Chronically critically ill pediatric patients represent an emerging population in NICUs and PICUs. Chronic critical illness has been recognized and defined in the adult population, but the same attention has not been systematically applied to pediatrics. This article reviews what is currently known about pediatric chronic critical illness, highlighting the unique aspects of chronic critical illness in infants and children, including specific considerations of prognosis, outcomes, and decision-making. We propose a definition that incorporates NICU versus PICU stays, recurrent ICU admissions, dependence on life-sustaining technology, multiorgan dysfunction, underlying medical complexity, and the developmental implications of congenital versus acquired conditions. We propose a research agenda, highlighting existing knowledge gaps and targeting areas of improvement in clinical care, research, and policy.
As more patients cared for in ICUs survive their acute illnesses, a new population of chronically critically ill patients has emerged. Adult chronic critical illness (CCI) is described as a syndrome of persistent multisystem dysfunction that arises when critical care interventions support patients through the acute phase of a life-threatening critical illness but cannot return them to a state of good health and function. These patients have ongoing significant morbidity, care burdens, and poor outcomes.1,2 The growing CCI population poses both clinical and resource management challenges.1,2

The literature describes “long-stay” pediatric patients as early as 1987, and increasing numbers of ICU patients have long-stay status and underlying chronic conditions.2,4 Feudtner and colleagues8,10 have shown that children with multiple complex chronic conditions (CCCs) are living longer than they were 2 decades ago, often spending substantial periods in the hospital and responsible for disproportionate utilization of ICU resources.11 Medically complex children are a very diverse population, with heterogeneous disease patterns and variable levels of disability, sites of care, and prognoses. Although the sickest among these children most likely represent the pediatric chronically critically ill (Fig 1), pediatric chronic critical illness (PCCI) has received little systematic attention.12-15

This subject is a missed opportunity to apply what we have learned about adult CCI to the care of infants and children. The present article reviews what is currently known about PCCI, emphasizing similarities and differences between adult and pediatric patients. We synthesized data from NICUs and PICUs, for although these patient populations are generally studied separately, the hospitalizations of children with PCCI often span both locales. Current challenges in understanding PCCI prognoses and outcomes, and the implications for clinician and family decision-making, are outlined. Targeting the gaps in knowledge, we offer a definition of PCCI to guide clinical care, systematic data collection, and resource application. Finally, a PCCI research agenda is suggested.

ADULT CCI

Adult CCI patients typically have limited physiologic reserves related to age and/or comorbidities when they develop severe acute illness. Critical care interventions help them to survive an acute event, but persistent inflammatory dysregulation is believed to contribute to ongoing multiorgan system dysfunction, as well as technology and/or functional dependence.2,3

A 2015 study estimated the prevalence of CCI in adults at 7.6% of all ICU admissions.2 After prolonged ICU stays, CCI patients are often transferred to respiratory, intermediate- or long-term acute care facilities or nursing homes. In-hospital mortality reaches 60%, and postdischarge mortality is >50% at 6 months.4 Related in-hospital costs exceed $25 billion in the United States annually.2

Various definitions of CCI have included both length of ICU stay and prolonged mechanical ventilation or tracheostomy. The use of a uniform definition for adult CCI has been essential to strengthening the medical knowledge regarding these patients and for directing health system reimbursement and policy.5,16,17 A 2014 consensus definition from the RTI International defines adult CCI patients as those hospitalized at least 8 days in an ICU and with at least 1 of 5 conditions: prolonged acute mechanical ventilation, tracheostomy, sepsis/other severe infection, severe wounds, or multiple organ failure.18 A consistent definition of CCI allows clinicians and families to recognize the transition from an acute critical illness to CCI, which can inform evolving ICU goals of care. A CCI definition can also streamline research agendas and highlight gaps in medical knowledge. At the systems level, the ability to define and identify this patient population creates opportunities for improved care delivery and outcomes for adult CCI patients and their families.

ADAPTING THE ADULT CCI DEFINITION

The benefits of a uniform definition for CCI are not yet available for pediatric patients. The hallmarks of adult CCI—prolonged mechanical ventilation, tracheostomy, and ICU length of stay (LOS)—are not clearly definitional features of PCCI. Respiratory insufficiency requiring mechanical ventilation is routine for many neonatal conditions, for example, only some of which herald poor outcomes. The expected duration of mechanical ventilation and NICU stay varies widely depending on degree of prematurity but is commonly >1 month for the most premature infants. In addition, among older infants and children who are ventilator dependent due to a variety of underlying medical conditions, expanded home ventilation programs allow many of these children to thrive outside of the hospital setting.19-21

Tracheostomies also have different implications for pediatric patients versus adult patients. Although tracheostomies function similarly for all patients (ie, permit long-term ventilator support, bypass upper airway obstruction, maintain pulmonary hygiene), they involve more complications in children.22-24 Current practice is to perform tracheostomy early (<14 days) in adults who need prolonged mechanical ventilation; this approach makes tracheostomy a useful early indicator of adult CCI.25-27 In pediatrics, the median time to tracheostomy is later and more variable (range, 22–41.5 days),25-27 undermining its value as an early marker of PCCI.

ICU LOS is essential to any definition of CCI but cannot independently define PCCI. LOS
can be mediated by factors external to a patient’s clinical status, including hospital bed availability. Although true for patients of any age,28 this scenario is particularly so for children due to institutional variability in inpatient venues for children with chronic ventilator dependence, as well as the paucity of available non-ICU pediatric intermediate- and long-term care settings and the regional variability in home care services. The variability in definition of “prolonged LOS” in the literature (Table 1) reflects this complexity and the need for a more consistent approach.

**PEDIATRIC CCI: UNIQUE CONSIDERATIONS**

In addition to the aforementioned adaptations, we found data to suggest 3 additional pediatric considerations that may inform the definition of PCCI: underlying medical complexity; recurrent ICU hospitalizations; and the impact of age and developmental status on pediatric disease processes.

Medical complexity is clearly important to PCCI. Many children with repeated and prolonged hospitalizations have “special health care needs” or “medical complexity.” Multiple schemas, such as the CCC algorithm and Pediatric Medical Complexity Algorithm, have been developed to describe and identify this subset of the pediatric population.29–32 These schemas describe a range of underlying medical conditions, including children with medical complexity (CMC), who comprise >50% of the patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Setting</th>
<th>Case Definition</th>
<th>Findings/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pollack et al5</td>
<td>1987</td>
<td>United States; single PICU</td>
<td>&gt;13 d</td>
<td>7.1% of patients, used ~50% of PICU resources; at 1 y follow-up, 58% died or with severe disability</td>
</tr>
<tr>
<td>Marcin et al8</td>
<td>2001</td>
<td>United States; 32 PICUs</td>
<td>&gt;12 d (&gt;95th percentile)</td>
<td>LSP 2.1%–8.1% of population; occupy 15.2%–57.8% of PICU bed days; significantly higher mortality rate</td>
</tr>
<tr>
<td>Brown et al37</td>
<td>2003</td>
<td>London, UK; tertiary pediatric cardiac surgical center</td>
<td>≥14 d (&gt;95th percentile)</td>
<td>LSP 12% of population; mortality 3 times higher; identified preoperative, intra-operative, and postoperative features predictive of long-stay status</td>
</tr>
<tr>
<td>van der Heide et al31</td>
<td>2004</td>
<td>Amsterdam, the Netherlands; single PICU</td>
<td>≥ 30 d</td>
<td>No significant difference between baseline characteristics or mortality of LSP and matched control subjects; higher incidence of complications for LSP</td>
</tr>
<tr>
<td>Briassoulis et al38</td>
<td>2004</td>
<td>Athens, Greece; single PICU</td>
<td>&gt;14 d</td>
<td>20% of patients accounted for 55% of PICU patient days; &gt;3 mo</td>
</tr>
<tr>
<td>Conlon et al36</td>
<td>2009</td>
<td>Dublin, Ireland; single PICU</td>
<td>≥ 28 d</td>
<td>3.1% of total patients over study period; 21.2% PICU mortality, 14% postdischarge mortality; long-term HRQOL normal for majority of survivors</td>
</tr>
<tr>
<td>Naghib et al39</td>
<td>2010</td>
<td>Rotterdam, the Netherlands; single PICU</td>
<td>≥28 d</td>
<td>4.4% of patients had prolonged stay; 3% of admissions account for 63% of PICU patient days; mortality 5 times higher for LSP</td>
</tr>
<tr>
<td>Pagowska-Klimek et al30</td>
<td>2011</td>
<td>Lodz, Poland; single PICU</td>
<td>&gt;14 d (&gt;95th percentile)</td>
<td>Cardiac surgery patients only; identified risk factors associated with long stay</td>
</tr>
<tr>
<td>Edwards et al35</td>
<td>2012</td>
<td>54 US PICUs</td>
<td>&gt;15 d</td>
<td>Children with CCMs at greater risk for prolonged LOS and PICU mortality</td>
</tr>
<tr>
<td>Namachivayam et al7</td>
<td>2012</td>
<td>Melbourne, Australia; single PICU</td>
<td>≥ 28 d</td>
<td>1% of admissions, used 18.5% bed days; bed occupancy of LSP 8% in 1989; increased to 21% in 2008; unfavorable outcome (moderate to severe disability or death) in more than two-thirds of patients; favorable outcome for 54% of survivors</td>
</tr>
<tr>
<td>Namachivayam et al31</td>
<td>2015</td>
<td>Australia and New Zealand; all PICUs</td>
<td>≥28 d</td>
<td>No improvement in outcomes for CCI patients over a 10 year period</td>
</tr>
</tbody>
</table>

HRQOL, health-related quality of life; LSP, long-stay patient.
admitted to PICUs. Some CMC have functional impairment or chronic dependence on technology, including mechanical ventilation, surgical feeding tubes, cerebrospinal fluid shunts, or indwelling venous catheters, to sustain long-term vital functioning. In addition to increased risk of ICU admission, CMC are also at high risk of prolonged ICU stays. Many existing studies show that long-stay PICU status, variably defined as >12 to ≥30 days (Table 1), is associated with underlying chronic medical conditions and increased mortality. However, medical complexity is not synonymous with PCCI; other studies have shown that the presence of chronic medical conditions is not alone associated with a longer LOS. The children who develop PCCI represent a subset of the population of CMC; that is, those who spend the majority of their time in the hospital setting.

The adult CCI definition does not include recurrent ICU hospitalization. This use makes sense, given that most adults with CCI die during their ICU admission or within 6 months. In contrast, many children with CCI can survive for months to years, albeit with recurrent needs for intensive medical care, which, depending on the hospital, can be delivered in an ICU or other inpatient setting (eg, step-down unit, chronic ventilator unit). As noted earlier, CMC are at an increased risk for ICU admission. Dosa et al reported that, in their tertiary PICU, the only children with >1 unscheduled ICU admission over a 1-year period were those with underlying chronic conditions and that children who receive technology-assisted care may be as many as 300 times more likely to have an unscheduled ICU admission than children without underlying health problems. Edwards et al also found an increased rate of ICU readmission among children with more complex and chronic conditions. Namachivayam et al reported that many long-stay pediatric patients had multiple separate ICU admissions. These data suggest that repeated admission to the ICU may be an indicator of PCCI.

Finally, the definition of PCCI must also account for the differential evolution of pediatric pathologies based on age and developmental status. As with most pediatric disease processes, PCCI is clearly influenced by pediatric physiologic and behavioral development. The evolution and features of PCCI in a premature neonate differ from those in a toddler with leukemia or a previously well teenager with acute trauma. The finding that so many children with PCCI have static or progressive neurodevelopmental disabilities is also relevant to the child and family experience of prolonged ICU stays and additive ICU interventions.

**SIGNALING THE ONSET OF PCCI: WHY DOES IT MATTER?**

A primary benefit of recognizing when a patient transitions from an acute critical illness to CCI is that the prognostic implications of CCI can inform goals of care and decision-making. A definition of PCCI that can be applied in real time, rather than based on discharge data, supports this endeavor. Nelson et al found that families of adult patients with prolonged hospitalizations feel least informed about long-term functional prognosis and alternatives to aggressive treatment. Lacking clear signals about illness course, families may erroneously believe that making a decision for an intervention to chronically sustain a vital function (eg, home ventilation) is a sign of disease improvement. In our previous research, we describe the ways in which ICU processes and ICU clinician training can undermine clear communication about the transition from an acute critical illness to CCI. Being clear about PCCI onset, and the diminishing prognosis for recovery, is essential to making meaningful medical decisions with families.

Although adult patients who develop CCI have a 60% in-hospital mortality rate, PCCI mortality is more variable and may not be the single most important outcome. Mortality rates in NICUs fluctuate, ranging from >60% for the most premature infants to <7% for mildly premature infants. Overall mortality in PICUs is reported to be <2.5%. It is clear that long-stay PICU patients have increased mortality compared with other PICU patients. Namachivayam et al examined 5-year survival of children with a PICU LOS ≥28 days. Overall 5-year survival was 65.5%; among patients with single ventricle physiology, 5-year survival was 47.2%, and among bone marrow transplant recipients, it was 22.8%. Importantly, this 2015 study also showed that mortality has not improved for long-stay PICU patients over the past decade, even as overall PICU mortality rates have decreased. Other studies have noted similar poor mortality outcomes for long-stay PICU patients, with 18% to 21% mortality at time of discharge from the PICU and worse mortality at follow-up. The Modified Glasgow Outcome Scale stratifies functional outcome. One study found that 65% of children who experienced PICU stays >28 days had an unfavorable outcome, including moderate disability, severe disability, or death according to the Modified Glasgow Outcome Scale.

Clearly, outcomes beyond mortality are important in PCCI. The impact of PCCI on global child development, for example, is without a corollary in adult CCI. Prolonged critical illness often delays or deprives children of important developmental experiences in multiple domains. The long-term effects of repeated painful stimuli, anesthesia, and long-term sedation on early brain development remain areas of open investigation. Prolonged confinement to hospital beds or restricted movement related to life-supporting technologies interferes with gross and fine motor development. Chronic illness without prolonged hospitalization among school-aged children can affect school attendance and performance; it is reasonable to extrapolate that prolonged hospitalizations will result in further social isolation and school absenteeism, interrupting social and academic development. Achievement or recovery of developmental milestones after PCCI is largely unexplored. The developmental morbidities associated with PCCI are important because they are at the center of the child’s ability to interact with his or her family and community; developmental morbidities also have implications for indefinite dependence on adult supervision for activities of daily living. These essential experiences often shape goals of care.
Many families of children with PCCI have likely faced at least one serious decision to pursue a therapy with uncertain benefit-to-burden ratio. Evolving medical complexity and therapeutic complications make identifying the best interests of these children increasingly difficult. Clinicians may assume that a family’s initial decision to pursue an intervention (decisions perhaps made with incomplete information or intense emotion) constitutes a “buy-in” of continued interventions. As Siegel et al described, many critical care interventions, including decisions for life-sustaining therapies, occur by default. Rapid ICU staff turnover; the involvement of multiple subspecialty teams, emphasis on daily decisions rather than long-term ones, and the lack of a medical home can all contribute to default medical management.

There is strong evidence that early integration of palliative care in the adult ICU can help ease symptoms and minimize ICU interventions without increasing mortality. Including PCCI as an ICU trigger for palliative care involvement can help families and medical teams prioritize quality of life and goals of care, no matter the prognosis. The American Academy of Pediatrics recommends that the care of all children with life-limiting or life-threatening illnesses include the involvement of pediatric palliative care specialists from the time of diagnosis. Providing extra decision support may help families consider a potentially less effective but less burdensome treatment, therapies that prioritize time outside the ICU, or medicines that promote quality parent–child interactions within the ICU.

WHAT WE NEED TO LEARN

The emergence of CCI is an unintended consequence of improved critical care interventions. As we continue to make strides in critical care delivery to infants and children, we must simultaneously learn more about PCCI to prevent its occurrence where possible, improve outcomes when it occurs, and improve our care delivery systems so as to better meet the specific needs of children with CCI. We envision a broad PCCI research and practice agenda (Table 2) that targets patient care, family, medical team and health system challenges, and societal implications. Our proposed research questions mirror many of those in adult CCI and also seek to answer questions of specific concern in the pediatric population. Developing and testing a working definition of PCCI are critical first steps in this effort.

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<tr>
<th>TABLE 2</th>
<th>Research Agenda for PCCI</th>
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<tr>
<td>Domains</td>
<td>Research Questions</td>
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<tr>
<td>CCI definition</td>
<td>• Does the proposed definition of PCCI capture the appropriate patient population?</td>
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<tr>
<td>• Is there a PCCI syndrome analogous to CCI in adults (including neurologic, metabolic, endocrine, and musculoskeletal sequelae)?</td>
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<td>• Can the PCCI definition be validated by using a large database?</td>
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<tr>
<td>• Is the definition successful in various types of databases (eg, hospital chart review, administrative databases)?</td>
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<tr>
<td>Patient</td>
<td>• Are there risk factors or patterns of illness/ injury that predispose to CCI?</td>
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<tr>
<td>• Are there features of PCCI that are preventable?</td>
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<td>• Would a “PCCI score” permit earlier diagnosis of PCCI and/or permit targeted interventions?</td>
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<tr>
<td>• What are the short- and long-term outcomes of PCCI?</td>
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<tr>
<td>• Are there lifelong physiologic implications of meeting diagnostic criteria for PCCI? Do children “recover” from PCCI?</td>
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<tr>
<td>Family, medical team, and health system</td>
<td>• What clinical and communication skills are needed to optimize the care of PCCI patients? How can they be taught?</td>
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<tr>
<td>• What are the specific palliative care needs of the PCCI population?</td>
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<tr>
<td>• What is the role of longitudinal care providers in the care of patients with PCCI?</td>
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<tr>
<td>• What are the appropriate care settings for children with PCCI?</td>
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<tr>
<td>• Where should hospital care be provided for older adolescents/young adults with PCCI?</td>
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<tr>
<td>• What are the effects of PCCI on families?</td>
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<tr>
<td>• What supports do families need when caring for a child with PCCI?</td>
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<tr>
<td>Outcomes</td>
<td>• How do we improve our assessment of global outcomes of PCCI?</td>
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<tr>
<td>• What can hospital indicators (eg, readmission rate, LOS), quality of life indices (eg, inpatient and outpatient HRQOL), functional status measures, and developmental assessments tell us about PCCI?</td>
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<tr>
<td>• What can indices of caretaker/family coping and satisfaction tell us about PCCI?</td>
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<tr>
<td>Societal</td>
<td>• What is the epidemiology of PCCI?</td>
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<td>• Are there regional variations in the incidence of, medical management, and care settings for children with PCCI?</td>
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<tr>
<td>• How do we appropriately and fairly allocate health care resources in PCCI? What ethical issues arise around PCCI?</td>
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HRQOL, health-related quality of life.

and societal implications. Our proposed definition for PCCI as a starting point for relevant clinical decisions and research efforts (Fig 2):

1. Pediatric patients who remain hospitalized in a NICU >28 days postterm corrected age, or in a PICU >14 consecutive days, or who have a history of prolonged ICU stay and ≥2 acute care or ICU admissions within 12 months;
and

2. Ongoing dependence on one or more technologies to sustain vital functions (eg, tracheostomy, invasive/noninvasive mechanical ventilation, gastrostomy/jejunostomy tube, dialysis) or persistent multiple vital organ system involvement.

We see 2 pathways for entry to CCI in children: neonatal and pediatric. Neonatal patients with CCI are those who are born with conditions that immediately require ICU care due to disease-related morbidity and mortality. These patients have predictable needs for critical care interventions, prolonged and/or frequent hospitalizations, and ongoing complex care needs. Their condition is accompanied by developmental and functional impairment and high risk of early death. Examples include severe congenital heart disease complicated by seizures, renal insufficiency and/or feeding intolerance; syndromes associated with chromosomal anomalies involving the development and function of multiple organ systems; and infants with extreme prematurity complicated by chronic lung disease, short gut syndrome, feeding difficulties, and/or neurologic or developmental impairment.

Pediatric patients with CCI are divided into 2 categories. Those with underlying vulnerabilities are children with medical complexity who may spend months to years in stable outpatient care before enduring progressive decline, triggered by acute critical illness. Examples include end-stage cystic fibrosis and progressive neuromuscular disorders with respiratory failure. These children are at risk for acute decompensations, prolonged ICU stays, and functional limitations. There may also be unique considerations for patients outside the typical pediatric age range (ie, >18 years old) whose chronic underlying conditions make them more similar to pediatric patients than adults. Those without underlying vulnerabilities are previously healthy children with an acquired illness or injury whose prolonged ICU stay may result from the initial condition or complications thereof; examples include traumatic brain injury and cancer.

The proposed definition clearly has its limits; any health care practitioner who cares for children with CCI can likely imagine a patient who either meets the criteria, but whom they would not consider to have CCI, or who does not meet the criteria, but seems obviously to have CCI. There are many challenges in defining this patient population, including its heterogeneity from a disease standpoint and the fact that pediatrics encompasses patients from neonates through adolescence. In addition, there is wide variability across the United States in how children with chronic conditions and technology dependence are cared for in hospitals (eg, some always in ICUs, some rarely in ICUs). There is much more work to be done in figuring out how to define this population to enable early identification in the clinical environment and to facilitate the application of administrative databases, building on existing CCC or Pediatric Medical Complexity Algorithm criteria, for ongoing research. Our intention in proposing this definition is to launch the conversation. We hope this definition serves as a starting point for further discussion and refinement, with the goal of achieving a PCCI definition meaningful for clinical care, research, and resource allocation.

CONCLUSIONS

PCCI patients experience increased morbidity and mortality compared with the general population of infants and children.
receiving critical care. Despite the fact that research over the past decade has shown the existence of this patient population, as well as their high health care costs, poor outcomes, and significant ongoing health care needs, practices in NICUs and PICUs have not evolved with respect to these patients. PICU mortality has improved for short-stay patients but remained stable for long-stay patients, suggesting that although we have improved delivery of acute critical care, we lag behind in improving provision of chronic critical care. Early identification of NICU and PICU patients who are at high risk for prolonged, complicated hospitalizations and relatively poor outcomes could help target interventions and resources for both patients and families. As a critical starting point for research in this arena, we have proposed a definition of PCCI that incorporates age, developmental status, and the existence of congenital or acquired underlying conditions and comorbidities. We have highlighted key elements of what is known about PCCI and identified critical areas of inquiry that will advance the care of this growing patient population.

Acknowledgments
We thank the additional members of the Pediatric Chronic Critical Illness Working Group (Rebecca Seltzer, Emily Hahn, Erin Williams, and Katherine Marcus) for their contributions to the research presented here.

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### Defining Pediatric Chronic Critical Illness for Clinical Care, Research, and Policy

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