003). Length of stay after infant heart surgery is related to cognitive outcome at age 8 years. *The Journal of Pediatrics*, 143(1), 67–73. 10.1016/S0022-3476(03)00183-5 [PubMed: 12915826]
- Nitchingham A, Kumar V, Shenkin S, Ferguson KJ, & Caplan GA (2017). A systematic review of neuroimaging in delirium: Predictors, correlates and consequences. *International Journal of Geriatric Psychiatry*. 10.1002/gps.4724
- Pandharipande PP, Girard TD, Jackson JC, Morandi A, Thompson JL, Pun BT, ... BRAIN-ICU Study Investigators. (2013). Long-term cognitive impairment after critical illness. *The New England Journal of Medicine*, 369(14), 1306–16. 10.1056/NEJMoa1301372 [PubMed: 24088092]
- Pollack MM, Holubkov R, Funai T, Berger JT, Clark AE, Meert K, ... Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network. (2015). Simultaneous prediction of new morbidity, mortality, and survival without new morbidity from pediatric intensive care: a new paradigm for outcomes assessment. *Critical Care Medicine*, 43(8), 1699–709. 10.1097/CCM.0000000000001081 [PubMed: 25985385]

- Rosa RG, Tonietto TF, da Silva DB, Gutierrez FA, Ascoli AM, Madeira LC, ... ICU Visits Study Group Investigators. (2017). Effectiveness and safety of an extended ICU visitation model for delirium prevention. *Critical Care Medicine*, 45(10), 1660–1667. 10.1097/CCM.0000000000002588 [PubMed: 28671901]
- Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, ... Kress JP (2009). Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *The Lancet*, 373(9678), 1874–1882. 10.1016/S0140-6736(09)60658-9
- Shehabi Y, Riker RR, Bokesch PM, Wisemandle W, Shintani A, & Ely EW (2010). Delirium duration and mortality in lightly sedated, mechanically ventilated intensive care patients. *Critical Care Medicine*, 38(12), 2311–2318. 10.1097/CCM.0b013e3181f85759 [PubMed: 20838332]
- Silver GH, Kearney JA, Kutko MC, & Bartell AS (2010). Infant delirium in pediatric critical care settings. *American Journal of Psychiatry*, 167(10), 1172–1177. 10.1176/appi.ajp.2010.09111606 [PubMed: 20889664]
- Silver G, Traube C, Gerber LM, Sun X, Kearney J, Patel A, & Greenwald B. (2015). Pediatric delirium and associated risk factors: a single-center prospective observational study. *Pediatric Critical Care Medicine*, 16(4), 303–309. 10.1097/PCC.0000000000000356 [PubMed: 25647240]
- Smith HAB, Gangopadhyay M, Goben CM, Jacobowski NL, Chestnut MH, Thompson JL, ... Pandharipande PP (2017). Delirium and benzodiazepines associated with prolonged ICU stay in critically ill infants and young children. *Critical Care Medicine*, 45(9), 1427–1435. 10.1097/CCM.0000000000002515 [PubMed: 28594681]
- Theall KP, Shirtcliff EA, Dismukes AR, Wallace M, & Drury SS (2017). Association between neighborhood violence and biological stress in children. *JAMA Pediatrics*, 171(1), 53–60. 10.1001/jamapediatrics.2016.2321 [PubMed: 27842189]
- Tottenham N, Hare TA, Quinn BT, McCarry TW, Nurse M, Gilhooly T, ... Casey BJ (2010). Prolonged institutional rearing is associated with atypically large amygdala volume and difficulties in emotion regulation. *Developmental Science*, 13(1), 46–61. 10.1111/j.1467-7687.2009.00852.x [PubMed: 20121862]
- Traube C, Silver G, Gerber LM, Kaur S, Mauer EA, Kerson A, ... Greenwald BM (2017). Delirium and mortality in critically ill children: Epidemiology and outcomes of pediatric delirium. *Critical Care Medicine*, 45(5), 891–898. 10.1097/CCM.0000000000002324 [PubMed: 28288026]
- Traube C, Silver G, Reeder RW, Doyle H, Hegel E, Wolfe HA, ... Bell MJ (2017). Delirium in critically ill children: an international point prevalence study. *Critical Care Medicine*, 45(4), 584–590. 10.1097/CCM.0000000000002250 [PubMed: 28079605]
- Turkel SB, Trzepacz PT, & Tavaré CJ (2006). Comparing symptoms of delirium in adults and children. *Psychosomatics*, 47(4), 320–324. 10.1176/appi.psy.47.4.320 [PubMed: 16844890]
- Watson RS, Choong K, Colville G, Crow S, Dervan LA, Hopkins RO, ... Curley MAQ (2018). Life after critical illness in children—Toward an understanding of pediatric post-intensive care syndrome. *The Journal of Pediatrics*. 10.1016/j.jpeds.2017.12.084
- Weinhouse GL, Schwab RJ, Watson PL, Patil N, Vaccaro B, Pandharipande P, & Ely EW (2009). Bench-to-bedside review: Delirium in ICU patients - Importance of sleep deprivation. *Critical Care*, 13(6), 234. 10.1186/cc8131 [PubMed: 20053301]
- White K, Haas JS, & Williams DR (2012). Elucidating the role of place in health care disparities: the example of racial/ethnic residential segregation. *Health Services Research*, 47(3 Pt 2), 1278–99. 10.1111/j.1475-6773.2012.01410.x [PubMed: 22515933]
- Wickrama KKAS, O'Neal CW, Lee TK, & Wickrama T. (2015). Early socioeconomic adversity, youth positive development, and young adults' cardio-metabolic disease risk. *Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association*, 34(9), 905–14. 10.1037/hea0000208

Summary Box

What does this paper contribute to the wider global clinical community?

- Delirium is a serious complication of critical illness with growing international interest.
- Despite efforts of the International Federation of Delirium Societies to raise awareness and stimulate practice change, critically ill pediatric populations are under-studied in delirium research.
- The Life Course Health Development Model serves as a theoretical research framework for pediatric delirium that challenges critical care clinicians and researchers to consider pediatric delirium from the viewpoint of long-ranging consequences across the lifespan.

Figure I.
Life course health development model. Adapted from the Maternal and Child Health Life Course Research Network.