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Pediatric Delirium: Recognition, Management, and Outcome

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Abstract
Purpose of Review This review seeks to provide an update on the diagnosis, management, and outcome of pediatric delirium.
Recent Findings Care of patients with delirium depends on correct diagnosis and treatment of its underlying cause. A variety of instruments are available to aid diagnosis. Management of delirium currently depends on atypical antipsychotics, while avoiding agents that may precipitate or exacerbate it.

While most critically ill children survive delirium, many children die or have worsening function after their illness. The longer the duration of delirium, the more severe its subsequent problems including postintensive care syndrome and posttraumatic stress disorder.
Summary Possible serious long-term consequences emphasize the importance of efforts to improve diagnosis and outcome in critically ill children suffering from delirium.

Keywords Delirium · Children · Adolescents · Assessment · Diagnosis · Management · Outcome

Introduction

This update on pediatric delirium primarily focuses on new studies from the past 5 years to review the most recent studies of the management and outcome of pediatric delirium. Delirium is a syndrome of severe, pervasive, cerebral dysfunction, a global encephalopathic process that represents a nonspecific, acute, fluctuating disturbance of consciousness and cognitive function. It may result from infection, drugs and toxins, metabolic dysfunction, malignancy, or other serious illness. Delirium has been linked to increased length of stay, morbidity, mortality, and long-term cognitive impairment [1, 2•, 3]. An overall 85% increase in pediatric intensive care unit (PICU) costs ($p < 0.0001$) is associated with caring for patients with delirium, and costs increase further with longer length of stay [4].

Interest in the study of delirium in pediatric patients has grown rapidly in the past decade, changing focus from definition and symptoms, to diagnostic instruments, to risk factors, to management, and finally to outcome. Consensus on ways to decrease the risk of developing delirium and ameliorate its negative consequences remains the active focus of current studies.

Pediatric Delirium: Recognition and Management

The characteristic core symptoms of delirium include impaired consciousness and awareness; inability to direct, focus, sustain, and shift attention; abnormalities of the sleep-wake cycle; disturbance of thought processes; behavioral dyscontrol; and fluctuating symptoms. The clinical presentation of delirium is essentially the same in all ages and typically begins with the acute onset of impaired consciousness and attention [2•]. Risk factors for developing pediatric delirium have been well described and include younger age, male gender, preexisting cognitive impairment or developmental delay, previous delirium, positive family history of delirium, and preexisting emotional and behavioral problems.

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Exacerbating environmental factors of physical restraints, high noise levels, poor lighting, frequent staff changes, and disease entities with high mortality risk are important, but delirium is most often related to agents used for sedation, including benzodiazepines, opioids, propofol, and ketamine [5••]. The continuous infusion of sedating agents has been linked to longer duration of mechanical ventilation, extended length of hospitalization, and refractory agitation, which is a marker for pediatric delirium [2•].

The diagnosis of delirium in pediatric patients focuses more on behavioral changes rather than cognitive impairment as in adults [5••]. Delirium is frequently preceded by "sickness behavior" with reduced appetite, fatigue, sleep disturbance, loss of interest, isolation, and exaggerated responses to pain [6].

Delirium is most common in the sickest patients who are typically cared for in intensive care units. However, not every patient in the pediatric intensive care unit is diagnosed with delirium. In a recent multi-institutional, multi-national study of over 800 subjects, 25% screened positive for delirium, 13% were comatose, and 62% were delirium- and coma-free. The highest rates of delirium were found with infectious or other inflammatory disorders [7•].

Delirium is usually diagnosed within the first few days of admission to the PICU. Its prevalence increases with PICU stays of 6 days or longer; with mechanical ventilation; with the need for physical restraints; with the use of benzodiazepines, narcotics, vasopressors, or antiepileptics; or if the patient is younger, no older than 5 years old [7•].

Delirium has been classified into hyperactive, hypoactive, and mixed. In adults, hyperactive delirium is more common. In contrast, about half of pediatric patients are described as hypoactive, about half as mixed, and less than 10% are classified hyperactive [8]. As symptoms fluctuate, it is common to find different levels of activity at different times during the PICU course in the same patient, reflecting different levels of sedation and changing clinical condition. Unlike in adults, motoric subtypes of delirium in children and adolescents do not differ from each other with respect to other symptoms, risk factors, or outcome [8].

Disrupted sleep-wake cycle is characteristic of delirium, especially in mechanically ventilated patients who receive sedative or analgesic medication at often very high doses. These agents decrease slow wave and rapid eye movement sleep and result in deterioration of sleep quality, decreased sleep efficiency, increased arousal frequency, and late sleep onset [9]. The circadian rhythm of melatonin secretion appears to be disrupted with delirium and with deep sedation. Melatonin and ramelteon, a synthetic selective melatonin receptor agonist, are useful in addressing the sleep disturbance characteristic of delirium and may be helpful in reducing the risk for delirium [2].

The symptoms of catatonia often overlap with those of delirium in medically ill patients [10], and incoherence, altered awareness, agitation, and behavioral change occur with both conditions [11]. Hypoactive delirium especially is more likely to be confused with catatonia [10]. New onset catatonia is typically considered to represent a primary psychiatric condition, especially a mood disorder, but the possibility of an underlying medical or neurologic condition such as encephalitis should also be investigated [11, 12]. Both delirium and catatonia may occur abruptly, both may be associated with an underlying medical condition, and both involve a profound disturbance of behavior and response to the environment [13]. Hallucinations and perceptual disturbances, disorientation, impaired memory, and retained language skills can help distinguish delirium from the mutism and waxy flexibility commonly seen with catatonia.

Confounding the issue, catatonia may occur with or following delirium in almost one third of patients [10]. It is important to make the appropriate diagnosis, since neuroleptics can address the symptoms of delirium and worsen catatonia, while benzodiazepines can worsen delirium and manage catatonia symptoms, even when catatonia is secondary to a medical condition [13].

Delirium may result from both the use of opioids and benzodiazepines and from their acute withdrawal [14]. Withdrawal symptoms are prevalent in the PICU population, and commonly used scales for withdrawal assess changes in activity and behavior which overlap with symptoms of delirium [15].

The treatment of delirium depends on its correct diagnosis, which is where diagnostic instruments and screens can be useful (Table 1). The new Vanderbilt Assessment for Delirium in Infants and Children was formulated to encourage a consistent approach to pediatric delirium assessment by psychiatrists using common terminology to facilitate comprehensive studies [16•].

The Delirium Rating Scale, developed in 1988 and revised 10 years later, was designed to assist psychiatrists in distinguishing between dementia, delirium, and schizophrenia [17]. Familiarity with psychiatric terminology is needed, so it is not optimal for regular screening by non-psychiatrists or nurses in a busy PICU.

The Pediatric Confusion Assessment Method (pCAM-ICU) was devised for verbal children 5 years or older [18], and the psCAM-ICU for younger children, from 6 months to 5 years [19]. The Cornell Assessment of Pediatric Delirium (CAP-D) was derived from the Pediatric Anesthesia Emergence Delirium (PAED) scale and is also applicable for younger or nonverbal children [20]. Both the pCAM-ICU and CAP-D are specific (98 and 100%) and sensitive (78 and 91%), both are designed for use by nurses and non-psychiatric physicians to screen for delirium, and both have become widely used [21••].

Educating nurses about delirium is critical, as screening instruments depend on nursing to administer them, but most

Table 1 Instruments used for screening or diagnosis in pediatric delirium

	Purpose	Staff	Patients > 5 years	Patients < 5 years
DRS	Diagnosis	Psychiatrist	Yes	Yes
DRS-R98	Diagnosis and research	Psychiatrist	Yes	Possibly
pCAM-ICU	Screen	Intensivist and RN	Yes	No
psCAM-ICU	Screen	Intensivist and RN	Yes	Yes
PAED	Emerging from anesthesia	Anesthesiologist	Yes	Possibly
CAP-D	Screen	Intensivist and RN	Yes	Yes
VADIC	Standardized assessment	Psychiatrists	Yes	Yes
WAT-1	Opioid withdrawal	RN	Yes	Yes
RASS	Agitation scale	RN	Yes	Yes

bedside nurses have significant gaps in their knowledge of delirium and its diagnosis [22].

Pediatric Delirium: Treatment

The treatment of delirium is fundamentally the treatment of its underlying cause. The management of delirium relies on the effective control of its potentially distressing and dangerous symptoms and requires the collaboration of different medical specialties, including intensivists, pediatricians, neurologists, and child psychiatrists. At our institution, since antipsychotic agents are most familiar to psychiatrists, child-adolescent psychiatrists confirm the diagnosis and provide medication management.

While the underlying etiology of delirium is being addressed, its symptoms should be controlled for the comfort of the patients and their families. Management starts with establishing a therapeutic environment (Table 2). Good lighting in the day and low light at night help with day-night distinction and maintenance of a diurnal sleep-wake cycle. Clocks, calendars, pictures, and familiar objects from home help reduce anxiety. Limiting staff changes, minimizing noise, frequent and repeated reassurance, and verbal reorientation by family or familiar staff decrease fear and confusion [5••]. Environmental management is often sufficient to manage the symptoms of delirium in young patients, and medication may not be needed.

The pharmacologic management of delirium primarily depends on the off-label use of antipsychotics to control its symptoms, while avoiding agents that may cause or worsen delirium, especially benzodiazepines [2•]. Benzodiazepines have been shown to precipitate or prolong delirium and agitation, especially in children [23]. They increase hospital length of stay and duration of intubation in the ICU and will exacerbate confusion, agitation, and disordered sleep [2•]. Symptoms of delirium are most effectively managed by the judicious use of antipsychotic drugs which usually effectively address confusion and agitation [24]. Benzodiazepines are themselves associated with agitation and should be avoided [23]. Antipsycyhotics allow for less prolonged use and lower doses of benzodiazepines and opioids, which in turn allows for improved oxygenation and more rapid weaning of ventilator support [1, 2•].

Table 2 Establishing a therapeutic environment

Familiar caregivers and staff
Day-night distinction: maintain diurnal cycle
Clocks and calendars
Familiar objects and pictures of family
Minimizing noise
Frequent reorientation and reassurance, especially on awakening

Haloperidol has been used clinically for many years, it is the most described in the literature, and it can be given orally or intravenously, while atypical antipsychotics, currently the first line pharmacologic agents, can only be given orally. Intramuscular administration is generally avoided in pediatric patients. A recent study of haloperidol to manage delirium confirmed its efficacy, noting more adverse side effects in girls than boys, and apparently no difference in adverse effects by age or severity of illness [25]. Because intravenous haloperidol avoids first pass through the liver, it is considered to be less likely to cause dystonia, but risk of arrhythmia remains high [2•].

Quetiapine, risperidone, and olanzapine have been the most studied atypical antipsychotics and are currently the first choice for managing delirium in pediatric patients [1, 2•, 24•]. Risperidone is equipotent to haloperidol [4] and available in oral disintegrating tablets and liquid which make it useful in infants or by enteral routes via nasogastric or gastrojejunal tubes [1]. Olanzapine [26] and quetiapine have been described for treating delirium in critically ill infants, children, and adolescents [27] (Table 3).

Quetiapine appears to be least likely to be associated with hepatic complications, and it is useful in patients with hepatic compromise, in hepatic failure, before or after liver transplant. The typical antipsychotic, fluphenazine, is reportedly associated with less risk of cardiac arrhythmia than other typical or

Table 3 Underlying disorder associated with pediatric delirium: frequency (%) [2•, 28]

	Total $n = 194$	
Infection	51	(26%)
Drug-induced	40	(20%)
Neoplasm	25	(13%)
Autoimmune	16	(8%)
Postoperative	15	(7.7%)
Organ failure	14	(7%)
Trauma	14	(7%)
Posttransplant	9	(5%)

atypical antipsychotics and can be used in small infants with congenital heart disease.

Light sedation or no sedation has become the therapeutic goal in caring for critically ill adults [29], but protocolized sedation (using a management algorithm) and sedation interruption have not been shown to improve incidence of delirium, clinical outcome, duration of mechanical ventilation, length of stay, or total sedative drugs administered, which is reported in adults [29], but not in children [30, 31].

The selective alpha-2 adrenergic agonist, dexmedetomidine, is increasingly favored in pediatric intensive care units. It provides sedation, anxiolysis, and sympatholysis without significant respiratory compromise, risk of hypotension, or increased risk for delirium [32]. It avoids use of benzodiazepines, has minimal depression of respiratory function, shortens length of mechanical ventilation, lowers opioid use, and decreases risk of delirium [33, 34]. It can be transitioned to oral clonidine, which is typically used to ameliorate opioid withdrawal [35, 36].

Pediatric Delirium: Consequences in Survivors

The majority of critically ill children survive their illness, but there are physical, functional, neurocognitive, and psychological consequences that have a substantial impact on survivors and their families. Quality of life declines and societal costs accrue as more children survive critical illness with significant dysfunction. The postintensive care syndrome designates new or worsening problems in physical, cognitive, or mental health status after a critical illness which persist beyond the acute hospitalization [37•]. The term postintensive care syndrome was coined at a conference convened by the Society of Critical Care Medicine and can be applied to either the intensive care survivor or family member [37]. Risk factors for developing the syndrome include younger age, lower socioeconomic status, increased number of invasive procedures or interventions, type of illness, and increased benzodiazepine and narcotic administration [37]. Postintensive care syndrome in children often resolves over time.

Critical illness can leave ICU survivors disabled, with cognitive decline of mild dementia in about one quarter of patients at 12 months. An episode of delirium increases the risk for subsequent delirium, anxiety, depression, delusional memories, and posttraumatic stress disorder [38]. The longer the duration of delirium, the more severe the subsequent cognitive and memory problems [39].

Posttraumatic stress disorder (PTSD) after PICU admission is recognized in 5–28% of survivors, and PTSD symptoms without meeting the full criteria for the disorder occur in 35–62% [40]. PTSD in a child is positively correlated with parental PTSD, with parental rates of PTSD of 10.5–21%, and symptom rates approaching 84% [41].

Adult survivors of intensive care most remember visual hallucinations and feeling afraid and confused, and a large majority are distressed by their experience (86%) [42]. While anxiety, depression, and PTSD rates may increase, the long-term risk of psychiatric illness in adults is not increased overall by an ICU stay [43].

Morbidity and mortality increase after discharge from the PICU, from 3.9% by hospital discharge to 7.8% at 6 months and to 10.4% at 3 years [44••]. About as many children die or have worsening functional status (38%) as survive without functional decline (44%) and a few (< 10%) have functional gains with time [44••]. Poor outcome is associated with greater severity of illness, mechanical ventilation, more ventilator days, use of vasoactive medications, and greater PICU length of stay [44••].

The highest risk for mortality following PICU stay is found in pediatric patients with an oncologic or neurologic diagnosis

Table 4 Antipsychotics used in delirium management [2•]

	P450	Half-life (h)	Starting dose	Forms
Haloperidol	3A4	8.5–36	0.1 mg	Tablet, IV Liquid, IM
Risperidone	2D6, 3A4	3–21	0.05–0.5 mg	Tablet, liquid, ODT
Olanzapine	1A2, 2D6	20–40	1–2.5 mg	Tablet, ODT, IM
Quetiapine	2D6, 3A4	6	6.25–12.5 mg	Tablet
Zisprasidone	3A4	3–10	No data	Tablet, IM
Aripiprazole	3A4, 2D6	75	No data	Tablet, liquid, ODT, IM

[45]. Highest functional/cognitive disability rates occur with a trauma diagnosis, an unscheduled admission, mechanical ventilation, renal replacement therapy, cardiopulmonary resuscitation, or extracorporeal oxygenation [45].

In assessing neuropsychologic function 3–6 months after PICU admission in school-aged children, those admitted to the PICU significantly underperformed compared to controls ($p < 0.02$). Teacher ratings noted worse educational performance, executive function, attention, and memory in younger survivors, those from lower social class, or who had seizures [46].

Our institution has been enrolling children in a prospective observational study of delirium and cognitive function. Children (5–17 years old) are screened daily by a research assistant using the pCAM and CAP-D; so far, 42% (21 patients) have screened positive for delirium on at least one measure. Our psychiatry team confirmed the diagnosis in 54%. Cognitive testing of all screened children at the time of transfer or discharge from the PICU has shown impairment in attention, concentration, and memory, regardless whether they had been diagnosed with delirium or not. This reinforces growing concern that children leaving intensive care are at risk for cognitive dysfunction.

Conclusion

The acute alteration in consciousness that characterizes delirium implies significant CNS dysfunction from a variety of etiologies (Table 4). Increasing awareness of delirium in pediatric patients has led to improved descriptions of its presentation and a variety of screening instruments to facilitate its diagnosis and allow improved management of its symptoms. Environmental interventions often are sufficient to ameliorate its distress. Avoidance of benzodiazepines may decrease its occurrence, and utilization of antipsychotic medications is effective in managing its symptoms. Despite these efforts, current methods appear to be inadequate in improving its outcome.

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Compliance with Ethical Standards

Conflict of Interest Susan Beckwitt Turkel declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Malas N, Brahmbhatt K, McDermot C, Smith A, Ortiz-Aguayo R, Turkel S. Pediatric delirium: evaluation, management, and special considerations. Curr Psychiatry Rep. 2017;19:65–79. https://doi.org/10.1007/s11920-017-0817-3.
2.• Turkel SB, Hanft A. The pharmacologic management of delirium in children and adolescents. Pediatr Drugs. 2014;16:267–74. https://doi.org/10.1007/s40272-014-0078-0. **Review. Review of diagnostic criteria and pharmacologic management of delirium in pediatric patients.**
3. Traube C, Silver G, Gerber LM, Kaur S, Maure EA, Kerson A, et al. Delirium and mortality in critically ill children: epidemiology and outcomes of pediatric delirium. Crit Care Med. 2017;45:891–8. https://doi.org/10.1097/CCM.0000000000002324.
4. Traube C, Mauer EA, Gerber LM. Costs associated with pediatric delirium in the ICU. Crit Care Med. 2016;44:e1175–9.
5.•• Van Tuijl SCL, van Cauteren TJM, Pikhard T, Engel M, Schieveld JNM. Management of pediatric delirium in critical illness: a practical update. Minerva Anestesiol. 2015;81:333–41. **As title notes, a practical and thorough update on pediatric delirium.**
6. Poon C-HD, Ho Y-S, Chui K, Wong H-L, Chang RC. Sickness: from the focus on cytokines, prostaglandins, and complement factors to the perspective of neurons. Neurosci Biobehav Rev. 2015;57:30–45. https://doi.org/10.1016/jbiorev.2015.015.Epub2015Aug5.
7.• Traube C, Silver G, Reeder RW, Doyle H, Hegel E, Wolfe HA, et al. Delirium in critically ill children: an international point prevalence study. Crit Care Med. 2017;45:584–90. https://doi.org/10.1097/CCM0000000000002250. **Up to date international study of prevalence which puts problem of pediatric delirium into perspective.**
8. Grover S, Ghosh A, Kate N, Malhotra S, Mattoo SK, Chakrabarti S, et al. Do motor subtypes of delirium in child and adolescent have a different clinical and phenomenological profile? Gen Hosp Psychiatr. 2014;36:187–91. https://doi.org/10.1016/jgenhosppsych.2013.10.005.Epub2013Oct14.
9. Kudchadka SR, Aljiohani OA, Punjabi NM. Sleep of critically ill children in the pediatric intensive care unit. Sleep Med Rev. 2014;18:103–10. https://doi.org/10.1016/jsmrv.2013.02.002.Epub2013May21.
10. Grover S, Ghosh A, Charmode D. Do patients of delirium have catatonic features? An exploratory study. Psychiatr Clin Neurosci. 2014;68:644–51. https://doi.org/10.1111/pcn.12168.Epub2014Apr13.
11. Oldham MA, Lee HB. Catatonia vis-à-vis delirium: the significance of recognizing catatonia in altered mental status. Gen Hosp Psychiatr. 2015;37:554–9. https://doi.org/10.1016/jgenhosppsych.2015.0b.011.Epub2015Jun18.
12. Smith JH, Smith DV, Philbrick KL, Kumar N. Catatonic disorder due to a general medical or psychiatric condition. J Neuropsychiatry Clin Neurosci. 2012;24:198–207. https://doi.org/10.1176/appi.neuropsych.1060120.
13. Wilson JE, Nui K, Nicolson SE, Levine SZ, Heckers S. The diagnostic criteria and structure of catatonia. Schizophr Res. 2015;164:256–62. https://doi.org/10.1016/jschres.2014.12.036.Epub2015Jan13.
14. Best KM, Boullata JI, Curley MA. Risk factors associated with iatrogenic opioid and benzodiazepine withdrawal in critically ill pediatric patients: a systematic review and conceptual model. Pediatr Crit Care Med. 2015;16:175–83. https://doi.org/10.1097/PCC.0000000000000306.

15. Madden K, Burns MM, Tasker RC. Differentiating delirium from sedative/hypnotic-related iatrogenic withdrawal syndrome: lack of specificity in pediatric critical care assessment tools. Pediatr Crit Care Med. 2017;18:580–8. https://doi.org/10.1097/PCC.0000000000001153.

16.• Gangopadhyay M, Smith H, Pao M, Silver G, Deepmala D, De Souza C, et al. Development of the Vanderbilt Assessment for Delirium in Infants and Children to standardize pediatric delirium assessment by psychiatrists. Psychosomatics. 2017;58:355–63. https://doi.org/10.1016/jpsym.2017.03.006.Epub2017Mar15. **Newest instrument to provide a standardized approach for psychiatrists assessing for delirium.**

17. Trzepacz PT, Mittal D, Torres R, Kanary K, Norton J, Jimerson N. Validity of the Delirium Rating Scale-revised 98: comparison with the delirium rating scale and the cognitive test for delirium. J Neuropsychiatr Clin Neurosci. 2001;13:229–42. https://doi.org/10.1176/jnp.13.2.229.

18. Smith HA, Boyd J, Fuchs DC, Melvin K, Berry P, Shintani A, et al. Diagnosing delirium in critically ill children: validity and reliability of the pediatric confusion assessment method for the intensive care unit. Crit Care Med. 2011;39:150–7. https://doi.org/10.1097/CCM.0000000000001428.

19. Smith J, Gangopadhyay M, Goben CM, Jacobowski NL, Chestnut MH, Savage S, et al. The preschool confusion assessment method of the ICU: valid and reliable delirium monitoring for critically ill infants and children. Crit Care Med. 2016;44:592–600. https://doi.org/10.1097/CCM.0000000000001428.

20. Traube C, Silver G, Kearney J, Patel A, Atkinson TM, Yoon MJ, et al. Cornell assessment of pediatric delirium: a valid, rapid observational tool for screening delirium in the PICU. Pediatr Crit Care Med. 2014;42:656–63. https://doi.org/10.1097/CCM.0b013e3182a66b76.

21.•• Daoud A, Duff JP, Joffe AR, Alberta Sepsis Network. Diagnostic accuracy of delirium diagnosis in pediatric intensive care: a systematic review. Crit Care. 2014;18:489. https://doi.org/10.1186/s13054-014-0489-x. **Review. Review of instruments used to screen for delirium and their limitations.**

22. Flaigle MC, Ascenzi J, Kudchadkar SR. Identifying barriers to delirium screening and prevention in the pediatric ICU: evaluation of PICU staff knowledge. J Pediatric Nursing. 2016;31:81–4. https://doi.org/10.1016/j.pedn.2015.07.009.Epub2015Sep9.

23. Schieveld JN, Staal M, Voogd L, Fincken J, Vos G, Van Os J. Refractory agitation as a marker for pediatric delirium in very young infants at a pediatric intensive care unit. Intens Care Med. 2010;36:1982–3. https://doi.org/10.1007/s00143-010-1989-z. Epub 2010Aug6.

24.• Turkel SB, Jacobson JR, Munzig E, Tavaré CJ. Atypical antipsychotic medications to control symptoms of delirium in children and adolescents. J Child Adol Psychopharmacol. 2012;22:126–30. https://doi.org/10.1089/cap.2011.0084. **Reviews current first line choices for antipsychotics used to manage symptoms of delirium in pediatric patients.**

25. Slooff VD, Spaans E, van Puijenbroek E, Jessurun N, van Beusekom BS, de Hoog M, et al. Adverse events of haloperidol for the treatment of delirium in critically ill children. Intensive Care Med. 2014;40:1602–3. https://doi.org/10.1007/s00134-014-344-x. Epub2014Sep3.

26. Sassano-Higgins S, Freudenberg N, Jacobson J, Turkel S. Olanzapine reduces delirium symptoms in the critically ill pediatric patient. J Pediatr Intens Care. 2013;2:49–54.

27. Joyce C, Witcher R, Herrup E, Kaur S, Mendez-Rico E, Silver G, et al. Evaluation of the safety of quetiapine in treating delirium in critically ill children: a retrospective review. J Child Adolesc Psychopharmacol. 2015;25:666–70. https://doi.org/10.1089/cap.2015.0093.Epub2015Oct15.

28. Turkel SB, Tavaré CJ. Delirium in children and adolescents. J Neuropsychiatry Clin Neurosci. 2003;15:431–5. https://doi.org/10.1176/jnp.15.4.431.

29. Mehta S. Protocolized sedation in critically ill children. JAMA. 2015;313:363–4. https://doi.org/10.1001/jama.2015.1.

30. Minhas MA, Velasquez AG, Kaul A, Salinas PD, Celi LA. Effect of protocolized sedation on clinical outcomes in mechanically ventilated intensive care unit patients: a systematic review and meta-analysis of randomized controlled trials. Mayo Clinic Proc. 2015;90:613–23. https://doi.org/10.1016/j.mayocp.2015.02.016.Epub2015Apr9.

31. Vet NJ, de Wildt SN, Verlaat CW, Knibbe CA, Mooji MG, van Woensel JB, et al. A randomized controlled trial of daily sedation interruption in critically ill children. Intensive Care Med. 2016;42:233–44. https://doi.org/10.1007/s00134-015-4136-2.Epub2015Nov24.

32. Curley MA, Wypij D, Watson RS, Grant MJ, Asaro LA, Cheifetz IM, et al. Protocolized sedation vs usual care in pediatric patients mechanically ventilated for acute respiratory failure: a randomized clinical trial. JAMA. 2015;313:379–89. https://doi.org/10.1001/jama.2014.18399.

33. Nelson S, Muzyk AJ, Bucklin MH, Brudney S, Gagliardi JP. Defining the role of dexmedetomidine in the prevention of delirium in the intensive care unit. BioMed Res Internat. 2015;635737. https://doi.org/10.1155/2015/635737.Epub2015Oct19.

34. Pan W, Wang Y, Lin L, Zhou G, Hua X, Mo L. Outcomes of dexmedetomidine treatment in pediatric patients undergoing congenital heart disease surgery: a meta-analysis. Paediatr Anaesth. 2016;26:239–48. https://doi.org/10.1111/pan.12820.

35. Weerink MAS, Struys MMRF, Hannivoort LN, Barends CRM, Absalom AR, Colin P. Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine. Clin Pharmacokinet. 2017;56:893–913. https://doi.org/10.1007/s40262-017-0507-7.

36. Gagnon DJ, Riker RR, Glisic EK, Kelner A, Perrey HM, Fraser GL. Transition from dexmedetomidine to enteral clonidine for ICU sedation: an observational pilot study. Pharmacotherapy. 2015;35:251–9. https://doi.org/10.1002/phar.1559.

37.• Herrup EA, Wieczorek B, Kudchadkar SR. Characteristics of postintensive care syndrome in survivors of pediatric critical illness: a systematic review. World J Crit Care Med. 2017;6:124–34. https://doi.org/10.5492/wjccm.v6.i2.124.eCdlection2017May4. **Describes features of post-intensive care syndrome in pediatric patients, first described in adult survivors.**

38. Needham DM, Davidson J, Cohen H, Hopkins RO, Weinert C, Wunsch H, et al. Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. Crit Care Med. 2012;40:502–9. https://doi.org/10.1097/CCM.06013e318232da75.

39. Tasker RC, Menon DK. Critical care and the brain. JAMA. 2016;315(8):749–50. https://doi.org/10.1001/jama.2016.0701.

40. Van den Boogaard M, Schoonhoven L, Evers AW, van der Hoeven JG, van Achterberg T, Pikkers P. Delirium in critically ill patients: impact on long-term health-related quality of life and cognitive functioning. Crit Care Med. 2012;40:112–8. https://doi.org/10.1097/CCM.0b013e31822e9fc9.

41. Nelson LP, Gold JI. Posttraumatic stress disorder in children and their parents following admission to the pediatric intensive care unit: a review. Pediatr Crit Care Med. 2012;13:338–47. https://doi.org/10.1097/PCC.06013e3182196a8f.

42. Grover S, Ghosh A, Ghormode D. Experience in delirium: is it distressing? J Neuropsychiatry Clin Neurosci. 2015;27:139–46. https://doi.org/10.1176/appineuropsych.13110329.Epub2014Oct31.

43. Wolters AE, Peelen LM, Welling MC, Kok L, de Lange DW, Cremer OL, et al. Long-term mental health problems after delirium in the ICU. Crit Care Med. 2016;44:1808–13. https://doi.org/10.1097/CCM.0000000000001861.

44.•• Pinto NP, Rhinesmiith EW, Kim TY, Ladner PH, Pollack MM. Long-term function after pediatric critical illness: results from the survivor outcomes study. Pediatric Crit Care Med. 2017;18:e122–30. https://doi.org/10.1097/PCC.0000000000001070. **Long-term function in survivors, an important area of active research.**

45. Bone MF, Feinglass KM, Goodman DM. Risk factors for acquiring functional and cognitive disabilities during admission to a PICU. Pediatr Crit Care Med. 2014;15:640–8. https://doi.org/10.1097/PCC0000000000000199.

46. Als LC, Nadel S, Cooper M, Pierce CM, Sahakian BJ, Garralda ME. Neuropsychologic function three to six months following admission to the PICU with meningoencephalitis, sepsis, and other disorders: a prospective study of school-aged children. Crit Care Med. 2013;41:1094–103. https://doi.org/10.1097/CCM.0b013e318275d032.