Published in final edited form as:
Arch Pediatr Adolesc Med. 2010 April ; 164(4): 377–385. doi:10.1001/archpediatrics.2010.10.

Psychiatric Morbidity in Pediatric Critical Illness Survivors: A Comprehensive Review of the Literature

Dimitry S. Davydow, M.D.[1], **Laura P. Richardson, M.D.**[2], **Douglas F. Zatzick, M.D.**[1,3], and **Wayne J. Katon, M.D.**[1]

[1]Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, WA, USA

[2]Department of Pediatrics, University of Washington School of Medicine, Seattle, WA, USA

[3]Harborview Injury Prevention and Research Center, University of Washington School of Medicine, Seattle, WA, USA

Abstract

Objective—To review the prevalence of psychiatric syndromes in pediatric critical illness survivors as well as to summarize data on vulnerabilities and pediatric intensive care unit (PICU) exposures that may increase risk of developing these syndromes.

Data Sources—Medline (1966–2009), the Cochrane Library (2009, Issue 3), and PsycInfo (1967–2009) as of August 9, 2009.

Study Selection—Case-control, cross-sectional, prospective cohort and retrospective cohort studies, as well as randomized-controlled trials.

Main Exposures—Hospitalization for the treatment of a critical illness.

Main Outcome Measures—Assessments of psychiatric symptoms/disorders at least once after discharge.

Results—Seventeen studies were eligible. The most commonly assessed psychiatric disorders were posttraumatic stress disorder (PTSD) and major depression. The point prevalence of clinically significant PTSD symptoms ranged from 10%–28% (5 studies). The point prevalence of clinically significant depressive symptoms ranged from 7%–13% (3 studies). Pre-illness psychiatric and/or developmental problems and parental psychopathology were associated with vulnerability to psychiatric morbidity. Neither a child's age nor gender consistently increased vulnerability to post-illness psychopathology. Exposure to increased severity of medical illness and PICU service-delivery characteristics (e.g., invasive procedures) were predictors of psychiatric illness in some, but not all, studies. Early post-illness psychiatric symptoms were predictors of later psychiatric morbidity.

Conclusions—Psychiatric morbidity appears to be a substantial problem for pediatric critical illness survivors. Future research should include more in-depth assessment of post-critical illness depressive, anxiety and psychotic symptoms, validate existing psychiatric instruments, and clarify how vulnerability factors, PICU service-delivery characteristics and severity of critical illnesses are associated with subsequent psychopathology.

Address for Correspondence: Dimitry S. Davydow, M.D., Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, 1959 NE Pacific St, Box 356560, Seattle, WA, USA 98195, Phone: (206) 616-0952, Fax: (206) 221-5414, ddavydo1@u.washington.edu.

Keywords

intensive care units; pediatric; stress disorder; posttraumatic; depressive disorder; major; critical illness; outcome assessment (health care)

INTRODUCTION

Over 200,000 children require admission to a pediatric intensive care unit (PICU) annually in the United States for the treatment of critical illnesses.1 With recent advances in pediatric critical care medicine, more children are surviving critical illnesses.2 Accompanying this increase in survival, research in the field has begun to focus on long-term outcomes of pediatric critical illness survivors, including physical health,3 health-related quality of life (HRQOL),[4, 5] and mental health.[6, 7]

Critical illnesses and their requisite therapies expose children to extreme stressors, including pain from invasive procedures, respiratory insufficiency, delirium with potential associated psychotic experiences, and separation from their families. Critical illnesses are also, by definition, life-threatening. Therefore, psychiatric disorders, which can be triggered by exposure to extreme stressors in a vulnerable population,[8] and are highly prevalent in children exposed to traumatic events,[8] are a potential concern in pediatric critical illness survivors. The recognition of psychological distress in these children is important for several reasons. Mental disorders carry an increased risk of suicide, and this risk, as well as the persistence of symptoms, can continue into adulthood.[9, 10] Also, psychiatric disorders in this population may impair functioning in school, family and social roles, lead to lags in development and negatively impact HRQOL.[11, 12]

In this report, we present the results of a review of: (1) the prevalence of psychiatric syndromes in children surviving critical illnesses, (2) youth and parental vulnerabilities that may increase the risk of psychopathology, and (3) features of medical illness presentation and PICU exposures that elevate the risk for psychiatric morbidity. Our report differs from prior reviews on this topic[6, 7] in its focus on psychiatric syndromes following critical illnesses as well as its comprehensive review of potential vulnerabilities and exposures that may increase the risk for psychiatric disorders.

METHODS

Search Strategy

To identify studies eligible for review, we searched Medline (1966–2009), the Cochrane Library (2009, Issue 3), and PsycInfo (1967–2009) as of August 9, 2009. Our search strategy included the following terms mapped to the appropriate MeSH subject headings and “exploded”: (“mental disorders” OR “psychometrics”) AND (“respiratory distress syndrome, adult” OR “critical care” OR “critical illness” OR “intensive care units” OR “sepsis” OR “burns”). We also included the following terms as text words: (“depress*” OR “stress” OR “anxi*”) AND (“respiratory distress syndrome” OR “ARDS” OR “acute lung injury” OR “ALI”). The search was limited to English-language articles.

Study Selection

We sequentially reviewed citations, abstracts, and full text articles to select eligible studies. Articles were selected for review if they met the following criteria: (1) the study population was comprised of pediatric critical illness survivors between the ages of 2–19, and (2) psychiatric assessments occurred at any time following illness resolution. Studies of neonatal

and adult ICU survivors were excluded, as were abstracts, case reports, and review articles. We also excluded studies that only included transplant surgery survivors due to concerns for the confounding of risk for psychiatric morbidity conferred by organ transplants (due to psychiatric side effects of immunosuppressant medications13 and the severity of chronic illness pre-transplant14).

Data Abstraction and Study Quality

For each eligible study, we abstracted information regarding study cohorts, psychiatric measures, and potential vulnerabilities and exposures. When necessary, we contacted authors of eligible studies for additional study data.

Study quality was assessed using five criteria adapted from the United States Preventative Task Force15 and a previous systematic review of heterogeneous outcome data:[16] (1) enrollment of consecutive patients; (2) no loss to follow-up of > 10% of study participants prior to first psychiatric symptom assessment; (3) description of patients lost to follow-up; (4) at least one statistical comparison between patients lost to follow-up and those remaining in the study; and (5) adjustment for confounders by stratification, statistical adjustment, or comparison with a matched population. Quality criteria were not used in decisions regarding inclusion or exclusion of eligible studies.

RESULTS

Study Characteristics and Quality

We reviewed 8,569, citations, 553 abstracts and 58 full text articles for inclusion. Forty-one articles were excluded for lack of child psychiatric outcomes. Seventeen studies describing sixteen unique cohorts of pediatric critical illness survivors were eligible for data abstraction. Table 1 shows baseline descriptive data for the seventeen studies, ordered by follow-up assessment times. Follow-up periods ranged from immediately following hospital discharge[17] to up to 16 years after acute care discharge.[29] The studies enrolled 1,067 unique patients. Seven of the studies were conducted in the UK,[22, 23, 25–28, 33] five in the US,[18,19, 21, 31, 32] two in The Netherlands,[24, 29] one in Canada,[18]one in India,[17] and one in Switzerland.[30]

Four of the studies excluded patients with a history of psychiatric disorders.[24–27] In three of these, patients were excluded only if they were admitted to the PICU for a suicide attempt.[24, 25, 27] In the other one, patients with any prior or ongoing psychiatric disorder were excluded.[26] One of the studies reported on a premorbid history of developmental problems.[23] Six percent of children in this study had a history of developmental problems. Another study explored prior psychiatric difficulties using the Strengths and Difficulties Questionnaire (SDQ), a validated measure of general psychopathology in children completed by their parents and teachers.[22] Two studies reported on premorbid temperament using validated parent report measures, the Temperament Measurement Schedule and the School-Age Temperament Inventory, in school-age children.[17, 19]

Only six of the seventeen studies were of consecutive samples (Table 2).[17, 19, 22, 23, 25, 29] A majority of studies demonstrated high retention, though only four of the studies described the characteristics associated with participant loss,[24, 25, 29, 32] and only four of the studies compared patients lost to follow-up and those that completed the study.[18, 20, 24, 29] Over half of the studies adjusted for potential confounders in analyses.[18–26, 29, 31, 33]

Measures of Psychiatric Symptoms

Eight hundred ninety-nine subjects completed at least one PTSD measure, 166 completed measures of other anxiety disorders and 224 subjects completed at least one depression measure. Twelve of the studies utilized in-person assessments with a clinician,[17–19, 22–25, 27, 28,30, 31], one used an in-person computer-based assessment,[32] three used mailed questionnaires,[20, 26, 33] and one had a combination of in-person assessments and mailed questionnaires.[29] One of the studies used only questionnaires completed by parents.[18] The remaining studies used reports from the children themselves with or without additional parental reports. Seven studies utilized diagnostic interviews to ascertain psychiatric morbidity.[19, 21, 23,26, 30–32] The remaining studies used only questionnaires to measure psychopathology (Table 3).

Prevalence of Psychiatric Symptoms/Disorders

In determining the median point prevalence of questionnaire-ascertained clinically significant psychiatric symptoms, one important challenge was that several of the included studies collected psychiatric symptom data at more than one time point. In these cases, we used the median value from each study in our calculation of the overall median point prevalences of disorders. Table 3 summarizes the prevalences of post-critical illness psychopathology. The most commonly assessed psychiatric syndromes were PTSD and major depression. The point prevalence of questionnaire-ascertained clinically significant PTSD symptoms in pediatric critical illness survivors ranged from 10%28 to 28%,25 with a median point prevalence of 16% (5 studies, n = 201). The prevalence of diagnostic interview ascertained PTSD after a critical illness was 0%23 to 21%,27 with a median prevalence of 13% (6 studies, n = 233). The lifetime prevalence of PTSD in a cohort of 30 pediatric burn injury survivors was 30%.31 The point prevalence of questionnaire-ascertained clinically significant depressive symptoms ranged from 7%27 to 13%17, with a median point prevalence of 10% (2 studies, n = 51).17, 27 The prevalence of major depression following a critical illness as ascertained by diagnostic interview was 0%23 to 6%,32 with a median prevalence of 3%[31](3 studies, n = 128). The lifetime prevalence of major depression in one study was 27%.[31]

Vulnerability Factors Associated with Risk for Psychiatric Symptoms/Disorders

Pre-critical illness psychopathology was a potential vulnerability factor for post-PICU psychiatric morbidity in two studies (Table 4).[19, 22] Less consistent pre-critical illness predictors of post critical-illness psychiatric disorders included a child's gender (one of six studies20, 23–25, 30, 33), younger age (one of eight studies[17, 20,21, 23–25, 29, 30), developmental problems,[23] and pre-PICU maternal negative life events.[23] The following pre-illness variables were not associated with youth post-critical illness psychopathology: family socioeconomic status, [17, 23, 30] ethnicity,23, [25] social deprivation (as ascertained by the Townsend Deprivation Index, a questionnaire derived from UK census data measures of familial social isolation),[25] birth order,23 youth level of education,17 pre-PICU level of family support,19 maternal education,[20] parental marital status,[23] pre-PICU temperamental difficulties,[17, 19] or pre-PICU cognitive level.[19]

Critical Illness and Treatment-Related Exposures

Exposure to invasive procedures predicted post-critical illness psychiatric morbidity in two of three studies,17, 20, [30] PICU length of stay (LOS) predicted later psychiatric symptoms in two of six studies[17, 19, 20, 23–25], and severity of illness at admission predicted later psychopathology in three of eight studies. [17, 20, 21,23–25, 29, 30] Emergent admission to the PICU,[25] hospital LOS in the absence of septic shock,[23] and no family visits during the PICU stay,[20] also predicted post-critical illness psychiatric morbidity. Maternal presence at the time a child sustained a serious burn injury was protective against PTSD in one study,[30] and maternal

participation in a program designed to enhance emotional regulation and diminish anxiety was associated with fewer behavioral problems in young PICU survivors.[18] The following critical illness and treatment-related exposures were not associated with post-critical illness psychiatric morbidity: PICU admission diagnosis,[17, 24] traumatic brain injury,[25] duration of mechanical ventilation,24 hospital LOS22, 30 (particularly in the presence of septic shock23), sepsis or septic shock,23, 25 or receipt of opiates and/or benzodiazepines for ≥ 2 days.25

Post-Critical Illness Factors

Psychiatric symptoms, memories of in-PICU psychotic/nightmare experiences, and cognitive difficulties in the days and months following a critical illness were significant prospective predictors or cross-sectional correlates of post-critical illness psychopathology.[21, 22, 24–26] Both child and parental retrospective perceptions of the threat to the child's life from the critical illness, and the severity of illness, were cross-sectional correlates of child PTSD symptoms.[27] Parental psychiatric symptoms were cross-sectional correlates of youth post-critical illness PTSD symptoms in three studies.[22, 24, 27]The timing of the post-acute care pediatric follow-up visit was not a predictor of PTSD symptoms in one study,[24] nor was the length of follow-up in another study.[30]

DISCUSSION

This review of psychiatric morbidity in pediatric critical illness survivors found that the point prevalence of substantial psychopathology, particularly PTSD symptoms, was high within the first year following hospitalization. To our knowledge, there are no general population estimates in children for the questionnaires discussed in this review. Nevertheless, it is interesting to note that the point prevalence of substantial PTSD symptoms in pediatric critical illness survivors is as high or higher than that of traumatically-injured children (14% at approximately 4 months34) and pediatric cancer survivors (12% of pediatric sarcoma survivors at a mean of 17 years after treatment35) using two of the same questionnaires, the Impact of Events Scale (IES)35 and the IES-Revised.34 Importantly, since premorbid psychopathology may confer vulnerability to post-illness psychiatric morbidity, and some of the studies reviewed excluded youth with prior psychiatric histories, our prevalence estimates of post-critical illness psychiatric disorders are likely underestimates.

Although fourteen studies examined potential vulnerabilities and exposures that could convey risk for post-critical illness psychiatric morbidity, many of the specific factors examined were unique to particular studies. Nonetheless, where similar factors were considered across multiple studies, some tentative conclusions can be made: a) neither gender nor age appear to be consistent vulnerabilities; b) pre-PICU youth psychiatric and/or developmental problems are fairly consistent vulnerabilities that increase the risk of subsequent PTSD symptoms; c) medical illness severity and PICU servicedelivery characteristics such as LOS and invasive procedures may increase risk; d) early post-illness psychiatric symptoms may predict later psychiatric symptoms; and e) parental psychiatric symptoms are strongly associated with their children's post-critical illness psychiatric morbidity. The findings regarding age, gender, and prior psychiatric conditions are in line with those of studies of adult general ICU survivors.[36, 37] However, studies of adults have not found that severity of physical illness was associated with risk for post-ICU psychopathology,[36, 37] and there are inconsistencies regarding whether ICU service-delivery characteristics such as LOS increase risk.[36–38]

The existing literature has several important limitations. First, only three small studies prospectively assessed depression, and only four studies assessed psychiatric disorders other than PTSD or major depression, leaving further questions about these important outcomes in critically ill children. Trauma-exposed youth are at increased risk of developing major depression and anxiety disorders comorbid with PTSD,[39] suggesting pediatric critical illness

survivors may have similar risks. Second, none of the questionnaires utilized to assess psychiatric symptoms in the studies described have been validated in pediatric critical illness survivors. Also, one of the studies found substantial difficulties with the psychometric properties of the IES, leading to changes in the final questionnaire used,20 as well the group's endeavors to create a new questionnaire to ascertain these symptoms.40 Third, all of the studies enrolled pre-school and elementary school age children, and there are concerns regarding the validity of the Diagnostic and Statistic Manual of Mental Disorders-IV PTSD diagnostic criteria in these age groups.41, [42] Fourth, none of the studies separated subjects by developmental stage (e.g., prepubescent, adolescent), so we could not assess this factor as a vulnerability to post-critical illness psychopathology. There is evidence to suggest that trauma-exposed adolescents are at greater risk for subsequent psychopathology than younger children. [39] Moreover, it is unclear if the psychiatric morbidity these children experience is primarily a result of pre-morbid factors, the critical illness itself, or of the subsequent treatment. Due to these methodological limitations, confidence regarding the precision and validity of this review's findings should be tempered.

Additional research is needed to understand vulnerabilities and exposures that may increase the risk of psychiatric morbidity in pediatric critical illness survivors. None of the reviewed studies assessed the impact of prior exposure to trauma as a predictor of psychopathology following a critical illness. Studies of adult traumatic injury survivors have found that increased prior trauma exposure is a potent predictor of PTSD following an injury.[43, 44] A similar association in pediatric critical illness survivors would be important to establish. Also, researchers have found an increased risk of psychiatric symptoms in adolescents with serious medical conditions.[45] Therefore, a potential intermediate conveying risk for post-critical illness psychopathology may be a child's preexisting medical illness severity. Potential proxies for preexisting medical illness severity to ascertain include the presence of multiple comorbid conditions,[46] previous medical hospitalizations and/or the number of prior emergency room visits. Furthermore, prospective studies of the effects of parental psychopathology on the psychiatric outcomes of their children following a critical illness are needed to clarify the nature of the associations found here and to identify potential avenues for intervention. If outcomes of childhood critical illnesses are worsened by parental psychiatric symptoms, then parents of children with post-critical illness psychiatric disorders should also be screened for psychopathology following their child's hospitalization. Parents of youth diagnosed with major depression have been found to have a high prevalence of psychopathology themselves,[47] and treatment of parental psychiatric disorders may improve the mental health outcomes of their children.[48] Studies screening parents of traumatically injured children for alcohol use disorders[49] and parents of depressed adolescents for major depression[50] have shown that such screening programs are not only feasible, but have also identified potential areas for intervention that may improve the health of both children and their parents.

As interest in the outcomes of pediatric critical illness survivors is increasing, we make several recommendations for future studies of psychiatric morbidity in these patients. First, studies assessing post-critical illness psychopathology should prospectively evaluate the prevalence of, and risk factors for, depressive, anxiety and psychotic symptoms. Second, studies should utilize diagnostic interviews to validate commonly used questionnaires and diagnostic criteria in children surviving critical illnesses. Third, studies prospectively examining psychiatric and functional morbidities in critical illness survivors under the age of two are needed. Studies of burned youth that included children as young as one year old have found that even very young children may also be at increased risk for psychiatric symptoms following a serious illness. [51, 52] Fourth, future studies should assess child developmental stage and utilize valid and reliable measures of temperament, prior trauma exposure, family psychiatric history and youth lifetime psychiatric and medical history as potential vulnerabilities to post-critical illness psychopathology, and incorporate these factors into a comprehensive model, including PICU

factors (e.g., invasive procedures, pain, delirium, illness severity) and post-hospitalization factors (e.g., parental psychopathology). Ultimately, such studies can lead to implementation of screening mechanisms which utilize validated instruments to target at-risk youth prior to acute care discharge, facilitating appropriate interventions and referrals before the development of substantial psychiatric morbidity.

In conclusion, pediatric critical illness survivors appear to have substantial psychiatric morbidity. Although further research is needed to more fully define factors that may increase the risk of post-critical illness psychopathology, we can preliminarily conclude that a child's age and/or gender are not vulnerabilities, pre-illness psychiatric and/or developmental problems are probable vulnerabilities, severity of illness and PICU service-delivery characteristics may be exposures that elevate risk, and early post-critical illness psychiatric symptoms, as well as parental psychiatric symptoms, are strong correlates of subsequent youth psychiatric morbidity. In the meantime, clinicians should recognize that psychiatric illnesses are common in pediatric critical illness survivors, requiring collaboration between pediatric intensivists, surgeons, pediatricians, child psychiatrists, pediatric psychologists and social workers, in a multidisciplinary team, to ensure prompt, comprehensive evaluation and treatment.

Acknowledgments

The authors wish to thank Gillian Colville, Bsc., MPhil., Elena Garralda, F.R.C.Psych., Julia Gledhill, F.R.C.Psych., Bernadette Melnyk, R.N., Ph.D., Janet Rennick, R.N., Ph.D., EMWJ Utens, Ph.D., and LCAC Vermunt, Ph.D., for providing additional data from their studies for this review.

This work was supported by grant NRSA-T32/MH20021-11 from the National Institute of Mental Health. The authors have no competing interests or relevant potential conflicts of interest to disclose. Dr. Davydow has had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1

Measurements of psychiatric symptoms/syndromes, ordered by follow-up time

			Mean (standard deviation) or *Median (interquartile range)* or [absolute range]				
Psychiatric Condition	**Study**	**Instrument**	**Follow-up in months**	**N at follow-up**	**Mean/Median**	**Cut-off score**	**Point Prevalence (%)**
PTSD	*Muranjan et al. 2008*[17]	IES-I	0	30	1.6 (2.2)	26	43
		IES-A			0.2 (0.8)		7
		IES-I	1	30	0.3 (0.6)		-
		IES-A			0 (0)		-
	Melnyk et al. 2004[18]	PHSI	1	-	-	7	-
			3	89			
			6	89			
			12	67			
	Connolly et al. 2004[19]	DISC	1.4 (0.5), [1–2]	43	n/a	n/a	12
	Rennick et al. 2002[20]	CIES	1.5	60	0.4 (0.2)	-	-
			6	60	0.3 (0.2)		
	Saxe et al. 2005[21]	Child PTSD Reaction Index	3	72	16.8 (13.1)	-	-
	Shears et al. 2005[22], [a]	IES	3	26	-	30	15
	Bronner et al. 2008[24]	CRTI	3	29	-	47	14
			9	28			18
	Colville et al. 2008[25]	IES-R	*3*, [1.8–5.7]	96	*9*, [0–26]	17	28
	Elison et al. 2008[26]	IES	4.8 (1.4)	15	27.3 (19.4), *27.5 (12.2, 37.2)*	-	-

			Mean (standard deviation) or *Median (interquartile range)* or [absolute range]				
Psychiatric Condition	**Study**	**Instrument**	**Follow-up in months**	**N at follow-up**	**Mean/Median**	**Cut-off score**	**Point Prevalence (%)**
	Rees et al. 2004[27]	CAPS-C	*7.7 (6.9, 8.6)*	19	n/a	n/a	21[b, 5c]
		IES		21	*10 (6, 24)*	30	17
	Judge et al. 2002[28]	IES	8.9, [3–12]	29	-	20	10
	Shears et al. 2007[23, a]	K-SADS-IV-R	11.9 (2.3)	48	n/a	n/a	0
	Vermunt et al. 2008[29]	PTSP	[48–192]	192	4.3	-	-
	Landolt et al. 2009[30]	CAPS-CA	53 (24)	43	n/a	n/a	19
	Stoddard et al. 1989[31]	DICA-C DICA-P	108	30	n/a	n/a	7[d, 30e]
	Thomas et al. 2009[32]	C-DISC4	125	50	n/a	n/a	2
Overanxious Disorder	*Stoddard et al. 1989*[31]	DICA-C DICA-P	108	30	n/a	n/a	30[d, 33e]
Separation Anxiety Disorder	*Shears et al. 2007*[23, a]	K-SADS-IV-R	11.9 (2.3)	48	n/a	n/a	3
	Stoddard et al. 1989[31]	DICA-C DICA-P	108	30	n/a	n/a	0[d, 7e]
Phobic Disorder	*Shears et al. 2007*[23, a]	K-SADS-IV-R	11.9 (2.3)	48	n/a	n/a	13
	Stoddard et al. 1989[31]	DICA-C DICA-P	108	30	n/a	n/a	47[d, 47e]

			Mean (standard deviation) or *Median (interquartile range)* or [absolute range]				
Psychiatric Condition	**Study**	**Instrument**	**Follow-up in months**	**N at follow-up**	**Mean/Median**	**Cut-off score**	**Point Prevalence (%)**
	Thomas et al. 2009[32]	C-DISC4	125	50	n/a	n/a	44
Depression	*Muranjan et al. 2008*[17]	BDS	0 1	30 30	6.9 (4.0) 5.0 (3.7)	13	13 -
	Rees et al. 2004[27]	BDS	*7.7 (6.9, 8.6)*	30	7.4 (4.7)	15	7
	Shears et al. 2007[23], *a*	K-SADS-IV-R	11.9 (2.3)	48	n/a	n/a	0
	Stoddard et al. 1989[31]	DICA-C DICA-P	108	30	n/a	n/a	3*d*, 27*e*
	Thomas et al. 2009[32]	C-DISC4	125	50	n/a	n/a	6
	Pope et al. 2007[33]	BDI-II	141	36	10.4 (9.7)	20	-
Dysthymic Disorder	*Stoddard et al. 1989*[31]	DICA-C DICA-P	108	30	n/a	n/a	10*d*, 10*e*
Tic Disorder Psychosis	*Shears et al. 2007*[23], *a*	K-SADS-IV-R	11.9 (2.3)	48	n/a	n/a	6
	Stoddard et al. 1989[31]	DICA-C DICA-P	108	30	n/a	n/a	3*d*, 6*e*
ADHD	*Stoddard et al. 1989*[31]	DICA-C DICA-P	108	30	n/a	n/a	0*d*, 13*e*
	Thomas et al. 2009[32]	C-DISC4	125	50	n/a	n/a	2
Oppositional Defiant Disorder	*Shears et al.*	K-SADS-IV-R	11.9 (2.3)	48	n/a	n/a	13

			Mean (standard deviation) or *Median (interquartile range)* or [absolute range]				
Psychiatric Condition	**Study**	**Instrument**	**Follow-up in months**	**N at follow-up**	**Mean/Median**	**Cut-off score**	**Point Prevalence (%)**
	2007 [23], *a*						
	Stoddard et al. 1989 [31]	DICA-C DICA-P	108	30	n/a	n/a	[23]*d*, 23*e*
	Thomas et al. 2009 [32]	C-DISC4	125	50	n/a	n/a	0
Conduct Disorder	*Stoddard et al. 1989* [31]	DICA-C DICA-P	108	30	n/a	n/a	[7]*d*, 17*e*
	Thomas et al. 2009 [32]	C-DISC4	125	50	n/a	n/a	12
Behavioral problems	*Melnyk et al. 2004* [18]	BASC-composite index	1	-	-	-	-
			3	89			-
			6	89			-
			12	67			11%

Abbreviations (in alphabetic order): BASC = Behavioral Assessment Scale for Children; BDI-II = Beck Depression Inventory-II; BDS = Birleson Depression Scale; CAPS-C = Clinician-Administered PTSD Scale for Children; CAPS-CA = Clinician-Administered PTSD Scale for Children and Adolescents; C-DISC = Computerized Diagnostic Interview Schedule for Children-4th edition; CIES = Children's Impact of Events Scale; CRTI = Children's Response to Trauma Inventory; DICA-C = Diagnostic Instrument for Children and Adolescents – Child Version; DICA-P = Diagnostic Instrument for Children and Adolescents – Parent Version; DISC = Diagnostic Interview Schedule for Children; IES = Impact of Events Scale; IES-R = Impact of Events Scale-Revised; K-SADS-IV-R = Schedule for Affective Disorders and Schizophrenia for School-Age Children-IV-Revised; n/a = not-applicable; PHSI = Post-Hospital Stress Index for Children; PTSD = posttraumatic stress disorder; PTSP = Posttraumatic Stress Problems Scale; "-"= not reported.

[a] The two studies by Shears et al.[22, 23] reported data on the same cohort but at different follow-up times.

[b] Point prevalence of CAPS-C PTSD in the year following PICU admission.

[c] Point prevalence of CAPS-C PTSD at the time of follow-up assessment.

[d] Point prevalence of disorder at the time of interview.

[e] Lifetime prevalence of disorder.

Table 2

Potential vulnerability and/or exposure factors for psychiatric morbidity

Study	Measure of Association	Potential vulnerability and/or exposure factors	Psychiatric symptoms/disorder
Muranjan et al. 2008 (n = 30) 17	Spearman's rank test	**a.** TISS score **b.** age, SES, education, nature of illness, illness severity, PICU LOS, premorbid temperament	IES-I at hospital discharge **a.** R = 0.51, P = 0.004 **b.** n.s.
Melnyk et al. 2004 (n = 67) 18	χ^2	Mother not participating in COPE program	BASC-composite index P < 0.01
Connolly et al. 2004 (n = 43) 19	Quantile regression Wilcoxon signed-rank	**a.** ≥ 48 h ICU LOS **b.** premorbid cognitive level **c.** negative reactivity **d.** approach/withdrawal **e.** dimensions of temperament **f.** family support **g.** PTSD symptoms pre-op	PTSD **a.** r^2 = 0.19, P = 0.001 **b.** P = 0.49 **c.** P = 0.95 **d.** P = 0.89 **e.** P = 0.83 **f.** P = 0.83 **g.** $z = -2.62$, P = 0.009
Rennick et al. 2002 (n=60) 20	Multiple regression	**a.** child age **b.** invasive procedures **c.** severity of illness **d.** length of stay **e.** maternal education (f) child age (g) invasive procedures (h) severity of illness (i) length of stay (j) maternal education (k) child's sex (l) family visiting	CIES at 6 weeks **a.** $\beta_{st} = -0.14$, n.s. **b.** $\beta_{st} = 0.29$, P < 0.05 **c.** $\beta_{st} = 0.02$, n.s. **d.** $\beta_{st} = -0.08$, n.s. **e.** $\beta_{st} = -0.05$, n.s. CIES at 6 months (f) $\beta_{st} = -0.01$, n.s. (g) $\beta_{st} = 0.0006$, n.s. (h) $\beta_{st} = 0.0004$, n.s. (i) $\beta_{st} = -0.002$, n.s. (j) $\beta_{st} = 0.004$, n.s. (k) $\beta_{st} = 0.03$, n.s. (l) $\beta_{st} = -0.08$, P < 0.05
Saxe et al. 2005 (n = 72) 21	Pearson's correlation	**a.** age **b.** TBSA burned **c.** separation anxiety post-burn **d.** dissociation post-burn	PTSD at 3 months **a.** r = −0.17, n.s. **b.** r = 0.49, P < 0.001 **c.** r = 0.68, P < 0.001 **d.** r = 0.36, P < 0.01

Study	Measure of Association	Potential vulnerability and/or exposure factors	Psychiatric symptoms/disorder
		e. PTSD symptoms 10 days post-burn	**e.** r = 0.45, P < 0.001
Shears et al. 2005 (n = 26)[22], *a*	Spearman's rank test	**a.** days in hospital **b.** premorbid SDQ **c.** follow-up SDQ **d.** maternal IES	IES at 3 months **a.** r = 0.01, P = 0.95 **b.** r = 0.48, P = 0.01 **c.** r = 0.50, P = 0.007 **d.** r = 0.42, P = 0.03
Shears et al. 2007 (n = 31) [23], *a*	Multivariate logistic regression	**a.** PICU admission **b.** shock **c.** developmental problems **d.** impact of maternal premorbid negative life events **e.** days in hospital **f.** GMSPS **g.** shock by GMSPS **h.** shock by days in hospital (i) PICU admission (j) shock (k) developmental problems (l) premorbid SDQ impact score (m) GMSPS (n) days in PICU (o) shock by days in PICU (p) age, gender, social class, ethnicity, parental marital status, birth order position	Psychiatric disorder in the year after meningococcal disease **a.** UOR = 7.35, 95%CI(1.3–42.0) **b.** UOR = 4.66, 95%CI(1.0–20.9); AOR = 0.02, 95%CI(0–64.7), P = 0.34 **c.** UOR = 1.55, 95%CI (0.4–6.3) **d.** AOR = 1.61, 95%CI(1.1–2.4), P = 0.02 **e.** AOR = 2.53, 95%CI(1.1–5.7), P = 0.03 **f.** AOR = 0.29, 95%CI(0.09–0.9), P = 0.03 **g.** AOR = 7.61, 95%CI(1.4–42.4), P = 0.02 **h.** AOR = 0.38, 95%CI(0.2–0.9), P = 0.03 Psychiatric disorder at the time of 12 month follow-up (i) UOR = 4.8, 95%CI(1.0–23.3) (j) UOR = 5.5, 95%CI(1.7–17.6) AOR = 9.15, 95% CI(0.95–88.2), P = 0.055 (k) UOR = 3.4, 95%CI(1.2–9.9) (l) AOR = 2.46, 95%CI(1.0–6.2), P = 0.06 (m) AOR = 1.54, 95%CI(1.1–2.1), P = 0.008 (n) AOR = 1.48, 95%CI(0.9–2.4), P = 0.11 (o) AOR = 0.55, 95%CI(0.32–0.95), P = 0.03 (p) n.s.
Bronner et al. 2008 (n = 29) 24	Spearman's rank test	**a.** PICU LOS **b.** length of MV (n = 18) **c.** reason for PICU admission **d.** PIM **e.** follow-up time **f.** gender **g.** age **h.** mother's psychological distress score (n = 25) **i.** mother's SRS-PTSD score (n = 27)	CRTI at 3 months **a.** R = −0.12, n.s. **b.** R = −0.20, n.s. **c.** R = −0.00, n.s. **d.** R = 0.11, n.s. **e.** R = 0.00, n.s. **f.** R = 0.13, n.s. **g.** R = 0.02, n.s. **h.** R = 0.48, P < 0.05 **i.** R = 0.64, P < 0.01 **j.** R = 0.37, n.s.

Study	Measure of Association	Potential vulnerability and/or exposure factors	Psychiatric symptoms/disorder
	Linear regression	**j.** father's psychological distress score (n = 23) **k.** father's SRS-PTSD score (n = 19) (l) PICU LOS (n = 28) (m) length of MV (n = 20) (n) reason for PICU admission (n = 28) (o) PIM (n = 28) (p) follow-up time (n = 28) (q) gender (n = 28) (r) age (n = 28) (s) CRTI at 3 months (n = 21) (t) mother's psychological distress score (n = 25) (u) mother's SRS-PTSD score (n = 27) (v) father's psychological distress score (n = 21) (w) father's SRS-PTSD score (n = 22) (x) mother's SRS-PTSD score (n = 27) (y) CRTI at 3 months (n = 21)	**k.** R = 0.43, n.s. CRTI at 9 months (l) R = 0.25, n.s. (m) R = 0.28, n.s. (n) R = 0.15, n.s. (o) R = 0.06, n.s. (p) R = −0.01, n.s. (q) R = 0.17, n.s. (r) R = 0.31, n.s. (s) R = 0.77, P < 0.01 (t) R = 0.52, P < 0.01 (u) R = 0.73, P < 0.01 (v) R = 0.70, P < 0.01 (w) R = 0.37, n.s. (x) β = 1.40, t = 4.09, P = 0.001 (y) β = 0.38, t = 2.77, P = 0.02
Colville et al. 2008 (n = 96) 25	Linear regression Mann-Whitney *U*	**a.** age **b.** male **c.** white UK ethnicity **d.** social deprivation (n = 95) **e.** PICU LOS > 2 days **f.** emergency admission **g.** PIM (n = 94) **h.** opiates/benzos ≥ 2 days **i.** sepsis **j.** TBI **k.** factual memory **l.** delusional memory **m.** delusional memory vs. factual memory + delusional memory	IES-R at 3 months **a.** β = −0.29, 95%CI(−0.8–0.2), P = 0.28 **b.** β = −1.7, 95%CI(−4.7–1.2), P = 0.25 **c.** β = 0.21, 95%CI(−2.7–3.2), P = 0.89 **d.** β = 0.15, 95%CI(−2.8–3.1), P = 0.92 **e.** β = −0.52, 95%CI(−3.5–2.4), P = 0.73 **f.** β = 6.1, 95%CI(2.3–10), P = 0.002 **g.** β = 0.18, 95%CI(0.02–0.3), P = 0.03 **h.** β = 1.1, 95%CI(−1.8–4), P = 0.45 **i.** β = 1.4, 95%CI(−2.8–5.5), P = 0.51 **j.** β = 1.8, 95%CI(−1.2–4.8), P = 0.24 **k.** β = −0.48, 95%CI(−3.5–2.5), P = 0.76; Aβ = 1.3, 95%CI(−1.7–4.3), P = 0.39 **l.** β = 3.0, 95%CI(−0.05–6.1), P = 0.054; Aβ = 3.0, 95%CI(0.06–5.9), P = 0.04 **m.** *median 7.5* vs. *12*, P = 0.71
Elison et al. 2008 (n = 14)[26]	Spearman's rank test	CANTAB Pattern recognition memory score	IES R = −0.57, P = 0.03

Study	Measure of Association	Potential vulnerability and/or exposure factors	Psychiatric symptoms/disorder
Rees et al. 2004 (n = 21)[27]	Spearman's rank test	**a.** child-perceived severity of illness **b.** child-perceived life threat **c.** parent-perceived severity of illness **d.** parent-perceived life threat **e.** parental IES score	IES **a.** R = 0.40, P = 0.009 **b.** R = 0.36, P = 0.002 **c.** R = 0.30, P = 0.01 **d.** R = 0.40, P = 0.004 **e.** R = 0.40, P = 0.006
Vermunt et al. 2008(n = 192)	Linear regression	**a.** PRISM score **b.** age when mother was informant **c.** age when father was informant	PTSD **a.** n.s. **b.** $\beta = -0.36$, $P < 0.05$ **c.** $\beta = -0.43$, $P < 0.05$
Landolt et al. 2009 (n = 43) 30	Spearman's rank test	**a.** age at injury **b.** age at assessment **c.** female gender **d.** SES **e.** fire injury **f.** mother present at accident **g.** burn size **h.** face burned **i.** days in hospital **j.** number of skin graft procedures **k.** length of follow-up	PTSD **a.** R = −0.08, n.s. **b.** R = −0.06, n.s. **c.** R = −0.10, n.s. **d.** R = −0.02, n.s. **e.** R = 0.02, n.s. **f.** R = −0.35, P < 0.05 **g.** R = 0.11, n.s. **h.** R = −0.15, n.s. **i.** R = 0.13, n.s. **j.** R = 0.07, n.s. **k.** R = −0.04, n.s.
Pope et al. 2007 (n = 36)[33]	Analysis of Variance	female gender	BDI-II $F_{1, 75} = 8.85$, P = 0.004

Abbreviations (in alphabetical order):AOR = adjusted odds ratio; Aβ = linear regression coefficient in multivariable model adjusted for specified confounders; β = linear regression coefficient in multivariable model; BASC = Behavioral Assessment Scale for Children; BDI-II = Beck Depression Inventory – II; CANTAB = Cambridge Neuropsychological Test Automated Battery ; CI = confidence interval; CIES = Children's Impact of Events Scale; COPE = Creating Opportunities for Parent Empowerment Program; CRTI = Children's Response to Trauma Inventory; GMSPS = Glasgow Meningococcal Septicemia Prognostic Score; IES = Impact of Events Scale; IES-R = Impact of Events Scale-Revised; LOS = length of stay; MV = mechanical ventilation; n.s. = not significant; PICU = pediatric intensive care unit; PIM = Pediatric Index of Mortality; PRISM = Pediatric Risk of Mortality; PTSD = Posttraumatic stress disorder; SDQ = Strengths and Difficulties Questionnaire; SES = socioeconomic status; SRS-PTSD = Self-Rating Scale for Posttraumatic Stress Disorder; TBI = traumatic brain injury; TBSA = Total Body Surface Area; TISS = Therapeutic Intervention Scoring System; UOR = unadjusted odds ratio.

[a]The two studies by Shears et al.[22, 23] reported data on the same cohort but at different follow-up times.