



Functional Outcomes and Physical Impairments in Pediatric Critical Care Survivors: A Scoping Review*

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Objective: Although more children are surviving critical illness, little is known about long-term physical impairment. This scoping review aims to critically appraise existing literature on functional outcome measurement tools, prevalence, and risk factors for physical impairments in pediatric critical care survivors.

Data Sources: PubMed, Embase, and Cumulative Index to Nursing and Allied Health Literature, using a combination of MeSH terms and keywords (critical illness, intensive care, and functional outcomes/status).

Study Selection: All human studies reporting functional outcomes in children 0–18 years old admitted to the PICU. Non-English language, adult and preterm infant studies were excluded.

Data Synthesis: Three global assessment tools and eight multidimensional measures were used to measure functional outcome in pediatric survivors of critical illness. Rates of acquired functional impairment in a general pediatric intensive care cohort ranged from 10% to 36% at discharge and 10% to 13% after more than 2 years. Risk factors for acquired functional impairment include illness severity, the presence of organ dysfunction, length of ICU stay, and younger age. There is some evidence that physical impairment may be more severe and persistent than psychosocial components.

Conclusions: Functional impairment may be persistent in pediatric survivors of critical care. Unfortunately, studies varied largely in measurement timing and tools used. The lack of differentiation between impairment in different functional domains limited the generalizability of data. Further studies using a combination of standardized measures at various time points of the disease process can help establish more comprehensive rates of physical impairment. (*Pediatr Crit Care Med* 2016; 17:e247–e259)

Key Words: critical illness; functional status; intensive care; morbidity; outcomes assessment; pediatrics

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Pediatric critical care mortality has decreased secondary to evidence-based use of invasive ventilation, complex procedures, and medications (1), with current crude mortality rates of 3–5% (2, 3). However, survivors can experience disabilities and poorer health status (2), with significant associated healthcare costs. Children with chronic conditions are more likely to be readmitted to PICUs (2) and have longer stays compared with previously healthy children (4, 5). Growing demand for PICU care is evident—the United States saw a 24% increase in PICU beds between 1995 and 2001, disproportionately faster than pediatric population growth rates (3, 6).

With improved life expectancy, mortality may not be the most meaningful outcome measure (7). Of greater relevance is the level of disability following critical illness and the corresponding social and economic burden (8). Awareness of psychologic, social, and physical impairments can guide care in returning children to their preadmission state—a worthy goal from both an individual and a public health perspective (7, 8).

TABLE 1. Functional Outcome Measures Used in Critically Ill Children

Measurement Tool	Purpose	Characteristics
Global measures		
POPC, pediatric cerebral performance (59)	Measure short-term overall and cognitive disability after critical illness or injury in children; POPC may be more reflective of physical impairments	Six-point measure (good, mild disability, moderate disability, severe disability, coma or vegetative state, and brain death); assessed by healthcare provider. Time to administer: < 5 min
Modified Glasgow Outcome Scale (46)	Assess functional outcome in PICU survivors	Six-point measure (normal, functionally normal, mild handicap, moderate handicap, severe handicap, and died); assessed using standard questionnaire by healthcare provider Time to administer: < 5 min
Royal Alexandra Hospital for Children Measure of Function (93)	Measure HRQOL in hospitalized children	One- to 100-point rating scale about function; assessed by healthcare provider. Adapted from a measure of overall function Time to administer: < 5 min
Multidimensional measures—health-related quality of life		
HUI (HUI1, HUI2, and HUI3) (67, 68)	HUI1: evaluate HRQOL in VLBW infants HUI2 ^a : originally to measure HRQOL in childhood cancer survivors, now used for both clinical and general populations HUI3 ^a : measure HRQOL in both clinical and general populations	HUI1: four- to eight-point scale in each of four domains (physical, role, social emotional, and health problems) HUI2: three- to five-point scale in each of six domains (sensation, cognition, emotion, pain, mobility, and self-care) HUI3: five- to six-point scale in each of eight domains (vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain) Self/proxy reports available Time to administer: 5–10 min
Pediatric Quality of Life Inventory 4.0 (66)	Measure HRQOL in healthy and ill children (2–18 yr)	23 items in five domains (physical, psychosocial, emotional, social, and school) Self/proxy reports available Time to administer: 5 min
Child Health Questionnaire (65)	Measure HRQOL in healthy and ill children (5–18 yr)	28–87 questions targeting 14 different concepts: physical and psychosocial domains, including family functioning Self/proxy reports available Time to administer: 5–25 min
Stein-Jessop Function Status II (Revised) (62)	To assess behavioral function in children with chronic illness (0–16 yr)	43 questions, proxy report. Scores summarized into global health and stage-specific domains (responsiveness, activity, and interpersonal functioning) Time to administer: 15–30 min
Multidimensional measures—adaptive behavior		
Vineland Adaptive Behavior Scales, version 2 (74)	Measure adaptive behavior in children with disabilities (0–18 yr)	Four domains (communication, daily living, socialization, and motor) Time to administer: 45 min
Functional Status Scale (60)	To assess functional outcome in hospitalized children based on adaptive behavior (0–18 yr)	Five-point scale in each of six domains (mental, sensory, communication, motor, feeding, and respiratory status); assessed by healthcare provider Time to administer: < 5 min

PCPC = pediatric cerebral performance category, HUI = Health Utility Index, HRQOL = health-related quality of life, VLBW = very low birth weight.

^aHUI 2 and 3 are meant to be complementary.

Validation	Advantages	Limitations
Good interrater reliability, POPC correlates well with motor development and adaptive function in PICU population but less precise (5, 59)	Fast to administer, validated, and widely used in PICU outcome studies	Subjective, requires knowledge on child development, does not differentiate between aspects of function, ceiling effect possible for those with significant disability, unable to definitively identify rates of physical impairment
Not stated	Fast to administer	Subjective, requires knowledge on child development, does not differentiate between aspects of function, validation unclear
Moderate interrater reliability, moderate parent/clinician agreement in a pediatric hospital setting (49)	Fast to administer	Poor validity for nonschooling age, subjective, does not differentiate between different aspects of function/health status
HUI1: good reproducibility but high-responder confusion HUI2 and 3: validated in multiple patient cohorts including ex-VLBWs, childhood cancer survivors, and neurologic disorders (94, 95)	HUI2 and 3 widely used, suitable for various populations and ages, available in many languages. When used together, HUI2 and 3 provide a comprehensive view of various aspects of function and disability	HUI1: no longer in use HUI2 and 3: not valid in young children < 5 yr old, more suitable for community surveys as more sensitive to changes in the higher functioning range
Good correlation between parent and patient scores, scores significantly different between chronic and healthy children (96)	Has disease-specific questionnaires to complement generic questionnaires, available in many languages, wide pediatric age range	May not be as sensitive to small changes in areas of function
Good internal consistency, variable test-retest reliability, good construct validity, moderate discriminant validity in children with chronic disease (97, 98)	Widely used, available in many languages, normative values available	Not validated for use in children < 5 yr
Moderate correlation with illness susceptibility and hospital length of stay, and moderate discriminant validity for chronic disease (62)	Wide age range	Not as well validated, unable to differentiate specifically between domains of function
Good interrater, test-retest reliability, and good validity against other functional measures (99, 100)	Addresses developmental skills in children, large age range, age norms available	Relatively long administration time, requires trained administrators
Moderate to good interrater reliability in high-risk PICU population, correlates with adaptive behavior (60) and POPC (75)	Relatively fast to administer, more objective and precise than POPC	Not applicable to non-PICU patients or relatively well PICU patients

Early assessment of health status and long-term outcomes other than mortality in children focused on premature infants and children with chronic diseases (9–11). Impairments in physical, psychologic, and social behavior demonstrated the importance of function and health in evaluating medical treatment (9–11). Over the past decade, the burden of disability after critical illness has also gained attention as long-term functional impairments have become apparent in adults. Physical limitations seem to outlast the neuropsychologic deficits (12–15) and impact activities of daily living and return-to-work rates (16–18). Survivors attributed their physical limitations to muscle wasting (12), which is now widely studied, and it seems to be a cause of significant medical, financial, and social burden to ICU survivors and their families (19–22).

Risk factors associated with ICU muscle wasting and weakness in adults—sepsis (21, 23), organ dysfunction (21), prolonged mechanical ventilation (21), acute lung injury (20), hyperglycemia (24), and high corticosteroid dose (21)—also affect children (25–29), raising the possibility of muscle wasting and corresponding physical impairment following critical illness in children. Transient physical impairments, such as motor delays or lowered ability to perform daily activities, may not be alarming if children can eventually catch up to their peers. A prolonged impairment, however, would place considerable burden on the patient and family (30).

Quantifying physical and mental deficits in adult critical illness survivors has posed methodological difficulties for investigators in the past (31, 32). Recent studies have offered a variety of assessments of cognitive dysfunction complementing health-related quality of life (HRQOL) questionnaires (13, 15). However, the best assessment of physical disability in the same population remains unclear (33). This scoping review sets out to assess the potential tools available for quantification of PICU survivor functional and physical disability.

METHODS

The process of a scoping review recommended by Armstrong et al (34) was used. A search was performed to identify all studies on functional outcomes and tools used in children admitted to the PICU. PubMed, EMBASE, and CINAHL databases were reviewed from the earliest available date until January 2015 using a combination of MeSH terms and key words: “functional outcomes,” “functional status,” “critical illness,” and “intensive care.” Results were filtered for human studies and English language. Studies pertaining to premature infants and primarily adult populations (> 18 yr) were excluded. Full articles were retrieved, and articles not meeting our definition of functional status (e.g., endocrine and cardiac function) were excluded. Reference lists were searched for any other articles, and all articles that described the functional status of critically ill children (but not necessarily as the primary aim of the study) were included. Two authors (C.O. and J.H.L.) reviewed all short-listed titles and abstracts for inclusion in this review. Data extraction and synthesis using the final list of studies were then performed. Because of heterogeneity of the studies, no statistical synthesis was conducted, and a narrative approach was used instead to interpret the literature.

Included studies were reviewed for the following characteristics: functional outcome tool used, PICU population type, rates and type of functional impairment, time of assessment, and risk factors for functional impairment. Signs of possible physical impairment were highlighted wherever possible. Although other functional impairments do exist, in particular neuropsychologic ones, we did not describe them in detail as it was not the intention of this review.

RESULTS

A total of 297 titles were screened; of which, 39 full articles and reference lists were reviewed (**Supplemental Fig. 1**, Supplementary Digital Content 1, <http://links.lww.com/PCC/A238>; legend: selection of studies.). Twenty-five articles were finally included in our review. In the following sections, we describe the tools used and report the prevalence and risk factors for functional impairment in the PICU.

Types of Measures

Three global measures and eight multidimensional measures have been used to assess functional outcomes in the PICU population (**Table 1**) (5, 35–58), and their aims and limitations are discussed below.

Clinician-Derived Global Measures. The most commonly used tool was the pediatric overall performance category (POPC), a six-point score adapted from the adult traumatic brain injury Glasgow Outcome Scale (59). POPC can be used together with the pediatric cerebral performance category (PCPC) scale to identify both neurologic deficits and impairment in overall function (5, 37, 40, 42, 43). When used together, the difference in the POPC and PCPC scores can reflect the presence of physical impairment although not conclusively. Another similar global assessment tool is the six-point modified Glasgow Outcome Score (MGOS). However, MGOS has not been as widely used as the POPC, and its validity in the PICU population requires further study. The Royal Alexandra Hospital for Children Measure of Function (RAHC MOF) requires clinicians to score a child on a 0–100 scale with the aid of descriptions on various functional skills (49, 50).

Overall, these abbreviated scales are easy to administer, allowing collection of large population data to study trends. However, they are subjective, leading to larger interobserver variation, and assessment requires the ability to identify age-appropriate developmental milestones (59, 60). Despite consideration of various aspects of function, these measures provide a single summary score, which fails to reveal the most affected functional domains.

Multidimensional Measures. **HRQOL.** HRQOL tools were used to measure various aspects of physical and psychosocial functional outcomes and behavior in pediatric critical care survivors (38, 51–57). Although HRQOL and functional ability are not identical, they have overlapping constructs and are thus often used interchangeably (61). The assumption is that the burden of illness can manifest in behavioral changes, thus affecting functional status (62). HRQOL then captures how a child's health and functional status affects quality of life (61, 63).

Multidimensional HRQOL tools used in the PICU population include the Health Utilities Indexes (HUI) 1, 2 and 3, the Pediatric Quality of Life Inventory version 4.0 (PedsQL), the Stein-Jessup Functional Status II (Revised), and the Child Health Questionnaire (CHQ) (38, 51–57). Multidimensional HRQOL tools are more detailed than the RAHC MOF, differentiating between components of physical, mental, social, and emotional health (63, 64). Cumulative scores can compare a child’s function longitudinally or among established age-matched norms. In HRQOL measures, physical function components include motor function, ambulation or physical activity, pain, and self-care or role function (65–69) (Table 2).

Adaptive behavior. Appropriate growth and development is crucial in children, often assessed through tests of age-appropriate skills and behavior (70, 71). In children with disabilities, adaptive function (i.e., how appropriately a child behaves in daily life) may be more relevant than isolated developmental impairments (72, 73). The Vineland Adaptive Behavior Scale 2 (VABS-2) (43) is administered and scored by a psychologist or graduate-level trained professional (74). Similar to HRQOL questionnaires, VABS-2 differentiates between various components of physical (motor and self-care) and psychosocial (social and communication) functional domains (74). Unfortunately, the need for specific trained personnel and lengthy administration time inhibits scalability.

To overcome this, the National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network (CPCCRN) designed the Functional Status Score (FSS) (58, 60). FSS tasks abilities on a five-point scale across six domains of function, correlating well with a

validated adaptive behavior assessment tool (60), as well as POPC but with more precision (75).

The various measures covered 11 different but related components of function, not specific to the type of measure (HRQOL or adaptive behavior). No single tool encompassed all components, and no two tools measured the exact same constructs, each varied in their purpose and focus on the type of function. Thus, these measures are not interchangeable but can be used to complement one another to cover a variety of physical and psychosocial components, depending on the information researchers intend to capture.

Functional Outcomes in PICU Survivors

Prevalence. Functional impairment has been extensively described in children post critical illness (Table 3) (5, 35–58). Of particular importance is the rate of acquired functional impairment from critical illness as opposed to preexisting disease (76, 77). Acquired functional impairment in a general PICU population ranged from 10% to 36% at discharge, to 26% at 6 months, and 10% to 13% when followed up at more than 2 years (5, 37, 39, 41, 44, 46, 47, 50). A longitudinal study demonstrated that some impairment resolves with time as acquired impairment dropped from 26% at 6 months to 19% at 2 years after PICU admission (50).

Functional impairment rates differed across measures. Within the same patient population, absolute impairment was lower using multidimensional measures compared with global measures (43, 47). The reduced precision of global measures versus multidimensional measures (75) may result in overestimation of impairment. Another possible explanation is

TABLE 2. Domains Covered by Multidimensional Measures

Domain	Physical						Psychosocial				
	Role/ Self Care	Physical Activity/ Ambulation	Sensory	Pain	Motor	Respiratory	Emotional	Social	School	Cognitive	Communication
Child Health Questionnaire	✓	✓	✓	✓			✓	✓	✓		
Functional Status Scale	✓		✓		✓	✓	✓			✓	✓
Functional Status II (Revised)	✓	✓					✓	✓	✓		✓
Health Utilities Index 1	✓	✓	✓	✓			✓	✓	✓		
Health Utilities Index 2	✓	✓	✓	✓			✓			✓	
Health Utilities Index 3		✓	✓	✓			✓			✓	
Pediatric Quality of Life Inventory	✓	✓	✓	✓	✓		✓	✓	✓		
Vineland Adaptive Behavior Scales 2	✓				✓			✓			✓

TABLE 3. Functional Outcomes in Pediatric Survivors of Critical Illness

Study Reference	Population Characteristics	Measures Used	Follow-Up	Absolute Functional Disability Rates	Acquired Functional Disability Rates	Risk Factors for Acquired Functional Impairment
Pollack et al (35)	<i>n</i> = 24 Long stay, > 13 d; age: median, 13 mo	4 categories: functionally independent, functionally dependent, severely mentally disabled, or death	1 yr post ICU discharge	46%	25% overall	None identified
Fiser et al (5)	<i>n</i> = 10,598 Multicenter general PICU; age: mean, 53.8–86.9 mo across centers	POPC, PCPC	ICU discharge	68%	24% overall (14% cognitive; ≥ 10% physical)	Longer ICU stay Higher PRISM scores
van der Heide et al (36)	Long stay (57 ± 52 d), <i>n</i> = 19 vs control (12 ± 11 d), <i>n</i> = 15; age: mean, 10.7 ± 5.4 yr vs 7.3 ± 4.7 yr	POPC	Mean, 4.7 ± 1.7 yr from admission	58% in long stay, 47% control	Long stay: 1 (8%); control: 0	No significant difference in overall outcome between groups
de Mos et al (37)	<i>n</i> = 23 (not all assessed) In PICU cardiac arrest; age: median, 13 mo (range, 1 d to 17.7 yr)	POPC, PCPC	ICU discharge; 1 yr post discharge	Discharge: 100% Follow-up: 67%	Discharge: 36% overall (29% cognitive; ≥ 7% physical)	Increasing cardiac arrest duration
Keenan et al (38)	Inflicted vs noninflicted traumatic brain injury; age: median, 1.5 yr (IQR, 1.3–2 yr)	POPC, FSII(R)	1 yr post discharge	POPC: 54% overall POPC and FSII(R) lower in inflicted than noninflicted traumatic brain injury	Not stated	Baseline function not assessed
Alievi et al (39)	<i>n</i> = 443 General; age: median, 12 mo (4–45 mo)	POPC, PCPC	ICU discharge	85%	36% overall (25% cognitive; ≥ 11% physical)	Higher PIM score Longer ICU stay
Knoester et al (40)	<i>n</i> = 186 Previously healthy children; age: median, 1.4 yr (range, 0.1–17.3)	POPC, PCPC	ICU discharge, 3 mo post ICU discharge	Discharge: 99% Follow-up: 69%	Discharge: 91% overall (73% cognitive; ≥ 18% physical) Follow-up: 50% overall (21% cognitive; ≥ 29% physical)	Not stated
Mestrovic et al (41)	<i>n</i> = 493 General; age: median, 36.5 mo	POPC	ICU discharge	58%	25% overall	Higher PIM scores Previously well or nonneurologic chronic disease

(Continued)

TABLE 3. (Continued). Functional Outcomes in Pediatric Survivors of Critical Illness

Study Reference	Population Characteristics	Measures Used	Follow-Up	Absolute Functional Disability Rates	Acquired Functional Disability Rates	Risk Factors for Acquired Functional Impairment
Typo et al (42)	<i>n</i> = 21,465 Multicenter; age: range, 1 mo to 18 yr	POPC, PCPC	ICU discharge	21%	Not stated	Chronic diseases (noncongenital heart disease, neurologic, immune, and oncologic disease) Day 1 number and type of multiple organ dysfunction (hematologic, neurologic, and hepatic)
Ebrahim et al (43)	<i>n</i> = 65 Urgent admissions; age: median, 52 mo (range, 1–211)	POPC, PCPC, VABS-2, PedsQL 4.0	1 mo post ICU admission	POPC: 37% VABS-2: 28% PedsQL: poor mean HRQOL score	Not stated	Not stated
Farris et al (44)	<i>n</i> = 384 Multicenter, international survivors of severe sepsis; age: range, 0–17 yr	POPC	28 d after ICU admission	52%	34% overall	Intra-abdominal or CNS infection, trauma, cardiopulmonary resuscitation, and history of malignancy or immune-compromised Ethnicity (Hispanic) Higher PRISM score
Bone et al (45)	<i>n</i> = 29,352 Multicenter; age: range, 1 mo to 18 yr	POPC, PCPC	Baseline, ICU discharge	59%	10% overall (3% cognitive; ≥ 7% physical)	Unscheduled admission Higher PIM2 score Longer ICU stay (especially > 2.5 d) Invasive mechanical ventilation, cardiopulmonary resuscitation, renal replacement therapy, and extracorporeal membrane oxygenation
Butt et al (46)	<i>n</i> = 775 General; age: 28% < 1 mo, 37% 1 mo to 2 yr, and 35% > 2 yr	MGOS	30–36 mo post ICU discharge	25%	10% overall (in children > 1 mo)	Not stated
Taylor et al (47)	<i>n</i> = 626 General; age: median, 19.3 m (range, 0–29.3 yr)	MGOS, HUI1	Median, 3.5 yr (range, 2.3–6 yr) post ICU discharge	MGOS: 30% HUI1: 16%	13% overall	Not stated

(Continued)

TABLE 3. (Continued). Functional Outcomes in Pediatric Survivors of Critical Illness

Study Reference	Population Characteristics	Measures Used	Follow-Up	Absolute Functional Disability Rates	Acquired Functional Disability Rates	Risk Factors for Acquired Functional Impairment
Namachivayam et al (48)	Long stayers ≥ 28 d; age: median, 4.2 mo (IQR, 0.38–41.5 mo)	MGOS	Median, 4 yr (IQR, 1.4–7.6 yr) post ICU discharge	68% overall (of $n = 96$)	33% overall (of $n = 72$)	Not stated
Morrison et al (49)	$n = 405$ General; age: median, 2.3 yr	RAHC MOF	3–24 mo post ICU discharge	37%	Not available	Preadmission HRQOL not studied
Polic et al (50)	$n = 200$ General; age: median, 15.5 yr (range, 10–18 yr)	RAHC MOF	Preadmission, 6 mo, 24 mo post ICU admission	6 mo: 37% 24 mo: 31%	6 mo: 26% overall 24 mo: 19% overall	Higher PIM 2 score Preexisting neurodevelopment disability
Ambuehl et al (51)	$n = 484$ General; age: median, 11.3 mo (IQR, 0.5–5.5 yr)	HUI1	12 mo, 24 mo post ICU discharge	12 mo: 20% 24 mo: 23%	Not available	Preadmission HRQOL not assessed
Gemke et al (52)	$n = 226$ General; age: mean, 55 mo	HUI2	1 yr post ICU discharge	69% overall (physical: sensation 22%; mobility 50%; self-care 40%; pain 20%; psychosocial: emotion 40%; cognition 40%)	27% overall (physical: sensation 12%; mobility 11%; self-care 12%; pain 11%; psychosocial: emotion 22%; cognition 13%)	Not stated
Jones et al (53)	$n = 1,455$ Multicenter PICU; age: median, 4.7 yr (IQR, 1.7–10.1 yr)	HUI2	6 mo post ICU admission	73% overall (Physical: sensation 43%; pain 35%; mobility 31%; self-care 33%; psychosocial: cognition 30%; emotion 33%)	Not available	Preadmission HRQOL not studied
Cunha et al (54)	$n = 210$ Multicenter general PICUs; age: range, ≥ 6 yr	HUI3	Preadmission, 6 mo post ICU admission	Not stated	41% overall	Trauma Normal baseline pain and emotion scores
Conlon et al (55)	$n = 70$ Long stayers ≥ 28 d; age: median, 39 d (IQR, 2–234 d)	PedsQL 4.0	2–11 yr post ICU discharge	43% (physical: 31%; psychosocial: emotional 37%; social 37%; school 45%)	Not available	Preadmission HRQOL not assessed

(Continued)

TABLE 3. (Continued). Functional Outcomes in Pediatric Survivors of Critical Illness

Study Reference	Population Characteristics	Measures Used	Follow-Up	Absolute Functional Disability Rates	Acquired Functional Disability Rates	Risk Factors for Acquired Functional Impairment
Colville et al (56)	<i>n</i> = 72 Multicenter; age: median, 11 yr (range, 7–17 yr)	PedsQL 4.0	3 mo, 12 mo post ICU discharge	Physical and school functioning significantly below norms at 3 mo. School function normalized and physical function improved but remained impaired at 12 mo	Not available	Preadmission HRQOL not assessed
Buysse et al (57)	<i>n</i> = 47 Meningococcal septic shock; age: median, 3.7 yr (range, 0.1–16.1 yr)	Child Health Questionnaire	Median, 14 mo (range, 10–28 mo) post ICU discharge	Significantly lower physical abilities and health compared with norm values	Not available	Preadmission HRQOL not assessed
Pollack et al (58)	<i>n</i> = 4,798 Multicenter, general PICU; age: median, 3.7 yr (IQR, 0.8–10.9 yr)	Functional Status Scale	Hospital discharge	33%	18% overall (physical: feeding 8%; motor 7%; respiratory 4%; sensory 2%; Psychosocial: communication 3%; mental 3%)	Younger age (< 1 yr) Type of operation (top 3: general, cardiac, and neurosurgery) System of primary dysfunction (top 3: neurologic, acquired cardiovascular, and cancer)

IQR = interquartile range, POPC = pediatric overall performance category, PCPC = pediatric cerebral performance category, FSII(R) = Stein-Jessup Functional Status II (Revised), VABS = Vineland Adaptive Behavior Scale, PedsQL = Pediatric Quality of Life Inventory, MGOS = modified Glasgow Outcome Scale, HUI = Health Utility Index, RAHC MOF = Royal Alexandra Hospital for Children Measure of Function, HRQOL = health-related quality of life, PRISM = Pediatric Risk of Mortality, PIM = Pediatric Index of Mortality.

that this is a reflection of differences in subdomain coverage between tools (47).

Physical Impairment. A comparison between POPC and PCPC scores indicates that at least 19–70% of acquired impairment was physical (5, 37, 39, 40, 45). These included pulmonary issues and scarring (because of operations and meningococcal disease) (40), but it was unclear from this study whether other aspects of physical function (e.g., self-care or mobility) were affected.

Distinction between physical and psychosocial impairments was shown by multidimensional tools. One study using the HUI2 found acquired emotional impairments to be most common (22%), followed by cognitive impairments (13%) (52). Rates of physical impairment were lower, with 11–12% of the population having impairments in mobility, self-care, pain, and sensation. However, emotional impairments were mostly

mild with the most severe impairment being in the domain of self-care (52). In a larger multicenter study, rates of acquired physical impairment at hospital discharge were more prevalent than psychosocial ones (feeding 8% and motor 7% vs communication 3% and mental 3%) (58). Similar to the previous study, the most severe impairments were also seen in the physical domains, specifically respiratory and motor functions.

Factors Associated With Acquired Functional Disability

Several risk factors for acquired functional impairment have been proposed, but there are conflicting data. Preexisting neurodevelopmental disease was a risk factor in one study (50), but this was contradicted in another study (41). In the first study, patients were at relatively good baseline function and neurologic deficits were likely mild (50), whereas in the second

study, majority of the children had severely poor function prior to admission (41). This suggests that critical illness can be debilitating for children who were in good premorbid functional health and is a direct effect of the critical illness instead of exacerbation of an underlying disease state. Indeed, in a group of previously healthy critically ill children, the majority (91%) suffered functional deterioration at discharge as measured by the POPC (40). Children with preexisting functional impairment are not necessarily spared, but perhaps the tool used (POPC) was unable to capture changes in function because of a ceiling effect (41).

Nonneurologic chronic diseases were proposed as risk factors for functional impairment in a large multicenter study ($n = 21,465$) (42). Yet, the difference was not clinically significant, and authors attributed functional impairment to an increased risk of multiple organ dysfunction instead, in keeping with three other studies (44, 45, 58). All types of organ dysfunction (cardiovascular, hematologic, hepatic, neurologic, renal, and respiratory) were associated with acquired functional impairment (42, 44, 45).

Age may also be important—one study showed significantly higher impairment rates measured by FSS in those below 1 year old than those above 1 year old (7% vs 4%) (58). Greater illness severity as measured by the Pediatric Index of Mortality and Pediatric Risk of Mortality scores and longer PICU stay were also associated with acquired functional impairment (5, 39, 41, 44, 45, 50).

Only one study explored factors affecting recovery from acquired functional impairment (50) and found that children with chronic diseases were more likely to have persistent functional impairments 24 months after PICU admission.

DISCUSSION

We examined 11 unique but overlapping tools for the assessment of functional outcomes in pediatric critical care. Using these tools, 10–36% of children can experience functional impairment as a result of critical illness, which persists in 10–13% of survivors after more than 2 years (46, 47), indicating prolonged disability. Risk factors include younger age, greater illness severity, and organ dysfunction, two of which echo those found in adult ICU survivors with functional impairment (12, 18, 21). However, several gaps in PICU survivorship research currently limit the generalizability of our findings.

First, different interpretations exist in the definition of functional outcomes, a difficulty that has been reported in pediatric chronic illness research (61, 63, 78). Technically, functional status reflects one's actual ability to perform tasks, whereas HRQOL indicates one's perception of their functional ability (61, 63, 78). However, the HRQOL tools used have also included questions about a child's behavior and ability to perform certain everyday tasks, making it difficult to differentiate between the two (78). A necessary step in PICU survivor assessment is defining functional impairment unique to the pediatric critical illness population. Attention to development should be emphasized as hospitalization has been shown to affect behavior in children, particularly in those 2–5 years olds

(79, 80). Recent expanded definitions of “function” in children look beyond that of biologic, psychological, and social aspects to include contextual factors, such as caregiver assistance and environmental support because of their influence on child functioning (81, 82). Tools accounting for caregiver and environmental factors, and at different stages of growth and development (perhaps via adaptive behavior), would, thus, provide a more comprehensive view of outcome throughout critical illness and recovery.

Follow-up functional assessment varied from ICU discharge to 11 years after, adding to the difficulty of identifying true rates of acquired functional impairment (41, 55). **Supplemental Figure 2** (Supplementary Digital Content 2, <http://links.lww.com/PCC/A239>; legend: hypothesized trajectory of functional impairment in children with critical illness) demonstrates a possible trajectory of function in children during and after critical illness. Moving forward, serial measurements of functional status at baseline (of preadmission function), discharge, and after discharge (possibly up to 2 yr) would help identify impairment as a result of critical illness and to determine impairment trajectory (77). This would also enable early identification of functional impairment and timely intervention in prevention of developmental delay. Tools also need to capture heterogeneity of function among healthy and children with chronic disease and be mindful of potential floor and ceiling effects (31). Children with chronic diseases may require special attention as they seem to be at greater risk of prolonged functional impairment (50). Awareness of the difference between proxy and self-reported function and HRQOL at various ages is also important; new challenges related to higher executive function in adolescence can impact HRQOL (83). Achieving consensus on the best tool(s) to use may best be achieved by pooling of data (84). The FSS, designed as a standardized outcome measurement tool for the CPCCRN, may be useful in large studies and deserves further study (60). A recent review of HRQOL measures in critically ill children identified the most appropriate questionnaires (PedsQL 4.0, KIDSCREEN-27, CHQ parent form-28, and KINDL) based on factors, such as sensitivity to change, response burden, and interpretability of scores (84), a point of consideration for future PICU research.

The lack of distinction between types of functional disability remains a major limitation, partially because of the more common use of global functional measures. Global measures are useful for screening of functional impairment and large population outcome studies. However, multidimensional tools would enable a deeper analysis of the problem, guiding intervention and monitoring therapy efficacy. From the limited evidence available, physical impairments seemed more significant and persistent than psychosocial ones (52, 58), and risk factors are similar in children and adults (12, 18). Long-term physical impairments have been observed in survivors of burns and acute lymphoblastic leukemia where muscle wasting is common (85, 86). Physical limitations, including diminished strength, running speed, and agility, could affect a child's self-esteem and social function (87). This interaction demonstrates the extended effect of physical impairments on psychosocial

health. Studies are needed to determine the true prevalence of physical impairments in PICU survivors and effects on long-term developmental abilities and social functioning.

Our review was limited in that we explored physical outcomes. Psychosocial impairments are by no means less detrimental in critically ill children; psychologic and intellectual impacts have been widely studied in various groups of children admitted to the PICU (88–90). Although clearly important, it was not the intention of this article to focus on the psychosocial impairments, and we refer readers to other excellent reviews on this topic (91, 92). Furthermore, as discussed, the contribution of physical impairment to psychosocial impairment in this pediatric population remains unclear. In addition, the heterogeneity of these studies prevented a meaningful statistical synthesis of the results. Given such heterogeneity, an integrative approach was undertaken to allow a more comprehensive summary of the evidence. Nevertheless, to the best of our knowledge, this is the first in-depth review describing the tools used to measure functional outcomes in pediatric survivors of critical care, in particular physical impairments. We demonstrate the need for standardization and consensus in PICU outcome studies and integration of functional outcome measures.

CONCLUSIONS

Functional impairment may be persistent in pediatric survivors of critical illness. The evidence is scarce in this population especially in regard to the type and extent of functional impairment. Studies on general impairment using global measures are substantial, and domain-specific outcome research seems to be a necessary next step. Future directions include determining the best tools while accounting for age-appropriate development and the spectrum of chronically ill and healthy children, identifying risk factors and mechanisms for the functional impairment, and subsequently interventions to prevent prolonged functional impairment in critically ill children.

REFERENCES

- Pollack MM, Alexander SR, Clarke N, et al: Improved outcomes from tertiary center pediatric intensive care: A statewide comparison of tertiary and nontertiary care facilities. *Crit Care Med* 1991; 19:150–159
- Namachivayam P, Shann F, Shekerdemian L, et al: Three decades of pediatric intensive care: Who was admitted, what happened in intensive care, and what happened afterward. *Pediatr Crit Care Med* 2010; 11:549–555
- Randolph AG, Gonzales CA, Cortellini L, et al: Growth of pediatric intensive care units in the United States from 1995 to 2001. *J Pediatr* 2004; 144:792–798
- Marcin JP, Slonim AD, Pollack MM, et al: Long-stay patients in the pediatric intensive care unit. *Crit Care Med* 2001; 29:652–657
- Fiser DH, Tilford JM, Roberson PK: Relationship of illness severity and length of stay to functional outcomes in the pediatric intensive care unit: A multi-institutional study. *Crit Care Med* 2000; 28:1173–1179
- Watson RS, Hartman ME: Epidemiology of critical illness. In: *Pediatric Critical Care Medicine: Basic Science and Clinical Evidence*. Wheeler DS, Wong HR, Shanley TP (Eds). London, Springer, 2007
- Kneyber MC: Prognostic scoring in critically ill children: What to predict? *CMAJ* 2010; 182:1155–1156
- Taylor A, Butt W: The evaluation of outcome following paediatric intensive care: The major issues identified. *Clin Intensive Care* 2000; 11:239–244
- Lansky LL, List MA, Lansky SB, et al: Toward the development of a play performance scale for children (PPSC). *Cancer* 1985; 56:1837–1840
- Ditesheim JA, Templeton JM Jr: Short-term v long-term quality of life in children following repair of high imperforate anus. *J Pediatr Surg* 1987; 22:581–587
- Shapiro S, McCormick MC, Starfield BH, et al: Changes in infant morbidity associated with decreases in neonatal mortality. *Pediatrics* 1983; 72:408–415
- Herridge MS, Cheung AM, Tansey CM, et al: Canadian Critical Care Trials Group: One-year outcomes in survivors of the acute respiratory distress syndrome. *N Engl J Med* 2003; 348:683–693
- Hopkins RO, Weaver LK, Collingridge D, et al: Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2005; 171:340–347
- Rothenhäusler HB, Ehrentraut S, Stoll C, et al: The relationship between cognitive performance and employment and health status in long-term survivors of the acute respiratory distress syndrome: Results of an exploratory study. *Gen Hosp Psychiatry* 2001; 23:90–96
- Pandharipande PP, Girard TD, Jackson JC, et al: BRAIN-ICU Study Investigators: Long-term cognitive impairment after critical illness. *N Engl J Med* 2013; 369:1306–1316
- van der Schaaf M, Dettling DS, Beelen A, et al: Poor functional status immediately after discharge from an intensive care unit. *Disabil Rehabil* 2008; 30:1812–1818
- Bienvenu OJ, Colantuoni E, Mendez-Tellez PA, et al: Depressive symptoms and impaired physical function after acute lung injury: A 2-year longitudinal study. *Am J Respir Crit Care Med* 2012; 185:517–524
- Iwashyna TJ, Ely EW, Smith DM, et al: Long-term cognitive impairment and functional disability among survivors of severe sepsis. *JAMA* 2010; 304:1787–1794
- Herridge MS, Tansey CM, Matté A, et al: Canadian Critical Care Trials Group: Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med* 2011; 364:1293–1304
- Puthucherry ZA, Rawal J, McPhail M, et al: Acute skeletal muscle wasting in critical illness. *JAMA* 2013; 310:1591–1600
- De Jonghe B, Sharshar T, Lefaucheur JP, et al: Groupe de Réflexion et d'Etude des Neuromyopathies en Réanimation: Paresis acquired in the intensive care unit: A prospective multicenter study. *JAMA* 2002; 288:2859–2867
- Needham DM, Davidson J, Cohen H, et al: Improving long-term outcomes after discharge from intensive care unit: Report from a stakeholders' conference. *Crit Care Med* 2012; 40:502–509
- de Letter MA, Schmitz PI, Visser LH, et al: Risk factors for the development of polyneuropathy and myopathy in critically ill patients. *Crit Care Med* 2001; 29:2281–2286
- Hermans G, Wilmer A, Meersseman W, et al: Impact of intensive insulin therapy on neuromuscular complications and ventilator dependency in the medical intensive care unit. *Am J Respir Crit Care Med* 2007; 175:480–489
- Watson RS, Carcillo JA, Linde-Zwirble WT, et al: The epidemiology of severe sepsis in children in the United States. *Am J Respir Crit Care Med* 2003; 167:695–701
- Schlapbach LJ, Straney L, Alexander J, et al: ANZICS Paediatric Study Group: Mortality related to invasive infections, sepsis, and septic shock in critically ill children in Australia and New Zealand, 2002–13: A multicentre retrospective cohort study. *Lancet Infect Dis* 2015; 15:46–54
- Faustino EV, Apkon M: Persistent hyperglycemia in critically ill children. *J Pediatr* 2005; 146:30–34
- Zimmerman JJ, Akhtar SR, Caldwell E, et al: Incidence and outcomes of pediatric acute lung injury. *Pediatrics* 2009; 124:87–95
- Giuliano JS Jr, Faustino EV, Li S, et al: Northeast Pediatric Critical Care Research Consortium (NEPCCRC): Corticosteroid therapy in critically ill pediatric asthmatic patients. *Pediatr Crit Care Med* 2013; 14:467–470

30. Eisenhower AS, Baker BL, Blacher J: Children's delayed development and behavior problems: Impact on mothers' perceived physical health across early childhood. *Soc Sci Med* 2009; 68:89–99
31. Parry SM, Granger CL, Berney S, et al: Assessment of impairment and activity limitations in the critically ill: A systematic review of measurement instruments and their clinimetric properties. *Intensive Care Med* 2015; 41:744–762
32. Puthuchery Z, Harridge S, Hart N: Skeletal muscle dysfunction in critical care: Wasting, weakness, and rehabilitation strategies. *Crit Care Med* 2010; 38:S676–S682
33. Denehy L, de Morton NA, Skinner EH, et al: A physical function test for use in the intensive care unit: Validity, responsiveness, and predictive utility of the physical function ICU test (scored). *Phys Ther* 2013; 93:1636–1645
34. Armstrong R, Hall BJ, Doyle J, et al: Cochrane Update. 'Scoping the scope' of a cochrane review. *J Public Health (Oxf)* 2011; 33:147–150
35. Pollack MM, Wilkinson JD, Glass NL: Long-stay pediatric intensive care unit patients: Outcome and resource utilization. *Pediatrics* 1987; 80:855–860
36. van der Heide P, Hassing MB, Gemke RJ: Characteristics and outcome of long-stay patients in a paediatric intensive care unit: A case-control study. *Acta Paediatr* 2004; 93:1070–1074
37. de Mos N, van Litsenburg RR, McCrindle B, et al: Pediatric in-intensive-care-unit cardiac arrest: Incidence, survival, and predictive factors. *Crit Care Med* 2006; 34:1209–1215
38. Keenan HT, Runyan DK, Nocera M: Child outcomes and family characteristics 1 year after severe inflicted or noninflicted traumatic brain injury. *Pediatrics* 2006; 117:317–324
39. Alievi PT, Carvalho PR, Trotta EA, et al: The impact of admission to a pediatric intensive care unit assessed by means of global and cognitive performance scales. *J Pediatr (Rio J)* 2007; 83:505–511
40. Knoester H, Bronner MB, Bos AP, et al: Quality of life in children three and nine months after discharge from a paediatric intensive care unit: A prospective cohort study. *Health Qual Life Outcomes* 2008; 6:21
41. Mestrovic J, Polic B, Mestrovic M, et al: Functional outcome of children treated in intensive care unit. *J Pediatr (Rio J)* 2008; 84:232–236
42. Typpo KV, Petersen NJ, Hallman DM, et al: Day 1 multiple organ dysfunction syndrome is associated with poor functional outcome and mortality in the pediatric intensive care unit. *Pediatr Crit Care Med* 2009; 10:562–570
43. Ebrahim S, Singh S, Hutchison JS, et al: Adaptive behavior, functional outcomes, and quality of life outcomes of children requiring urgent ICU admission. *Pediatr Crit Care Med* 2013; 14:10–18
44. Farris RW, Weiss NS, Zimmerman JJ: Functional outcomes in pediatric severe sepsis: Further analysis of the researching severe sepsis and organ dysfunction in children: A global perspective trial. *Pediatr Crit Care Med* 2013; 14:835–842
45. Bone MF, Feinglass JM, Goodman DM: Risk factors for acquiring functional and cognitive disabilities during admission to a PICU*. *Pediatr Crit Care Med* 2014; 15:640–648
46. Butt W, Shann F, Tibballs J, et al: Long-term outcome of children after intensive care. *Crit Care Med* 1990; 18:961–965
47. Taylor A, Butt W, Ciardulli M: The functional outcome and quality of life of children after admission to an intensive care unit. *Intensive Care Med* 2003; 29:795–800
48. Namachivayam P, Taylor A, Montague T, et al: Long-stay children in intensive care: Long-term functional outcome and quality of life from a 20-yr institutional study. *Pediatr Crit Care Med* 2012; 13:520–528
49. Morrison AL, Gillis J, O'Connell AJ, et al: Quality of life of survivors of pediatric intensive care. *Pediatr Crit Care Med* 2002; 3:1–5
50. Polic B, Mestrovic J, Markic J, et al: Long-term quality of life of patients treated in paediatric intensive care unit. *Eur J Pediatr* 2013; 172:85–90
51. Ambuehl J, Karrer A, Meer A, et al: Quality of life of survivors of paediatric intensive care. *Swiss Med Wkly* 2007; 137:312–316
52. Gemke RJ, Bonsel GJ, van Vught AJ: Long-term survival and state of health after paediatric intensive care. *Arch Dis Child* 1995; 73:196–201
53. Jones S, Rantell K, Stevens K, et al; United Kingdom Pediatric Intensive Care Outcome Study Group: Outcome at 6 months after admission for pediatric intensive care: A report of a national study of pediatric intensive care units in the United Kingdom. *Pediatrics* 2006; 118:2101–2108
54. Cunha F, Mota T, Teixeira-Pinto A, et al: Factors associated with health-related quality of life changes in survivors to pediatric intensive care. *Pediatr Crit Care Med* 2013; 14:e8–e15
55. Conlon NP, Breatnach C, O'Hare BP, et al: Health-related quality of life after prolonged pediatric intensive care unit stay. *Pediatr Crit Care Med* 2009; 10:41–44
56. Colville GA, Pierce CM: Children's self-reported quality of life after intensive care treatment. *Pediatr Crit Care Med* 2013; 14:e85–e92
57. Buysse CM, Raat H, Hazelzet JA, et al: Surviving meningococcal septic shock: Health consequences and quality of life in children and their parents up to 2 years after pediatric intensive care unit discharge. *Crit Care Med* 2008; 36:596–602
58. Pollack MM, Holubkov R, Funai T, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network: Pediatric intensive care outcomes: Development of new morbidities during pediatric critical care. *Pediatr Crit Care Med* 2014; 15:821–827
59. Fiser DH: Assessing the outcome of pediatric intensive care. *J Pediatr* 1992; 121:68–74
60. Pollack MM, Holubkov R, Glass P, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network: Functional Status Scale: New pediatric outcome measure. *Pediatrics* 2009; 124:e18–e28
61. Drotar D: Validating measures of pediatric health status, functional status, and health-related quality of life: Key methodological challenges and strategies. *Ambul Pediatr* 2004; 4:358–364
62. Stein RE, Jessop DJ: Functional status II®. A measure of child health status. *Med Care* 1990; 28:1041–1055
63. Eiser C, Morse R: A review of measures of quality of life for children with chronic illness. *Arch Dis Child* 2001; 84:205–211
64. Msall ME: Measuring functional skills in preschool children at risk for neurodevelopmental disabilities. *Ment Retard Dev Disabil Res Rev* 2005; 11:263–273
65. Landgraf JM, Maunsell E, Speechley KN, et al: Canadian-French, German and UK versions of the Child Health Questionnaire: Methodology and preliminary item scaling results. *Qual Life Res* 1998; 7:433–445
66. Varni JW, Seid M, Rode CA: The PedsQL: Measurement model for the pediatric quality of life inventory. *Med Care* 1999; 37:126–139
67. Feeny D, Furlong W, Barr RD: Multiattribute approach to the assessment of health-related quality of life: Health Utilities Index. *Med Pediatr Oncol* 1998; Suppl 1:54–59
68. Boyle MH, Furlong W, Feeny D, et al: Reliability of the Health Utilities Index–Mark III used in the 1991 cycle 6 Canadian General Social Survey Health Questionnaire. *Qual Life Res* 1995; 4:249–257
69. Klassen AF, Landgraf JM, Lee SK, et al: Health related quality of life in 3 and 4 year old children and their parents: Preliminary findings about a new questionnaire. *Health Qual Life Outcomes* 2003; 1:81
70. Bayley N: Bayley Scales of Infant and Toddler Development – Third Edition. San Antonio, TX, Harcourt Assessment, 2006
71. Newborg J, Stock JR, Wnek L, et al: Battelle Developmental Inventory. Allen, TX, DLM Teaching Resources, 1984
72. Liss M, Harel B, Fein D, et al: Predictors and correlates of adaptive functioning in children with developmental disorders. *J Autism Dev Disord* 2001; 31:219–230
73. Ottenbacher KJ, Msall ME, Lyon N, et al: Measuring developmental and functional status in children with disabilities. *Dev Med Child Neurol* 1999; 41:186–194
74. Sparrow S, Cicchetti D, Balla D: Vineland Adaptive Behavior Scales – Second Edition. Circle Pines, MN, American Guidance Service, Inc., 2005
75. Pollack MM, Holubkov R, Funai T, et al: Relationship between the functional status scale and the pediatric overall performance category and pediatric cerebral performance category scales. *JAMA Pediatr* 2014; 168:671–676

76. Puthuchery ZA, Denehy L: Exercise interventions in critical illness survivors: Understanding inclusion and stratification criteria. *Am J Respir Crit Care Med* 2015; 191:1464–1467
77. Iwashyna TJ, Netzer G, Langa KM, et al: Spurious inferences about long-term outcomes: The case of severe sepsis and geriatric conditions. *Am J Respir Crit Care Med* 2012; 185:835–841
78. Eiser C, Morse R: Quality-of-life measures in chronic diseases of childhood. *Health Technol Assess* 2001; 5:1–157
79. Haslvm MN: Length of preschool hospitalization, multiple admissions and later educational attainment and behaviour. *Child Care Health Dev* 1988; 14:275–291
80. Shannon FT, Fergusson DM, Dimond ME: Early hospital admissions and subsequent behaviour problems in 6 year olds. *Arch Dis Child* 1984; 59:815–819
81. World Health Organization: International Classification of Functioning, Disability, and Health: Children & Youth Version: ICF-CY. Geneva, World Health Organization, 2007
82. Kostanjsek N: Use of the International Classification of Functioning, Disability and Health (ICF) as a conceptual framework and common language for disability statistics and health information systems. *BMC Public Health* 2011; 11(Suppl 4):S3
83. Eiser C: Children's quality of life measures. *Arch Dis Child* 1997; 77:350–354
84. Aspesberro F, Mangione-Smith R, Zimmerman JJ: Health-related quality of life following pediatric critical illness. *Intensive Care Med* 2015; 41:1235–1246
85. Sheridan RL, Hinson MI, Liang MH, et al: Long-term outcome of children surviving massive burns. *JAMA* 2000; 283:69–73
86. van Brussel M, Takken T, van der Net J, et al: Physical function and fitness in long-term survivors of childhood leukaemia. *Pediatr Rehabil* 2006; 9:267–274
87. Wright MJ, Halton JM, Martin RF, et al: Long-term gross motor performance following treatment for acute lymphoblastic leukemia. *Med Pediatr Oncol* 1998; 31:86–90
88. Rennick JE, Dougherty G, Chambers C, et al: Children's psychological and behavioral responses following pediatric intensive care unit hospitalization: The caring intensively study. *BMC Pediatr* 2014; 14:276
89. Rees G, Gledhill J, Garralda ME, et al: Psychiatric outcome following paediatric intensive care unit (PICU) admission: A cohort study. *Intensive Care Med* 2004; 30:1607–1614
90. Connolly D, McClowry S, Hayman L, et al: Posttraumatic stress disorder in children after cardiac surgery. *J Pediatr* 2004; 144:480–484
91. Rennick JE, Rashotte J: Psychological outcomes in children following pediatric intensive care unit hospitalization: A systematic review of the research. *J Child Health Care* 2009; 13:128–149
92. Knoester H, Grootenhuis MA, Bos AP: Outcome of paediatric intensive care survivors. *Eur J Pediatr* 2007; 166:1119–1128
93. Dossetor DR, Liddle JL, Mellis CM: Measuring health outcome in paediatrics: Development of the RAHC measure of function. *J Paediatr Child Health* 1996; 32:519–524
94. Torrance GW, Boyle MH, Horwood SP: Application of multi-attribute utility theory to measure social preferences for health states. *Oper Res* 1982; 30:1043–1069
95. Neumann PJ, Kuntz KM, Leon J, et al: Health utilities in Alzheimer's disease: A cross-sectional study of patients and caregivers. *Med Care* 1999; 37:27–32
96. Varni JW, Seid M, Kurtin PS: PedsQL 4.0: Reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Med Care* 2001; 39:800–812
97. Wake M, Hesketh K, Cameron F: The Child Health Questionnaire in children with diabetes: Cross-sectional survey of parent and adolescent-reported functional health status. *Diabet Med* 2000; 17:700–707
98. Waters EB, Salmon LA, Wake M, et al: The health and well-being of adolescents: A school-based population study of the self-report Child Health Questionnaire. *J Adolesc Health* 2001; 29:140–149
99. de Bildt A, Kraijer D, Sytema S, et al: The psychometric properties of the Vineland Adaptive Behavior Scales in children and adolescents with mental retardation. *J Autism Dev Disord* 2005; 35:53–62
100. Kanne SM, Gerber AJ, Quirnbach LM, et al: The role of adaptive behavior in autism spectrum disorders: Implications for functional outcome. *J Autism Dev Disord* 2011; 41:1007–1018