

Physical Functioning After Admission to the PICU: A Scoping Review

OBJECTIVES: To conduct a scoping review to 1) describe findings and determinants of physical functioning in children during and/or after PICU stay, 2) identify which domains of physical functioning are measured, 3) and synthesize the clinical and research knowledge gaps.

DATA SOURCES: A systematic search was conducted in PubMed, Embase, Cumulative Index to Nursing and Allied Health Literature, and Cochrane Library databases following the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for Scoping Reviews guidelines.

STUDY SELECTION: Two investigators independently screened and included studies against predetermined criteria.

DATA EXTRACTION: One investigator extracted data with review by a second investigator. A narrative analyses approach was used.

DATA SYNTHESIS: A total of 2,610 articles were identified, leaving 68 studies for inclusion. Post-PICU/hospital discharge scores show that PICU survivors report difficulties in physical functioning during and years after PICU stay. Although sustained improvements in the long-term have been reported, most of the reported levels were lower compared with the reference and baseline values. Decreased physical functioning was associated with longer hospital stay and presence of comorbidities. A diversity of instruments was used in which mobility and self-care were mostly addressed.

CONCLUSIONS: The results show that children perceive moderate to severe difficulties in physical functioning during and years after PICU stay. Longitudinal assessments during and after PICU stay should be incorporated, especially for children with a higher risk for poor functional outcomes. There is need for consensus on the most suitable methods to assess physical functioning in children admitted to the PICU.

KEY WORDS: children; clinical outcomes; pediatric intensive care; pediatric postintensive care syndrome; physical functioning

A wide range of poor physical, neurocognitive, and psychologic functioning outcomes have been identified in adults during and after ICU stay (1). Impairments in functioning outcomes after ICU stay are known as postintensive care syndrome (PICS) (1–4). Similar to adults, children admitted to the PICU are at risk for such long-term impairments and ongoing morbidity after hospital discharge. This holds both for previously healthy children as well as for those with underlying chronic diseases (5–9).

In order to systematically identify the risks for long-term impairments, recently, the PICS in children (PICS-p) framework has been developed (10–12). This framework identifies potential risks for the development of long-term impairments in children after PICU admission, including deterioration in physical functioning (PF) (11). On the PICU, children are exposed to factors that increase the risk for impairments in PF, including physical (e.g., respiratory and muscle weakness),

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environmental (e.g., mechanical ventilation, immobilization), and pharmacologic (e.g., sedatives) risk factors. A previous cohort study has shown that more than 70% of the children admitted to the PICU reported functional health problems 6 months after PICU discharge (13). Although long-term studies are limited, children may develop new PF disabilities in the long term (10). Poor levels of PF may have substantial impact on both future short- and long-term health such as in adult ICU survivors (1, 10, 14). Optimizing the level of PF in children after PICU discharge is of major importance to improve their developmental trajectories and for the prevention of, and recovery from, various health problems across lifespan (15, 16). Early evaluation of PF after PICU discharge could provide crucial information for treatment decisions and to monitor personalized intervention responsiveness. According to parents and healthcare professionals, PF should therefore be universally assessed and treated to optimize recovery from critical illness (9, 17, 18).

The level of PF in childhood can be classified according to the International Classification of Functioning, Disability and Health-Children and Youth framework (ICF-CY) (19). According to the ICF-CY, PF encompasses body functions and structures, activities, and participation related to movement and is a result of the interaction between the child's health condition and both personal and environmental factors (**Appendix 1**, <http://links.lww.com/CCX/A690>). In clinical practice, PF measurement tools should preferably cover all domains to identify changes in PF that may occur during and after PICU stay. A previous review by Ong et al (20) showed persistent functional impairment and a wide variety of measurement tools in pediatric critical care survivors. Whether and to what extent these outcome measures cover the different PF-related ICF -CY domains has yet to be evaluated. Therefore, the objective of this scoping review is three-fold: 1) to describe findings and determinants of PF in children admitted to the PICU evaluated during and/or after PICU stay using the ICF-CY as a frame of reference, 2) to identify and classify measurements according to the ICF-CY (sub)domains, and 3) to synthesize clinical and research knowledge gaps and recommendations.

METHODS

A comprehensive study protocol was written guided by the Preferred Reporting Items for Systematic Reviews

and Meta-analyses extension for Scoping Reviews guidelines (21) and the Joanna Briggs Institute methodology for conducting scoping reviews (22). The Preferred Reporting Items for Systematic Reviews and Meta-analyses checklist is provided as supplementary material (**Appendix 2**, <http://links.lww.com/CCX/A690>). The final protocol has been registered with the Open Science Framework (<https://osf.io/7xzv5/>).

Inclusion and Exclusion Criteria; Search Strategy

The design of the search strategy has been underpinned by key inclusion criteria, based on the broad Population, Concept and Context (PCC) framework, recommended by the Joanna Briggs Institute for scoping reviews (22). In the current review, we included English language studies reporting outcomes and/or determinants of PF in children admitted to the PICU from birth up to the age of 18 years evaluated during and/or after PICU stay. Nonempirical studies were also included for synthesizing clinical recommendations and knowledge gaps. Conference abstracts and study protocols were not included. Articles published from the earliest database records to 10th of October 2019 were included. A three-step search strategy was used (22). First, to identify keywords and index terms relevant to the topic, an initial limited search in PubMed was performed using a combination of MeSH terms and keywords referring to our PCC framework. Second, the search strategy was refined in collaboration with a university librarian, and searches were deployed in Medline via PubMed, Embase, Cumulative Index to Nursing and Allied Health Literature, and Cochrane Library. To capture all possible relevant studies, we decided to extend the search with the construct "quality of life (QoL)." Third, the reference lists of included studies were checked in order to identify additional relevant studies. The full electronic search strategy is detailed in **Appendix 3** (<http://links.lww.com/CCX/A690>).

Study Selection

All identified records were collated and uploaded into Covidence systematic review software (Veritas Health Innovation, Melbourne, VIC, Australia), and duplicates were removed. Two reviewers (D.B., R.M.d.B.) pilot-tested the inclusion criteria on a sample of 25 abstracts

and 25 full-text articles. Interrater agreement among the reviewers was determined, and if found insufficient (< 75% or Cohen's kappa < 0.5), inclusion criteria were redefined until the preset interrater agreement criteria were met (23). At the end of the screening process, an overall Kappa was recalculated. Next, all identified articles were independently screened by two reviewers on title and abstract. If an article met the inclusion criteria based on title and abstract, full-text articles were obtained and re-evaluated on meeting the inclusion criteria. Any unsolved disagreement between the two reviewers was resolved through discussion with a third reviewer (R.E.).

Data Extraction and Analyses

Data were extracted using a data extraction instrument developed by the authors (**Appendix 4**, <http://links.lww.com/CCX/A690>). Collected data comprised details on study characteristics (authors, country, year, design), patient characteristics (sample size, age, sex, primary reason PICU admission, comorbidity, hospital/PICU length of stay [LOS], mechanical ventilation), and PF-related assessment (measurement instrument, timing of assessment, extracted scale ICF-CY [sub]domain, findings of PF, and related determinants). In experimental studies, only data from the control group were used. The measurement instruments used in included empirical studies to report findings of PF were analyzed and classified to the ICF-CY domains and subdomains (available at <https://apps.who.int/classifications/icfbrowser>). In the first stage, data extraction of five randomly selected studies was performed independently and subsequently discussed by two researchers (D.B., R.M.d.B.). Data extraction of the remaining studies was performed by one researcher (R.M.d.B.). After extraction, patterns in the collected data were explored with the last author (R.E.). A narrative analyses approach was used to interpret the results of the included studies. Because of heterogeneity and the scope of this review, no aggregate and/or statistical analyses were conducted.

RESULTS

A total of 2,610 articles were identified. From independent screening of titles and abstracts, 156 potentially relevant articles were retrieved and subsequently assessed in full-text form. Of these, 93 studies did not

meet inclusion criteria and were excluded leaving a total of 68 studies for inclusion of which 56 were empirical studies (13, 24–78) and 12 were nonempirical studies in the form of literature reviews (1, 10, 12, 20, 79–86) (**Fig. 1**). The interrater agreement of the pilot full-text screening was 76% (Cohen's kappa: 0.52), with an overall agreement of 77% calculated on all studies included in the review (Cohen's kappa: 0.54). There was no need to redefine the inclusion criteria.

Study and Sample Characteristics

The study characteristics and sample characteristics of the 56 included empirical studies are presented in **Appendix 5** (<http://links.lww.com/CCX/A690>). The included studies were conducted in 18 different countries; 24 studies (42.9%) were conducted in the United States, eight (14.3%) in the Netherlands, and six (10.7%) in Canada. Year of publication ranged from 1995 to 2019, with half of the studies ($n = 28$; 50%) published between 2015 and 2019. Regarding study design of the empirical studies, there were 37 cohort studies (66.1%), seven cross-sectional studies (12.5%), six clinical trials (10.7%), four chart reviews (7.1%), and two case series (3.6%). A total of 31 studies (55.4%) reported only cross-sectional PF scores, with 12 studies (38.7%) reporting findings gathered post-(PICU) admission and 15 (48.4%) at PICU/hospital discharge. Longitudinal (change) scores were reported in 25 studies (44.6%). Of the 56 included empirical studies, 52 studies had unique samples involving 23,634 patients of which PF was reported. Of these, 25 studies (48.1%) included heterogeneous samples and 27 (51.9%) homogeneous samples (cardiac disease ($n = 9$; 33.3%), traumatic brain injury ($n = 6$; 22.2%), sepsis ($n = 4$; 14.8%), burns ($n = 3$; 12%), trauma ($n = 1$; 4%), pertussis ($n = 1$; 4%), liver transplant ($n = 1$; 4%), hematologic ($n = 1$; 4%), and bacterial meningitis ($n = 1$; 4%). The vast majority ($n = 38$; 83%) of the 46 studies that reported sex statistics included more males than females. Thirty-six studies (69.2%) reported PICU LOS, whereas 23 studies (44.2%) reported hospital LOS. PICU LOS ranged from 1.5 (24) to 43 days (40), and hospital LOS ranged from 1.5 to (13, 69) to 55 (41) days. A total of 19 studies (36.5%) reported on preexisting comorbidity and/or a chronic condition at admission, and merely 22 studies (42.3%) reported data (percentages and duration) on mechanical ventilation.

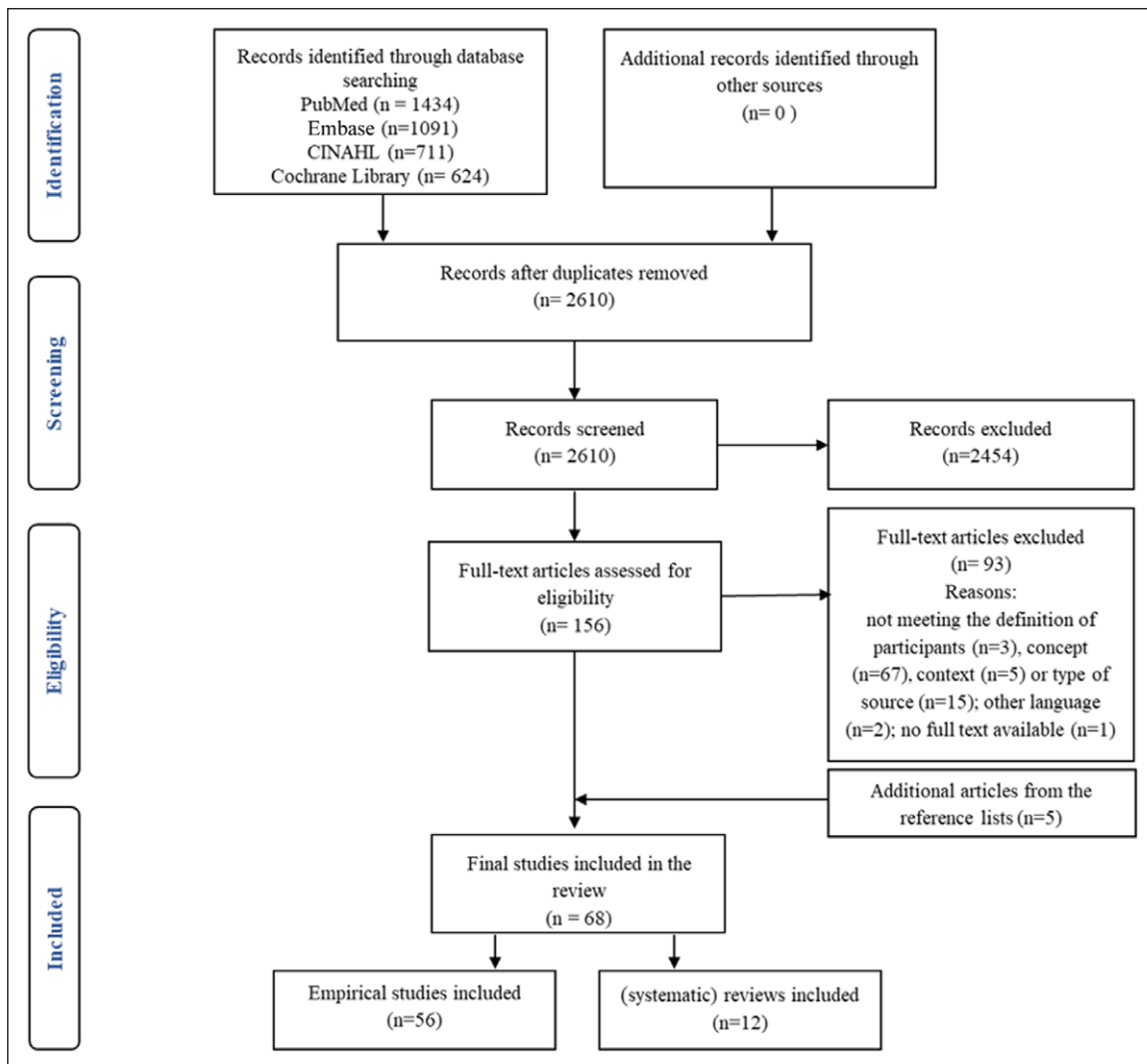


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram. CINAHL = Cumulative Index to Nursing and Allied Health Literature.

PF in PICU Patients

The cross-sectional and longitudinal PF scores are reported in **Appendix 6** (<http://links.lww.com/CCX/A690>). In 45 studies, cross-sectional PF data are reported at different occasions, from admission to long-term post-PICU/hospital discharge. All studies reported disabilities in PF during or after PICU/hospital stay. Post-PICU/hospital discharge scores (range, 1 mo to 10 yr) show that PICU survivors report difficulties in PF years after PICU discharge. These long-term disabilities scores differ widely across studies, ranging from mild disabilities (-1 SD) to severe disabilities (-3 SD). The course of PF, from PICU admission to follow-up, was reported in 25 studies. Studies that investigated the longitudinal trajectory of PF showed considerable decline of PF during PICU/hospital stay. Especially with respect

to body functions and structures, for example, significant muscular atrophy (48, 54, 72) and ICU-acquired weakness (27, 37, 38, 75). To illustrate, Glau et al (48) report a daily diaphragm atrophy rate of 3.4%, and Valla et al (72) found a statistically significant decrease of quadriceps femoris muscle thickness of 0.05 cm per day. Improvements of PF were mainly observed in the period following PICU/hospital discharge. Although several studies reported sustained improvements in the long term, most of the reported PF levels (e.g., eating, self-care, muscle strength) were lower compared with the reference and baseline values (25, 35, 37-39, 70).

Determinants of PF

Appendix 6 (<http://links.lww.com/CCX/A690>) present the cross-sectional and longitudinal relationships

between PF and its determinants. Notably, the vast majority of studies did not report longitudinal determinants of PF. The most frequently observed determinant associated with decreased PF was longer PICU/hospital stay (33, 45, 59, 63, 68). Other reported determinants include the presence of comorbidities (such as a preexistent neurodevelopmental condition), (blood) variables (e.g., hyperglycemia) (45, 50, 54), injuries, complications (such as postoperative seizures), and variables of prematurity (24, 33, 38, 45, 59, 63, 68). Admission-related interventions (such as duration of mechanical ventilation) were also associated with decreased levels of PF (54). Finally, three studies reported that older age was related to more physical disability (38, 54, 59), whereas another study among children who survived a septic shock showed a negative relationship between younger age and PF (31).

Measurement of PF

Appendix 7 (<http://links.lww.com/CCX/A690>) presents the extracted PF-related domains of measurement instruments across the ICF domains. A diversity of instruments was used to report PF findings, including 1) global health functioning instrument; 2) health-related QoL instruments; 3) biophysical instruments; 4) neuromotor development instruments; 5) PF scales, scores, and questionnaires; and 6) physical examinations/interviews by clinicians. The Functional Status Scale (FSS) was the most frequently used measurement instrument, followed by the Child Health Questionnaire (CHQ) and Pediatric Quality of Life (PedsQL) Inventory. In the included studies, the FSS was mostly used longitudinally during PICU/hospital stay and measures a narrow spectrum of the ICF model focusing solely on the subdomains muscle and movement functions of the concept “body functions.” PF as assessed with the CHQ or PedsQL focused primarily on the subdomain, of activities and participation of the ICF model at the level of perceived performance (i.e., level of PF subjectively experienced by patient/parents in current environment) (19). On the other hand, neuromotor development instruments measure PF in a standardized environment, also known as level of capacity. Notably, mainly all studies that have used Health-Related QoL and neuromotor development instruments have used these measurement instruments only once after discharge. Overall, the PF Scales, Scores, and Questionnaires covered the broadest spectrum of

the ICF model. The Pediatric Evaluation of Disability Inventory (PEDI), Barthel index, and the Functional Independence Measure for children (WeeFIM) were the only instruments that contain at least three of the four ICF domains and measure at the level of perceived and actual performance (PEDI) or solely actual performance (Barthel index, WeeFIM). Biophysical instruments and physical examinations are instruments that preliminary focused on structures related to movement, muscle functions, and movement functions of the ICF model. Biophysical instruments, such as assessment of muscle strength by dynamometry or muscle structure by ultrasound, mainly took place longitudinal during PICU/hospital stay. Overall, the most frequently identified ICF domains were mobility and self-care. In most cases, mobility was measured with items that address walking and moving around. Self-care was mainly evaluated with items that were related to eating, washing, and toileting.

Synthesis of Recommendations and Knowledge Gaps

We analyzed the discussion sections of the included studies in order to synthesize knowledge gaps and recommendations for future clinical research. In addition, we also analyzed the discussion sections of 11 (systematic) reviews (10, 20, 79–86). The most frequently addressed clinical recommendation pertained to the lack of standardized follow-up after PICU stay. PF assessments during and after PICU stay should be incorporated as part of usual care to define the long-term impact of PICU stay on PF. Long-term follow-up was especially warranted for children with a higher risk for poor functional outcomes, including for example children with chronic comorbidities (58). In line with this, further research was deemed necessary to determine the mechanisms and modifiable risk factors (such as LOS and invasive treatments), underlying the relation between PICU stay, and impairments in PF after PICU admission. Identification of modifiable factors within the PICU environment may be appropriate targets for future interventions aimed at increasing PF in children after PICU discharge. In adults for example mobilization and avoiding benzodiazepine sedation and preventing delirium during ICU stay result in improvement of both physical and psychological outcomes. We do not know the effects of these interventions in children admitted to a PICU. To evaluate

PF in children during and after PICU admission, consensus on the most suitable methods to assess PF in PICU survivors is needed. Study teams and clinicians are encouraged to collaborate and develop measurement guidelines with a combination of objective and self-reported measures in order to evaluate longitudinally the different PF dimensions according to the ICF-CY in children and adolescents who were admitted to the PICU.

DISCUSSION

Studies that investigated the longitudinal trajectory of PF showed considerable decline of PF during PICU/hospital stay, especially with respect to body functions and structures. Furthermore, post discharge scores show that PICU survivors report difficulties in PF years after PICU discharge. These long-term disabilities scores range from mild to severe disabilities. Although sustained improvements in the long-term have been reported, most of the PF levels were lower compared with reference and baseline values. This review shows that children with comorbidities, who undergo mechanical ventilation and longer PICU/hospital stay, are at higher risk for decreased PF. The results highlight the importance of post-PICU interventions for both children admitted to the PICU and their parents.

The PICS-p framework is now recognized for children (10–12), and standardized follow-up after PICU stay should be offered to PICU survivors. Based on the results of this review, longitudinal PF assessments during and after PICU stay should be incorporated in this standard follow-up care, especially for children with a higher risk for poor functional outcomes, such as children with chronic comorbidities. This is in line with the Delphi study of Fink et al (87), in which PF should be incorporated in the core outcome measurement set for pediatric critical care. Future research should investigate how these PF outcomes should be measured.

In addition, early recognition of children at risk for impairments of PF can help attempt to prevent these complications and develop suitable interventions to improve PF if these impairments persist. As about half of the PICU patients are admitted unexpectedly, evaluating PF status in these patients before PICU admission can only be performed through subjective questionnaires completed by parents during PICU stay.

In accordance with a recent review by Maddux et al (88), a diversity of instruments was used after PICU

stay of which the Health State Utility Index, the PedsQL Inventory, and the CHQ are most commonly deployed. The FSS is mainly used during PICU stay, in particular as longitudinal measurement. There is an urgent need for consensus on the most suitable methods to assess PF in children admitted to the PICU. In the adult PICS literature, more consensus is reached about functional diagnostic assessment as well as intervention. Recently, a Delphi method was used to focus on consensus in the rehabilitation of critical illness survivors after hospital discharge. A standard core set of outcomes was recommended that should test PF on different domains (i.e., exercise capacity, skeletal muscle strength, function in activities of daily living, mobility, quality of life and pain) (89).

In adults, length of ICU stay, mechanical ventilation, comorbidities (e.g., diabetes), and reason for ICU admission are associated with the development of chronic conditions after ICU discharge (90). As PF and other PICS morbidities are also seen in PICU survivors, these clinical variables can also be considered in the follow-up care of PICU survivors. As surviving critical illness can have long-term effects on both PICU survivors and parents, who play a key role in helping to recover, follow-up care for parents is necessary to be able to adequately support the patient and parents. Early mobility exercises, the practice of physical therapy during critical illness, and family engagement/empowerment are promising intervention strategies (91, 92).

In line with the findings of this systematic review, there is a need for more high-quality studies with larger sample sizes to better understand the course of PF and to investigate which determinants are related to cross-sectional and longitudinal PF scores in PICU children. Furthermore, more research is needed to establish the relationship between body function/structures and activities and participation in PICU survivors. A previous study reported associations between muscle layer thickness and muscle strength performance (93). Hence, ultrasound assessment of, for example, the quadriceps femoris muscle may be useful and feasible in PICU children. However, a deeper understanding is required how muscle thickness is actually related to muscle function.

Some limitations of this review should be discussed. First, we did not formally investigate the scientific quality and internal and external validity of individual

studies. Second, the search was limited since unpublished studies and reports were not included in this study. Third, due to the heterogeneous nature of the studies (population, design, outcome measures), it was challenging to synthesize the data and to draw conclusion for specific subgroups. To address this challenge, the two reviewers used standardized extraction forms and consensus meetings to synthesize the data in a structured manner.

CONCLUSIONS

We conclude that post-PICU/hospital discharge scores show that children admitted to the PICU report difficulties in PF years after PICU discharge, and long-term disabilities scores range from mild to severe disabilities. Studies that investigated the longitudinal trajectory of PF showed considerable decline of PF, especially with respect to body functions and structures. Decreased PF was associated with longer PICU/hospital stay and the presence of comorbidities. The results highlight the importance of post-PICU interventions for both PICU survivors and their parents. There is an intense need for consensus on the most suitable methods to assess PF in children and adolescents admitted to the PICU.

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