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REVIEW

Health-related quality of life outcome measures for children surviving critical care: a scoping review

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Abstract

Purpose Health-related quality of life (HRQL) has been identified as one of the core outcomes most important to assess following pediatric critical care, yet there are no data on the use of HRQL in pediatric critical care research. We aimed to determine the HRQL instruments most commonly used to assess children surviving critical care and describe study methodology, patient populations, and instrument characteristics to identify areas of deficiency and guide investigators conducting HRQL research.

Methods We queried PubMed, EMBASE, PsycINFO, Cumulative Index of Nursing and Allied Health Literature, and the Cochrane Registry for studies evaluating pediatric critical care survivors published 1970–2017. We used dual review for article selection and data extraction.

Results Of 60,349 citations, 66 articles met inclusion criteria. The majority of studies were observational (89.4%) and assessed HRQL at one post-discharge time-point (86.4%), and only 10.6% of studies included a baseline assessment. Time to the first follow-up assessment ranged from 1 month to 10 years post-hospitalization (median 3 years, IQR 0.5–6). For 26 prospective studies, the median follow-up time was 0.5 years [IQR 0.25–1]. Parent/guardian proxy-reporting was used in 83.3% of studies. Fifteen HRQL instruments were employed, with four used in >5% of articles: the Health Utility Index ($n=22$ articles), the Pediatric Quality of Life Inventory ($n=17$), the Child Health Questionnaire ($n=16$), and the 36-Item Short Form Survey ($n=9$).

Conclusion HRQL assessment in pediatric critical care research has been centered around four instruments, though existing literature is limited by minimal longitudinal follow-up and infrequent assessment of baseline HRQL.

Keywords Pediatric · Critical care outcomes · Patient reported outcome measures · Survivors · Health-related quality of life · Outcome assessment

Plain english summary

Many children who are hospitalized in an intensive care unit (ICU) have ongoing problems with their physical function, emotions, thinking, school performance, or relationships with family and friends after their discharge. The way that their heath affects these areas is called their health-related quality of life (HRQL). HRQL can be measured in children of all ages by asking them or their parents to fill out surveys with questions asking if they have problems in those areas. Many families and healthcare providers believe that HRQL is very important to measure after children have been in the ICU, but timing, approach, and the appropriate surveys to use remain unclear. In order to help make recommendations about how future studies should measure HRQL, we looked at all of the studies that have already been published about HRQL in children after ICU stays. We found that there have been only 66 studies published between 1970 and 2017, and

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that many different surveys have been used but that some of the surveys are probably better than others at measuring children's HRQL. Most of the studies only measured children's HRQL once after their ICU stay, and very few compared their HRQL after the ICU to how it was before the ICU. Based on these findings, we made recommendations that future studies should use the same set of surveys, measure HRQL multiple times after the ICU stay, and always try to compare HRQL to how it was before the hospitalization.

Introduction

Mortality rates among critically ill children have fallen consistently over the past several decades [1]. Cumulative morbidities facing pediatric intensive care unit (PICU) survivors, however, are increasingly recognized [2–4]. Sequelae can affect cognitive, social, physical, and emotional health and global health-related quality of life (HRQL) for survivors and their families, collectively termed Post-Intensive Care Syndrome-pediatrics (PICS-p) [3]. It is becoming increasingly evident that robust, longitudinal, and comprehensive follow-up is essential for evaluating the delivery and efficacy of pediatric critical care. Follow-up assessments must incorporate higher fidelity and more granular outcome measures beyond mortality, length-of-stay, or readmission rates [5]. There have been no recommendations, however, on which instruments or methodologic approaches future clinical trials and follow-up programs that aim to embrace the PICS-p framework should follow.

To improve our understanding of how post-discharge outcomes have been assessed in existing studies of pediatric critical illness, the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) network's POST-PICU Investigators (Online Resource 1) and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network (CPCCRN) collaborated to conduct a scoping review of pediatric critical care outcomes research. The scoping review identified the number of studies published, domains evaluated, and the study designs and instruments used in pediatric critical care medicine (PCCM) outcomes research. Outcomes assessed included overall health, emotional, physical, cognitive, health-related quality of life, social, and family domains [6]. This effort informed the development of a core outcome set (COS) for use in future research [7].

As part of the development of the COS, a Delphi process involving clinicians, researchers, families, and patient advocates identified HRQL as one of the core outcomes most important to assess following pediatric critical care [8]. There are no existing data, however, on what HRQL instruments are most commonly used in PCCM research or how they have been implemented. We thus conducted this subsequent review of the HRQL-specific instruments identified in the overall PCCM outcomes scoping review to provide additional details of the evaluation of HRQL following pediatric critical care. Our primary objectives were to (1) determine which HRQL measures have been used most frequently in PCCM outcomes research; (2) describe the study methodology and patient populations assessed in the published literature; and (3) identify areas of deficiency that might be addressed in future work to align investigators, clinicians, and families with the PICS-p framework. Our secondary objective was to describe the validation groups, subdomains, and practical considerations for usage of each identified instrument to provide a guide to investigators considering evaluation of HRQL among children surviving intensive care.

Materials and methods

For the overall PCCM outcomes scoping review, we identified studies evaluating outcomes of survivors or families after pediatric critical illness published between 1970 and 2017, inclusive [6]. Details of the protocol have been previously published [6]. We searched PubMed, EMBASE, PsycINFO, Cumulative Index of Nursing and Allied Health Literature, and the Cochrane Central Register of Controlled Trials Registry using search strategies that included a combination of keywords and controlled vocabulary for the concept of "pediatric" and "critical care/illness" combined with comprehensive terms for the domains of social, cognitive, emotional, physical, HRQL, and family functioning in alignment with the PICS-p framework (Online Resource 2) [3]. Reviewers were also encouraged to submit published articles for review and reconciliation with the formal inquiry. Grey literature was not queried. Articles were excluded if: (1) no post-discharge outcomes were assessed; (2) survival was the only outcome assessed; (3) only psychometric properties of an instrument were evaluated; (4) the outcome of a technical procedure/condition was evaluated without report of the relationship to ICU care; (5) the majority of the study sample was > 18 years old, preterm infants, neonates, or had not been definitively admitted to an ICU; (6) only one subject was included; or (7) the language was not English. The most recent search was conducted on 7/10/18.

Citations produced from the above search were imported into Covidence® (Veritas Health Innovation, Melbourne, Australia) and independently screened in a two-stage process. First, two reviewers screened each abstract and excluded ineligible manuscripts. Second, two reviewers screened each full-text manuscript to determine final eligibility. For both stages, discrepancies were resolved by a third reviewer.

For included articles, study characteristics and outcomes were independently extracted by two reviewers. Extracted data included: age, sex, and country of participants; study design (observational, interventional, qualitative, mixed-methods); study population (general PICU, acute respiratory failure, bone marrow transplant, cardiac arrest, congenital heart disease [CHD], renal failure, multiple organ dysfunction syndrome, oncology, sepsis, solid organ transplant, trauma, traumatic brain injury [TBI], other); number of patients eligible and enrolled; whether baseline data was collected; number and time range of follow-up evaluations; number of patients eligible and evaluated at each follow-up; outcome measures collected; and follow-up assessment method and data source. Extracted data were compared and consensus was achieved through discussion. When consensus could not be achieved, a member of the steering committee was consulted for final determination. Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Utah [9]. Outcome domains were identified based on the World Health Organization's International Classification of Functioning, Disability, and Health (ICF) framework for physical, emotional, cognitive, and HRQL outcomes [10].

For the current study of HRQL outcomes, the full text of all articles identified as assessing HRQL were reviewed by a single author (EYK) to confirm inclusion criteria, to verify the data extracted in the first round, and to extract additional information on the study population and follow-up methodology not collected in the overall scoping review process (years of data collection, prospective vs retrospective design, exact follow-up timepoints, whether follow-up evaluations occurred at specified times anchored to the admission or cross-sectionally, and more detailed population information). Categorical data were summarized as numbers and percentages, and continuous data were summarized as medians with the interquartile range.

For each of the identified HRQL instruments, a literature search to identify primary sources and subsequent validation studies was performed by at least two members of the POST-PICU HRQL subgroup (EYK or RJG, and one additional member) to extract psychometric properties of each instrument, with discrepancies resolved by a third member (EYK or RJG). Extracted instrument characteristics included module options, subdomains, target populations and ages, reporting sources (i.e., child and/or surrogate), number of items, approximate administration time, validation population (pediatric ICU, general pediatric, or adult populations), language availability, and cost.

Institutional Review Board approval was not required as the study did not include human subjects. Analyses were performed using SAS version 9.4 (Cary, NC) and Stata/SE version 14.2 (College Station, TX). The Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews (PRISMA-ScR) Checklist was followed (Online Resource 3).

Results

HRQL articles and study design

Seventy-three articles assessing HRQL were identified in the PCCM outcomes scoping review. Full-text review eliminated seven of these; five were determined to not evaluate HRQL, one only assessed families, and one evaluated only adult critical care survivors (Online Resource 4). This review thus included 66 articles (Online Resource 5). Studies excluded at the full-text stage are listed in Online Resource 6. Publication dates ranged from 1995 to 2017, with 82% published in the last 10 years of the study period (Fig. 1). These studies represented patients admitted to ICUs from 1984 to 2016, with enrollment periods ranging from 1 to 24 years long (median 4 years, interquartile range [IQR] 2–10).

Most studies were observational ($n=59$, 89.4%) while the remaining seven studies (10.6%) were interventional. Sixty two studies (93.9%) used quantitative analyses and four (6.1%) used mixed-methods analyses; no studies used only qualitative methods of analysis. Fourteen studies (21.2%) were multicenter, including five of the interventional studies. Patients were enrolled prospectively during their hospitalization in 40.9% ($n=27$) of studies, while in the remainder patients were first contacted and enrolled at the time of outcome assessment.

Among the cohorts prospectively enrolled during hospitalization, inpatient recruitment ranged from 21.4% to 100% of eligible patients (median 85.3%, IQR 61.9–98.8). After accounting for death or loss to follow-up, the final sample size of all studies ranged from 9 to 1455 patients with follow-up patient data (median 65 patients, IQR 31–140), representing 20.6–100% of eligible surviving patients (median 73.3%, IQR 63.0–88.9). For studies with multiple assessment points, attrition resulted in a median 19% (IQR 2.7–23.0) drop out of eligible surviving patients.

Patient populations assessed

General PICU populations were assessed in 28.8% of included studies ($n=19$) representing 69.9% of unique participants ($n=6631$), while the remainder of studies focused on a subgroup of patient diagnoses (Table 1). Subgroup evaluations most commonly focused on children who had sustained neurologic injury or carried cardiac diagnoses, with 15 articles each (22.7%). The single-most common diagnoses studied were traumatic brain injury (TBI) with 11 articles (16.7%) and 762 unique participants (8.0%) and

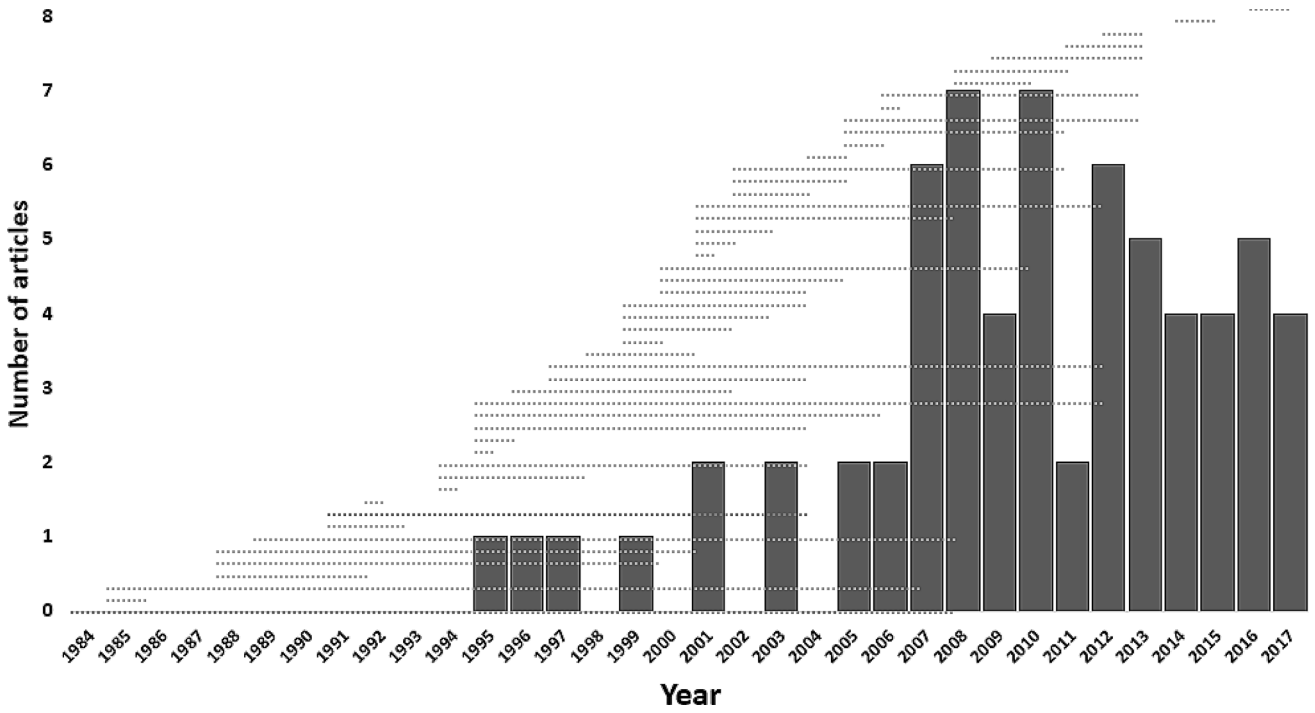

Fig. 1 Number of published articles evaluating HRQL outcomes 1995–2017. The PICU enrollment period for each included study is overlaid in grey dotted lines. Enrollment periods with multiple articles included: 1988–2011 ($n=6$ articles); 1998–2001 ($n=2$); 2000–2004 ($n=2$); 2000–2005 ($n=2$); 2002–2004 ($n=2$); 2008–2011 ($n=2$); 2012–2013 ($n=2$)

congenital heart disease with 7 articles (10.6%) and 1084 unique participants (11.4%).

The majority of studies enrolled patients across the typical age spectrum of pediatric ICUs from infants to teenagers at least 15 years old ($n=46$, 69.7%). The remainder had variable limitations on age range, including five studies that only enrolled infants or children ≤5 years and 4 with an upper age limit between 8 and 14 years, and 11 studies with a lower age limit between 2 and 8 years. On average, 56.3% of patients were male.

Studies were most frequently conducted in western Europe ($n=30$, 45.5%), including 12 articles from the Netherlands, eight from the United Kingdom, three from Germany, two from Portugal, and one each from Denmark, Finland, Ireland, Norway, and Switzerland. North America had the second highest contribution to HRQL articles ($n=26$, 39.4%), with 18 from the United States, seven from Canada, and one from both the US and Canada. Seven studies were conducted in Australia/New Zealand (10.6%). Only three studies were conducted outside of those regions, with one each from China, India, and Argentina.

Four study cohorts were used for multiple articles, impacting the frequency of HRQL measurement tool usage. Six of the included articles evaluated a single cohort of children with meningococcemia admitted from 1988 to 2001 in the Netherlands. Two articles evaluated a cohort of patients with TBI admitted from 1998 to 2001 in Germany, two articles evaluated a cohort with congenital heart disease admitted from 2000 to 2005 in Canada, and two articles evaluated the same general PICU cohort from 2002 to 2004 in Portugal.

Follow-up assessments

The majority of studies assessed HRQL at one post-discharge follow-up time point ($n=57$, 86.4%), while eight had two follow-up assessments (12.1%) and one had five follow-up assessments. Time to the first follow-up assessment ranged from 1 month to 10 years after hospitalization (median 3 years, IQR 0.5–6).

Twenty-six (39.4%) studies conducted follow-up assessments at specified intervals after the hospitalization, including one at 1 month, two at 2 months, nine at 3 months, seven at 6 months, five at 1 year, one at 2 years, and one at 5 years (median 0.5 years, IQR 0.25–1). The reference point for these intervals was variable, beginning with ICU admission ($n=10$, 38.5%), ICU discharge ($n=9$, 34.6%), hospital discharge ($n=3$, 11.5%), or unspecified discharge ($n=4$, 15.4%). Three studies assessed patients' HRQL at a particular age (4, 5, and 8 years of age), and the remainder ($n=37$, 56.1%) assessed HRQL as a cross-sectional assessment at a single time-point ranging from a mean or median of 6 months to 10 years after hospitalization (median 5.3 years, IQR 3–7.3). One study did not report the time to follow-up.

Table 1 Populations of critically ill pediatric patients included in health-related quality of life follow-up articles, by diagnosis group

Patient population	Number of articles *n* (%)	Total number of participants *n* (%)	Total number of unique participants[a] *n* (%)
Total	66	10,340	9483
General pediatric intensive care unit	19 (28.8)	6883 (66.6)	6631 (69.9)
All admissions	17[b] (25.8)	6748 (65.3)	6496 (68.5)
Urgent admissions	1 (1.5)	65 (0.6)	65 (0.7)
Long-stay patients	1 (1.5)	70 (0.7)	70 (0.7)
Cardiac	15 (22.7)	1399 (13.5)	1383 (14.6)
Congenital heart disease	7[b] (10.6)	1100 (10.6)	1084 (11.4)
Cardiac extracorporeal life support	4 (6.1)	132 (1.3)	132 (1.4)
Cardiac transplant	3 (4.5)	156 (1.5)	156 (1.6)
Heart failure	1 (1.5)	11 (0.1)	11 (0.1)
Neurologic injury	15 (22.7)	983 (9.5)	963 (10.2)
Traumatic brain injury	11[b] (16.7)	782 (7.6)	762 (8.0)
Traumatic brain injury and other neurologic injury	2 (3.0)	92 (0.9)	92 (1.0)
Encephalitis/meningitis	1 (1.5)	49 (0.5)	49 (0.5)
Other neurologic injury	1 (1.5)	60 (0.6)	60 (0.6)
Sepsis	8 (12.1)	768 (7.4)	199 (2.1)
Meningococcemia	7[c] (10.6)	718 (6.9)	149 (1.6)
General sepsis	1 (1.5)	50 (0.5)	50 (0.5)
General extracorporeal life support	4 (6.1)	126 (1.2)	126 (1.3)
Cardiac arrest	2 (3.0)	133 (1.3)	133 (1.4)
Burns	1 (1.5)	19 (0.2)	19 (0.2)
Drowning	1 (1.5)	29 (0.3)	29 (0.3)
General trauma	1 (1.5)	Not specified	Not specified

[a]Excluding duplicate participants from articles arising from the same cohort; [b]Includes two articles from the same cohort; [c]Includes six articles from the same cohort

Of the eight studies with two follow-up assessments, most conducted the first assessment at 3 months after hospitalization ($n=6$) with the second follow-up at 6 months ($n=3$), 9 months ($n=1$), or 1 year ($n=2$). The other 2 conducted assessments at 6 months and 1 year and at 1 and 2 years after hospitalization. The study with five follow-up assessments conducted them at 3, 6, 12, 18, and 24 months after hospitalization. Pre-hospital baseline HRQL data were collected in only 10.6% of studies ($n=7$), all of which had follow-up assessments conducted at a specified interval after the hospitalization.

Follow-up assessments were conducted in person in 36.3% of studies ($n=24$), by standard mail in 33.3% ($n=22$), phone in 30.3% ($n=20$), and email in 6.1% ($n=4$). Multiple follow-up methods were used in 16.7% of studies ($n=11$), most commonly standard mail plus phone. Follow-up method was not specified in 13.6% of articles ($n=9$).

Parent/guardian proxy-reporting was common, with 83.3% ($n=55$) using a parent or guardian as the source of data for patient HRQL. Patient report was used alone in 8 articles (12.1%) and in combination with parent/guardian proxy-report in 26 (39.4%). Overall, 34 articles (51.5%) included patient report. The source of data was not reported for three articles.

Instruments used

A total of 15 unique instruments were used for follow-up HRQL assessments, of which only four were used in >5% of articles (Table 2). The most commonly used HRQL instruments were the Health Utility Index [11] (HUI; also known as the Health State Utility Index, Health State Classification, and the Multi-Attribute Health State Classification) ($n=22$ articles, 33.3%), the Pediatric Quality of Life Inventory (PedsQL™; $n=17$, 25.8%), [12] the Child Health Questionnaire (CHQ; $n=16$, 24.2%), [13] and the 36-Item Short Form Survey (SF-36; $n=9$, 13.6%) [14]. The TNO-AZL Children's Quality of Life Questionnaire (TACQOL) [15] and the Youth Self-Report Form [16] were each used in three articles, and two used the Quality of Well-Being Scale [17]. The remaining eight instruments were each used in one study, including two instruments that were informal or unnamed. Multiple HRQL instruments were used in 16.7%

Table 2 Characteristics of health-related quality of life instruments used in included articles

Instrument formats by age or # of items	# Articles	Metrics by format			Score[a]	Report		Validation population			# languages	Fee for use
		Ages (yrs)	# items	Time (min)		Self (age)	Proxy	Adults	Children	PICU		
Health utility index [11][b]	22				−0.36–1.00	8+	Yes	x	x	x	40	Yes
15Q (self-administered)		5+	15	3–5								
40Q (interviewer-administered)		5+	39	8–10								
Pediatric quality of life inventory [12]	17				0–100	8+	Yes		x	x	51	Yes
Infant Scales: 0–12 months		0–1	36	6								
Infant Scales: 13–24 months		1–2	45	8								
Generic Core Scales		2–25	23	4								
Child health questionnaire [13]	16				0–100	10+	Yes		x		88	Yes
Parent-form 28		5–18	28	5–10								
Parent-form 50		5–18	50	10–15								
Child-form 45		5–18	45	11								
Child-form 87		5–18	87	14								
36-Item short form survey [14]	9	14+	36	10	0–100	14+	No	x			120	No
TNO AZL children's quality of life [15][c]	3				0–100	8+	Yes		x		10	No
TAPQOL: Preschool		0.5–6	43	10								
TACQOL: Child		6–15	56	10								
Youth self report form [16][c]	3	11–18	112	15–40	Proprietary	11+	No		x		65	Yes
Quality of well being Scale [17]	2	18+	71	15	0–1	18+	No	x			12	No
15D, 16D, 17D HRQoL [36]	1			10–30	0–1	8+	Yes	x	x		5	Yes
15D		16+	15									
16D		12–15	16									
17D		8–11	17									
Kidscreen [37]	1				Mean 50; SD 10	8+	Yes		x		38	No
Kidscreen-10		8–18	10	5								
Kidscreen-27		8–18	27	10–25								
Kidscreen-52		8–18	52	15–20								
KINDL [38]	1	3–17	24	10	0–100	4+	Yes		x		31	No

Table 2 (continued)

Instrument formats by age or # of items	# Articles	Metrics by format			Score[a]	Report		Validation population			# languages	Fee for use
		Ages (yrs)	# items	Time (min)		Self (age)	Proxy	Adults	Children	PICU		
Participation & Environment measure [18]	1				0–100	No	Yes		x		20	Yes
Young children		0–5	28	30								
Children and youth		5–17	25	25–40								
Quality of life assessment of growth hormone deficiency in adults [19]	1	18 +	25	5	0–25[d]	18 +	No	x			13	No
Quality of school life scale [39]	1	9–18	27	15–30	1–3	9 +	No		x		1	No

[a]Higher score indicates better quality of life unless indicated; [b]Also known as Health State Classification, Multi-attribute Health Status Classification, Health State Utility Index; [c]Adult versions available; proprietary scoring; [d]Higher score indicates worse quality of life

of studies (two instruments in 11 articles and three instruments in three articles).

Of the 13 named instruments, only the PedsQL™, the TACQOL, and the Participation and Environment Measure [18] were designed to measure HRQL across the entire spectrum of pediatric ages (with different versions by patient age), while the SF-36, the Quality of Well-Being Scale, and the Quality of Life Assessment of Growth Hormone Deficiency in Adults [19] were designed primarily for use in adults. The remaining seven instruments have a lower age limit between 3 and 11 years (Table 2). Eight of the instruments are available for use via proxy-reporting. Only the HUI [20] and the PedsQL™ [21] have been validated in PICU populations.

The utilized instruments assessed a wide range of quality of life domains, with the most common being emotional (12 of the 13 named instruments), physical function ($n=11$), and social ($n=11$) domains (Table 3). Pain and school functioning were each assessed in nine instruments, while cognition was assessed in seven. Fewer than half of the instruments assessed physical symptoms ($n=6$), family function ($n=5$), behavior ($n=3$), and general health ($n=2$).

Discussion

In this scoping review of nearly five decades of literature examining HRQL outcomes following pediatric critical care, we identified only 66 published studies despite HRQL having been identified by both families and healthcare professionals as one of the most important outcomes to assess among PICU survivors [22]. Of the seven outcome domains assessed in the PCCM outcomes scoping review, [6] the HRQL domain included the fewest number of identified articles. Attention to HRQL assessment in this population is clearly rising, however, with 82% of HRQL studies published in the last 10 years of the study period.

Longitudinal assessment of HRQL was quite limited, with 86% of studies only including a single post-discharge evaluation, and only one including more than two post-discharge evaluations. The majority of studies were conducted cross-sectionally by enrolling subjects after discharge with a single assessment time-point ranging from 6 months to 10 years after the hospitalization. Of the 39% of studies with follow-up at a prospectively specified time interval from hospitalization, the duration of follow-up was relatively short at a median of 6 months. Notably, there was no consistency among prospective studies regarding whether the follow-up interval was anchored from hospital admission, PICU discharge, or hospital discharge. Given that many patients experience extended ICU or hospital stays, a follow-up interval of 6 months from hospital admission could vary by weeks or months compared to a follow-up interval of 6 months after

Table 3 Domains assessed in the health-related quality of life instruments used in included articles

Instrument versions by domains assessed	# Declared domains[a]	Domain categories assessed									
		General health	Physical function	Physical symptoms	Pain	Emotional	Social	Cognitive	School	Family	Behavior
Health utility index [11]											
HUI 2	7		x		x	x		x			
HUI 3	8		x		x	x		x			
Pediatric quality of life inventory [12]											
Infant scales	5		x	x	x	x	x	x			
Generic core scales	4		x		x	x	x	x	x		
Child health questionnaire [13]	14	x	x		x	x	x		x	x	x
36-Item short form survey [14]	8	x	x		x	x	x				
TNO AZL children's quality of life [15]											
TAPQOL: Preschool	4		x	x		x	x	x			x
TACQOL: Child	7		x	x	x	x	x	x	x		
Youth self report form [16]	5		x	x	x	x	x	x	x	x	x
Quality of well being scale [17]	4		x	x	x	x	x	x			
15D, 16D, 17D HRQoL [36]											
15D	15		x	x	x	x		x			
16D	16		x	x	x	x	x	x	x		
17D	17		x	x	x	x	x	x	x		
Kidscreen [37]											
Kidscreen-10	1										
Kidscreen-27	5		x			x	x		x	x	
Kidscreen-52	10		x			x	x		x	x	
KINDL [38]	6		x	x	x	x	x		x	x	
Participation & environment measure [18]	3						x		x	x	
Quality of life assessment of growth hormone deficiency in adults [19]	7		x			x	x	x			
Quality of school life scale [39]	3					x			x		

[a]As reported by the instrument reference; may not equal the number of domain categories assessed per the table due to different categorization (e.g., the PedsQL™ includes pain in the physical function domain and cognitive function in the school domain)

hospital discharge, rendering comparisons of outcomes at specified time intervals across studies difficult. Additionally, patients' HRQL may change over time as is shown in longitudinal studies of children with burn injuries [23] and sepsis [24]. Together, these limitations highlight the need for consensus on study design to better understand the trajectory of HRQL recovery after pediatric critical illness. Prospective study design with enrollment during the acute hospitalization and selection of instruments designed for sequential measurement should be considered for future investigations.

In addition to limited longitudinal follow-up, the lack of baseline assessment in nearly 90% of studies is a major limitation to understanding the true impact of critical illness on HRQL. While baseline status typically must be ascertained based on recall due to the unanticipated nature of most ICU admissions, the assumption that baseline HRQL for children requiring ICU admission reflects published population norms for a given instrument cannot be assumed to be accurate and may result in misleading interpretation of post-hospitalization scores. Any effects of the illness and hospitalization would likely be underestimated for patients whose baseline was above the population mean and experienced HRQL deterioration following their hospitalization, and would be overestimated for patients whose baseline was below the population mean but did not decline further [25]. In a study of HRQL in children with sepsis, for example, Killien and colleagues found that only 69% of patients who had significant decline from baseline HRQL score would have been identified as being below the population mean, while 34% of the patients who were significantly below the population mean at follow-up were not significantly below their individual baseline score [26]. Improvement in HRQL after critical illness has also been reported, and this important phenomenon is unable to be captured when comparing to population norms [24, 26].

Baseline assessment of HRQL is particularly important because the population of children sampled to determine population norms may not be representative of the PICU population. Over half of children admitted to U.S. PICUs have complex chronic health conditions [27] and commonly have low HRQL scores at follow-up after an ICU admission [28, 29]. This may in part be reflective of low baseline scores; because most quantitative HRQL instruments were designed for typically developing children, patients with disabilities generally score lower especially in measures that rely heavily on assessment of physical function. Children with cerebral palsy, for example, have a mean baseline PedsQL™ score of 51.3 points, [30] two standard deviations below the population mean, [31] and children with chronic respiratory failure are also known to have significantly lower baseline HRQL scores than population norms [32, 33]. Very few HRQL studies used qualitative methods, but qualitative assessment may be a valuable way to gain a better understanding of how quality of life is impacted by critical illness in these populations.

The published studies demonstrate that reliance on parent/guardian proxy-reporting of child HRQL status is the norm among PICU populations. Only 12% of articles reported solely patient self-report, whereas half incorporated a parent and patient report. The reliance on parent-proxy may reflect the age of study patients as well as the high proportion of PICU patients with developmental delays or other complex medical conditions limiting their ability to complete a self-report. This is also a challenge with collecting baseline data based on patient report, as many patients may be too ill at the time of ICU admission to participate. The applicability of self-reported HRQL instruments to younger ages is also a limitation to collecting patient-reported data; the typical age for self-report for the included instruments is eight years or older. Both severity of illness as well as developmental capacity should be considered in future studies that include baseline assessments at the time of admission. Future studies could consider integrating self-reported HRQL instruments as the child recovers to complement parent-proxy reporting to facilitate participation and may be used to align age and developmentally-appropriate tools.

There was relatively high consensus among the published articles around the HRQL instruments used, with only four instruments used in at least 5% of articles. Together, 85% of articles used either the HUI, the PedsQL™, the CHQ, or the SF-36 to assess HRQL. Despite the frequency of use, however, the SF-36 was developed for patients age 14 and older, thus limiting its applicability to the general PICU population. A relatively narrow age range was a limitation for the majority of the 13 named instruments included in the published studies, with only three instruments designed for the entire range of PICU patients from infants to teenagers, and only eight are available by proxy-report. Notably, most of the instruments used have not been validated in the PICU population, and there has only been a single validation study each for the HUI [20] and PedsQL™ [21]. Additionally, studies were almost exclusively from high-income countries, with only three studies conducted outside of the United States, Canada, western Europe, and Australia/New Zealand, and thus the applicability of these instruments in other settings is unknown.

Most of the instruments used assess a wide variety of domains, including the core HRQL domains of physical, emotional, social, and cognitive or school function. Given the variation in domains assessed, target age range, ease of completion, available languages, and fees for use, there may be benefits to each HRQL instrument depending on the study. There is also value, however, to development of consensus in the pediatric critical care research community surrounding use of measures and follow-up methodology to facilitate comparison of studies conducted in centers around

the world. Work is ongoing within the PALISI and CPCCRN networks to identify specific instruments to recommend as part of a Core Outcomes Measurement Set. Ultimately, the current review and associated tabular summaries will assist future study design as investigators seek to harmonize subjects, investigation objectives, and psychometric properties of the proposed intstruments; links to the specific measures have been provided to facilitate more granular assessment of the latter. Based on the findings of this scoping review, there may also be value in future work to develop core methodology for HRQL outcomes studies with recommendations for baseline assessment and optimal timing and frequency of follow-up evaluation.

There are important limitations to this work. The scoping review was conducted by the PALISI and CPCCRN networks from 2018 to 2019, hence only articles published through 2017 were able to be included. Only articles published in English were included, thus comments on region- and culture-specific HRQL instruments and findings may be limited. This review only included studies in which the majority of the population studied were pediatric ICU patients, hence studies with heterogeneous populations that overlapped with PICU patients were excluded. Lastly, HRQL instruments that have been utilized in other general and subspecialty pediatric population may be relevant to PICU populations that were not included in the identified articles, such as the Patient-Report Outcomes Measurement Information System (PROMIS) measures [34] and Child Health Ratings Inventory [35].

Conclusions

Measurement of HRQL among children surviving critical care is becoming increasingly common; the existing literature, however, is limited by minimal longitudinal data collection with short duration of follow-up, infrequent assessment of baseline HRQL status, and disportionate representation of outcomes from high-income countries. While most studies used one of four HRQL instruments including the HUI, PedsQL, CHQ, and SF-36, these measures are not well-validated in the PICU population. Development of a consensus approach to measuring HRQL among critically ill children, emphasizing multiple longitudinal assessments anchored to baseline HRQL status, may better facilitate development of patient-centered, clinically meaningful interventions to promote recovery.

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Declarations

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