Collaborative Pediatric Critical Care Research Network (CPCCRN)*

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Pediatric critical care was formally recognized as a separate subspecialty in pediatrics in 1987. Since that time the numbers of pediatric intensivists, pediatric intensive care units, and pediatric intensive care beds in the United States have increased dramatically. Research efforts have lagged behind, however, as this new discipline has struggled to identify the necessary time, funding, and other resources to pursue clinical and laboratory investigation. In April 2004, the National Center for Medical Rehabilitation Research of the National Institute for Child Health and Human Development issued a request for applications to establish the Collaborative Pediatric Critical Care Research Network (CPCCRN). The CPCCRN provides an infrastructure to pursue collaborative clinical trials and descriptive studies in pediatric critical care medicine. Six pediatric centers involving seven intensive care units and a data-coordinating center were identified through a competitive application process. Network goals include the support of collaborative clinical trials otherwise impracticable in single institutions and the establishment of a framework for developing the scientific basis for pediatric critical care practice. This article describes how the CPCCRN was established, its organization, and its goals and future plans. (Pediatr Crit Care Med 2006; 7:301–307)

KEY WORDS: pediatric critical care; pediatric intensive care unit; clinical research; collaborative network; National Institutes of Health; National Institute of Child Health and Development

The first intensive care units developed primarily from the need to treat the acute and chronic respiratory problems incurred from a worldwide epidemic of polio in the 1950s (1). In the United States in the early 1950s, children were clustered for care in their "iron lungs" at Rancho Los Amigos Hospital in California (Fig. 1), although the first specifically designated pediatric intensive care unit (PICU) originated in Goteberg, Sweden, in 1955 (2). The first PICU in the United States was established at Children's Hospital of Philadelphia in 1967 followed within months by Boston Children's Hospital (2). The subspecialty emerged from the concordance of multiple disciplines, particularly anesthesiology, adult respiratory intensive care, pediatric pulmonology, pediatric surgery, cardiothoracic surgery, and neonatology.

The Society of Critical Care Medicine was formed in 1970 as a multidisciplinary organization focused on the care of the critically ill, including critically ill infants and children. Critical care nursing soon followed, with the establishment of the American Association of Critical Care Nurses in 1975 and the first certifying exam administered in 1976. The American Association for Respiratory Therapy (now the American Association of Respiratory Care) was established in 1973 and has maintained an intensive care focus since its inception. Critical care subspecialty programs for nurse practitioners, physician assistants, pharmacists, and allied health professionals have also developed.

In the United States, the American Board of Pediatrics first recognized pediatric critical care as a subspecialty in 1985, and the first certifying examination was administered in 1987. By the end of 2004, American Board of Pediatrics board certification had been conferred on 1,287 candidates (3). Currently the number of fellows entering subspecialty training in pediatric critical care in the United States is second only to neonatology (Table 1). Concomitant with the increase in pediatric intensivists, the number of PICUs and PICU beds has shown steady growth at a time when the number of pediatric ward beds and total pediatric discharges in the United States has been steadily decreasing (Fig. 2) (4, 5).

Although the role of the pediatric intensivist in the care of critically ill children is well established, pediatric critical care continues to evolve as a subspecialty and expand into other aspects of pediatric hospital care. In some hospitals, pediatric intensivists have assumed the broader role of "hospitalist," a role consistent with the fact that fewer but more severely ill pediatric patients are being hospitalized and intensivists are increasingly available in the hospital 24 hrs a day (5). As more imaging and therapeutic procedures are being performed on children, intensivists also find themselves in the role of administering sedation and analgesia both within and outside of the PICU (6,

*See also p. 386.

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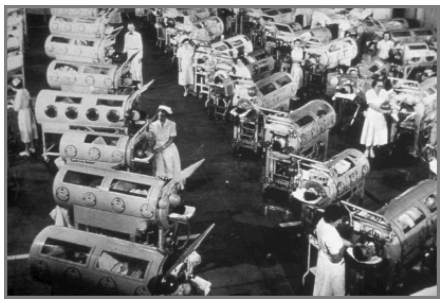

Figure 1. Iron lung unit at Rancho Los Amigos, Los Angeles, CA, circa 1952.

7). Finally, because most children who die in our hospitals die in the PICU, the role of pediatric intensivists in end-of-life care (palliative care) and bereavement has evolved through experience and by necessity (8).

The PICU patient population also continues to change. Current vaccines prevent or limit many diseases that were commonly seen in PICUs (e.g., epiglottitis, meningitis, pneumonia), improved vehicle design and trauma response measures have decreased the number and severity of trauma victims (9–11) (although new types of vehicles with associated injuries have emerged) (12), and new surgeries (e.g., for hypoplastic left heart syndrome) and therapies (e.g., bone marrow, liver, and heart transplant) have enabled survival for children who formerly perished. PICU mortality has decreased (13, 14), and the number of children with chronic medical conditions has proportionately increased (15). Survivors of pediatric intensive care increasingly require sophisticated medical support, many living with chronic medical conditions or disability.

NEED FOR AND BARRIERS TO RESEARCH

Many practices in pediatric critical care evolved without adequate study (16, 17) or were adopted uncritically from adult intensive care (fluid management, vasoactive drug support), anesthesiology (mechanical ventilatory support, neuromuscular blockade), or neonatology (extracorporeal membrane oxygenation, high-frequency ventilation). Indeed the risk vs. benefit of much of what we do remains largely unstudied and/or poorly understood (18–21). Consequently "practice variation" is the norm and has been shown to be associated with poorer outcomes and increased resource utilization (22, 23). Pediatric critical care also consumes a disproportionate share of pediatric health care expenditures, and yet little is known about the effectiveness of our care beyond the immediate period of hospitalization.

Examples of ongoing controversies in pediatric critical care that will require rigorous research for resolution abound; for example, beyond fluid resuscitation and appropriate antibiotic therapy we understand little about optimal therapy for sepsis; low tidal volume ventilation and strict blood glucose control have been uncritically adopted from studies in adults without examination in children; and although many of our patients have chronic medical illnesses little attention has been directed at what might prevent their deterioration to critical illness or how they fare once they leave the intensive care unit. Research in these and other areas of pediatric critical care is long overdue but requires collaborative, multiple-center longitudinal studies that have heretofore been unfeasible given the paucity of funding for clinical research.

Despite the obvious need, the barriers to research in pediatric critical care are many. It is a young field and most intensivists chose critical care because of a strong orientation toward clinical care rather than research. A recent survey found that on average pediatric intensivists spent <15% of their time in active research and <10% devote

Table 1. 2004 pediatric subspecialty fellows by training level (yr)[a]

Pediatric Subspecialty	1	2	3	4	Total
Adolescent medicine	24	28	22	1	75
Cardiology	116	89	86	15	306
Critical care medicine	139	108	83	5	335
Developmental-behavioral + neurodevelopmental	34	30	21	1	86
Emergency medicine	114	100	82	1	297
Endocrinology	71	72	57	1	201
Gastroenterology	73	62	52	3	190
Hematology/oncology	135	122	99	12	368
Infectious disease	65	60	52	2	179
Neonatal-perinatal medicine	224	195	173	4	596
Nephrology	46	42	27	1	116
Pulmonology	50	51	29	2	132
Rheumatology	24	20	14	0	58
Medicine/pediatrics	4	1	10	13	28
Subspecialties (all)					

[a] American Board of Pediatrics, 2004.

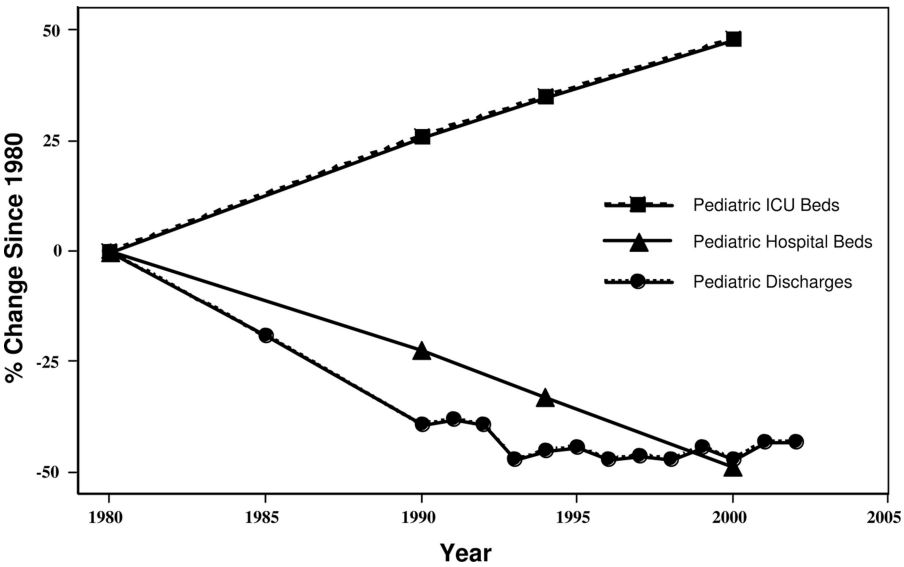

Figure 2. Changes in pediatric beds and discharges. Since 1980, total pediatric hospital beds decreased by 48% whereas pediatric intensive care unit (*ICU*) beds increased an identical percent. Total pediatric hospital discharges decreased by 47% over the same time period.

>50% of their time exclusively to laboratory or clinical investigation (24). The paucity of established researchers in the field makes identification of mentors problematic. Clinical research in our field is also difficult because of the relatively small numbers of any single type of patient, generally precluding meaningful single institution clinical studies and necessitating collaboration with other (often many) institutions. Such collaborative clinical studies require significant funding and research infrastructure and advance few careers beyond that of the primary investigator, both major issues in large-scale clinical trials. Defining adequate outcome measures is also challenging. Mortality in PICU patients is generally low (3–5%) (25), and acceptable intermediate outcome measures are not well established. Longitudinal studies are also necessary for more meaningful assessment of functional and rehabilitative outcome. These barriers are not insurmountable but, on the pessimistic side, the trend toward an expanded clinical role for pediatric intensivists (sedation, hospitalist, palliative care) as well as a general trend toward 24-hr "in-house" call may compromise our ability to respond to these research needs and portends poorly for our research future (26).

COLLABORATIVE PEDIATRIC CRITICAL CARE RESEARCH NETWORK (CPCCRN)

Conception and Development. In his 1992 historical review of the development of pediatric critical care, Jack Downs identified the absence of outcome studies on "all ages and major conditions including major trauma, sepsis, ARDS, and multiple organ failure" as a significant deficiency that would demand future attention (2). Development of clinical research networks to address these issues was a logical solution given the diversity of our patient population and the small numbers of a given patient type even at our largest institutions. Precedents existed in other pediatric subspecialties including oncology (Children's Oncology Group, Pediatric Oncology Group, etc.) and neonatology (Neonatal Research Network, VT Oxford Network) as well as other medical specialties (the ARDSnet in adult intensive care and the Maternal Fetal Medicine Units Network in Obstetrics). Loose associations of pediatric intensive care groups performed clinical trials in the middle 1980s (27), and shortly thereafter regional networks such as the Pediatric Critical Care Study Group (28–30) and the Mid-Atlantic Pediatric Critical Care Network (31, 32) enjoyed limited success but suffered from inadequate funding and infrastructure to sustain ongoing collaborative studies. However, multiple-institution research centered primarily on risk adjustment and assessment of quality using severity scoring methods, funded primarily by the Division of Maternal and Child Health, was quite successful (33–36). More recently, the National Association of Children's Hospitals and Related Institutions has sponsored two successful multiple-institution studies (37, 38). The Pediatric Acute Lung Injury and Sepsis Investigators network has also accomplished significant multiple-institution collaboration but relies entirely on individual investigators to obtain funding for specific projects (39–41).

In April 2004, the National Center for Medical Rehabilitation Research within the National Institute for Child Health and Development (NICHD) issued a request for applications to establish a pediatric critical care and rehabilitation research program "to initiate a multicentered program designed to investigate the safety and efficacy of treatment and management strategies to care for critically ill children, as well as the pathophysiological basis of critical illness and injury in childhood" (42). The program provides funding for six cooperative agreements for clinical sites as well as a data-coordinating center. Selection for the network was accomplished in January 2005, following a competitive peer-review process focused on the expertise of the principal investigator (required to be a pediatric intensivist), institutional resources for critical care and rehabilitation at the clinical site, quality of the submitted research proposal, and geographic and population diversity. The competition was limited to intensive care units within the United States.

Structure and Organization of the CPCCRN. Cooperative agreements were awarded to six clinical centers (seven sites) and the data-coordinating center (DCC) (Appendix). Each clinical center has principal and alternate investigators who are pediatric intensivists, as well as a research coordinator and data administrator. The principal investigator has overall responsibility for the center's participation and performance in the network. The research coordinator organizes and monitors the day-to-day tasks of the network studies, and the data administrator is responsible for data collection, cleaning, and entry. The DCC is led by a pediatric intensivist and includes biostatisticians, programmers, data analysts, and administrative personnel. The DCC is responsible for overall coordination of network logistics and assists in the planning and design of all projects. This includes assistance with statistical and study design, data collection, data analysis, record keeping, and oversight of the conduct of the study. The NICHD project scientist and program officer are responsible for the overall management and direction of the CPCCRN. This partnership between the NICHD and network investigators is designed to stimulate network productivity and ensure its focus on important research questions. The research infrastructure support as outlined not only allows the investigators the protected time and funding necessary to develop and pursue rigorous clinical research but also enables their collaboration with multiple investigators and gives them access to the network's large patient population—advantages largely deficient in previous collaborative networks in pediatric critical care.

The CPCCRN is directed by the Steering Committee, consisting of the principal investigators of the six clinical centers and the DCC, the NICHD project scientist, and an independent chairman appointed by the NICHD. Standing committees have been established to a) provide oversight of all publications and presentations; b) determine the priority given to studies approved by the Steering Committee; c) review all study budgets and assist the NICHD to determine capitated study costs; d) review all studies regarding ethical and regulatory issues; and e) review ongoing research external but relevant to the network (to ensure that clinical sites enroll patients preferentially into CPCCRN studies). Each approved study has an *ad hoc* committee to develop, implement, and monitor the study and write the resulting manuscripts.

CPCCRN study development follows a rigorous process shown in Figure 3. Studies pass through an initial concept phase to a more detailed mini-protocol and then to a complete protocol, each

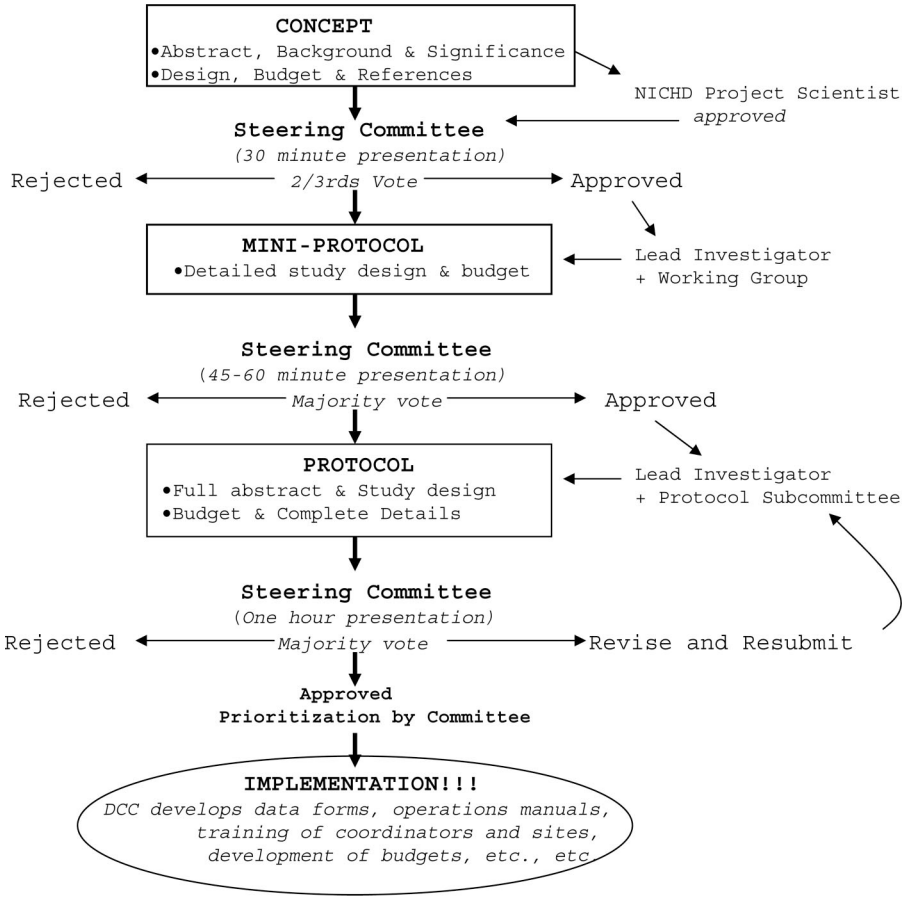

Figure 3. Study development and implementation in the Collaborative Pediatric Critical Care Research Network. *NICHD*, National Institute for Child Health and Development.

requiring Steering Committee approval before moving to the next stage. Once a protocol is approved, it is the task of the protocol subcommittee chair (generally the principal investigator of the study) to work with the DCC to develop case report forms, establish training procedures for participating centers, and finalize details regarding study design and statistical analysis. Studies are then implemented in an order determined by the prioritization committee and are funded by a capitation mechanism in an amount determined by the Capitation Committee, taking into account the available funds, the additional expenses incurred per patient enrolled in the proposed study, and the priorities of the NICHD and the CPCCRN. In the process of review and approval, ancillary or secondary studies may be attached to a primary (or "main") study but require the same approval process. Such secondary or ancillary studies may not detract from the primary study.

A member of the Steering Committee or one of the alternate investigators must be accountable for each study conducted within the network and functions as the lead investigator for the study. However, proposals from non-network investigators are welcomed for consideration, and interested investigators are encouraged to contact one of the Steering Committee members (Appendix). Non-network investigators may participate as an expert consultant on a specific study, as a collaborating investigator with a network principal investigator, or as an investigator for an ancillary or satellite site for a given study. Although the CPCCRN consists of only six clinical centers, some studies may require a larger sample size and patient recruitment from additional sites would be funded with subcontract mechanisms between those additional sites and an existing CPCCRN clinical center. In these instances, the CPCCRN principal investigator will be responsible to ensure that all federal requirements were fulfilled at ancillary or satellite sites. Additionally, the network would consider industry-funded studies of sufficient scientific merit providing funding is coordinated through the NICHD and the network retains control of the conduct of the study and publication of results. For all studies, the network will abide by all National Institutes of Health policies regarding conflict of interest.

The Data Safety and Monitoring Board and Advisory Board provide oversight of CPCCRN research. Both boards are appointed by the NICHD. The Data Safety and Monitoring Board is composed of experts in the fields of pediatric critical care, ethics, biostatistics, and other areas of special expertise as needed. The Advisory Board advises the Steering Committee regarding scientific merit and potential clinical impact of proposed studies and is composed of both experts in pediatrics as well as laypeople with experience and/or interest in pediatric critical care or pediatric rehabilitation.

Patient Population Available to the CPCCRN. The six clinical centers involving seven PICUs are geographically diverse tertiary pediatric hospitals and serve a mixture of urban, suburban, and rural patients. The CPCCRN patient population is described in Tables 2 and 3. This distribution is more heavily weighted toward minority populations than in the U.S. population in general but in that respect better represents the ethnic and racial composition of most PICU populations (43, 44). PICU patients are disproportionately poor, disabled, and younger than the general U.S. pediatric population. The distribution of patients by age is shown in Table 3.

Long-Term Goals of CPCCRN. The primary goal of the CPCCRN is to perform rigorous clinical research in pediatric critical care, with careful consideration of long-term functional outcome following critical illness. Any scientific question of significant relevance to the field of pediatric critical care would be considered, with an obvious emphasis on studies requiring multiple-institution collaboration and collaboration with our rehabilitation medicine colleagues. The network will enable studies that cannot be accomplished in single institutions and/or that require significant research infrastructure. It will also act as a platform on which to translate discoveries made in the laboratory into improvements in clinical care, as well as bringing clinical questions that arise in the course of caring for critically ill children back to the laboratory. Success should lead to the

Table 2. CPCCRN patient population 2003

Hospital	Ethnicity or Race (%)						Total No. of Admissions
	NHW	H	AA	NA	A/PI	Other	
Arkansas Children's Hospital	69.5	4.2	24.6	<1	<1	<1	1110
Children's Hospital Los Angeles and UCLA	20	55	6.2	0.6	7.7	10.7	1884 (CHLA) 1564 (UCLA)
Children's Hospital of Michigan	35	3	60	<1	2	<1	1392
Children's National Medical Center	19	10	67	1.3	2.7	<1	1313
Pittsburgh Children's Hospital	70	5	20	<1	5	<1	2064
Seattle Children's Hospital	64	9	5.1	1.3	5.2	13	1223
Total admissions (2003)							10,550

NHW, non-Hispanic White; H, Hispanic; AA, African-American; NA, Native American; A/PI, Asian or Pacific Islander.

Table 3. Age distribution and diagnostic categories from six centers

Diagnostic Category	Percent	Age Distribution, Yr	Percent
Trauma	7	<1	24.9
Surgical (non-trauma, non-cardiovascular)	29.4	1–5	29.3
Surgical (cardiovascular)	19.2	5–14	27.4
Medical non-BMT, non-Oncology	40.2	14–21	16.8
Medical BMT/oncology	4.3	>21	1.6

BMT, bone marrow transplant.

development of a sustainable clinical research infrastructure and the fostering of young investigators able to lead the next generation of pediatric intensivists and pediatric critical care investigators.

Studies currently in planning in the Network include: a) a randomized controlled trial of metaclopramide, zinc, selenium, and glutamine to improve immune competence and prevent nosocomial infection; b) a study of the epidemiology and outcomes in critical pertussis in infants; c) a study designed to develop and validate a functional status scale; and d) a study of bereavement and interventions to prevent pathologic grief. Other studies under discussion include a randomized controlled trial of steroids in septic shock; studies examining adjunctive agents to ameliorate narcotic tolerance and withdrawal; a study to develop a decision support tool for mechanical ventilation; and a collaborative effort with other networks and investigators to evaluate the possible efficacy of hypothermia after cardiac arrest. The results of all clinical trials would be reported on the National Institutes of Health database (http://clinicaltrials.gov). Periodic updates of ongoing network studies will be reported in *Pediatric Critical Care Medicine*.

The network also intends to join the conversation regarding the complex ethical issues of research in children. Pediatric intensivists have always recognized the difficulties inherent in clinical investigation in children but feel an ethical obligation to study rigorously the therapies and technologies used in pediatric critical care because much of our practice could legitimately be considered "experimental." Improving care can most effectively be accomplished by careful, well-designed clinical studies. Ultimate success of the CPCCRN will foster the spirit of continuing investigation in pediatric critical care and the eventual adoption of evidence-based medicine in our subspecialty.

CONCLUSIONS

Pediatric critical care has matured rapidly as a pediatric subspecialty. As with all new specialties in medicine, however, scientific investigation has lagged behind empirical clinical practice. Progress in research has been hindered by high clinical demands, inherent limitations in patient recruitment due to the nature of our patient population, and inadequate funding. In response to these difficulties, the NICHD has funded the CPCCRN to enable rigorous, multi-institutional clinical research. This report has outlined the structure, processes, and goals of this new network.

REFERENCES

1. Lassen HCA: A preliminary report on the 1952 epidemic of poliomyelitis in Copenhagen. With special reference to the treatment of acute respiratory insufficiency. *Lancet* 1953; 37–41
2. Downs JJ: The historical evolution, current status, and prospective development of pediatric critical care. *Crit Care Clin* 1992; 8:1–22
3. American Board of Pediatrics. Available at: http://www.abp.org/stats/numdips.htm
4. National Center for Health Statistics. Health, United States, 2003. Hyattsville, MD, 2003. Available at: http://www.cdc.gov/nchs/hus.htm
5. Randolph AG, Gonzales CA, Cortellini L, et al: Growth of pediatric intensive care units in the United States from 1995–2001. *J Pediatr* 2004; 144:792–798
6. Wheeler DS, Vaux KK, Ponaman ML, et al: The safe and effective use of propofol sedation in children undergoing diagnostic and therapeutic procedures: experience in a pediatric ICU and a review of the literature. *Pediatr Emerg Care* 2003; 19:385–392
7. Hertzog JH, Campbell JK, Dalton HJ, et al: Propofol anesthesia for invasive procedures in ambulatory and hospitalized children: Experience in the pediatric intensive care unit. *Pediatrics* 1999; 103. Available at: http://www.pediatrics.org/cgi/content/full/103/3/e30
8. Meert KL, Thurston CS, Briller SH: The spiritual needs of parents at the time of their child's death in the pediatric intensive care unit and during bereavement: A qualitative study. *Pediatr Crit Care Med* 2005; 5:420–427
9. Dowd MD, Keenan HT, Bratton SL: Epidemiology and prevention of childhood injuries. *Crit Care Med* 2002; 30(Suppl):S385–S392
10. Henry MC, Hollander JE, Alicandro JM, et al:

Prospective countrywide evaluation of the effects of motor vehicle safety device use on hospital resource use and injury severity. *Ann Emerg Med* 1996; 28:627–634
11. Vernon DD, Furnival RA, Hansen KW, et al: Effect of a pediatric trauma response team on emergency department treatment time and mortality of pediatric trauma victims. *Pediatrics* 1999; 103:20–24
12. Cvijanovich NZ, Cook LJ, Mann NC, et al: A population-based assessment of pediatric all-terrain vehicle injuries. *Pediatrics* 2001; 108: 631–635
13. Hallahan AR, Shaw PJ, Rowell G, et al: Improved outcomes of children with malignancy admitted to a pediatric intensive care unit. *Crit Care Med* 2000; 28: 3718–3721
14. Rossi R, Shernie SD, Calderwood S: Prognosis of pediatric bone marrow transplant recipients requiring mechanical ventilation. *Crit Care Med* 1999; 27:1181–1186
15. Graham RJ, Dumas HM, O'Brien JE, et al: Congenital neurodevelopmental diagnoses and an intensive care unit: Defining a population. *Pediatr Crit Care Med* 2004; 5:321–328
16. Newth CJ, Rachman B, Patel N, et al: The use of cuffed versus uncuffed endotracheal tubes in pediatric intensive care. *J Pediatr* 2004; 144:333–337
17. Anand KJ, Runeson B, Jacobson B: Gastric suction at birth associated with long-term risk for functional intestinal disorders in later life. *J Pediatr* 2004; 144:449–454
18. Carcillo JA: Pediatric septic shock and multiple organ failure. *Crit Care Clin* 2003; 19: 413–440
19. Anand KJ: Pain, plasticity, and premature birth: A prescription for permanent suffering? *Nat Med* 2000; 6:971–973
20. Vavilala MS, Lee LA, Boddu K, et al: Cerebral autoregulation in pediatric traumatic brain injury. *Pediatr Crit Care Med* 2004; 5:257–263
21. Markovitz BP, Goodman DM, Watson RS, et al: A retrospective cohort study of prognostic factors associated with outcome in pediatric severe sepsis: What is the role of steroids? *Pediatr Crit Care Med* 2004; 5:509
22. Willson DF, Horn SD, Hendley JO, et al: The effect of practice variation on resource utilization in infants hospitalized with viral lower respiratory illness (VLRI). *Pediatrics* 2001; 108:851–855
23. Willson DF, Jiao JH, Donowitz L, et al: invasive monitoring in infants with respiratory syncytial virus infection. *J Pediatr* 1996; 128: 357–362
24. Anderson MR, Jewett EA, Cull WL, et al: Practice of pediatric critical care medicine: Results of the Future of Pediatric Education II Survey of Sections Project. *Pediatr Crit Care Med* 2003; 4:412–417
25. Tilford JM, Roberson PK, Lensing S, et al: Differences in pediatric ICU mortality risk over time. *Crit Care Med* 1998; 26: 1737–1743
26. Nicholson CE, Gans BM, Chang AC, et al: Pediatric critical care medicine: Planning for our research future. *Pediatr Crit Care Med* 2003; 4:196–202
27. Oren J, Newth CJL, Hunt CE, et al: Ventilatory effects of almitrine bismesylate in congenital central hypoventilation syndrome. *Am Rev Respir Dis* 1986; 134:917–919
28. Moler FW, Steinhart CM, Ohmit SE, et al: Effectiveness of ribavirin in otherwise well infants with respiratory syncytial virus-associated respiratory failure. Pediatric Critical Care Study Group. *J Pediatr* 1996; 128: 422–428
29. Green TP, Timmons OD, Fackler JC, et al: The impact of extracorporeal membrane oxygenation on survival in pediatric patients with acute respiratory failure. Pediatric Critical Care Study Group. *Crit Care Med* 1996; 24:323–329
30. Timmons OD, Havens PL, Fackler JC: Predicting death in pediatric patients with acute respiratory failure. Pediatric Critical Care Study Group, Extracorporeal Life Support Organization. *Chest* 1995; 108: 789–797
31. Willson DF, Jiao JH, Bauman L, et al: Calf's lung surfactant extract in acute hypoxemic respiratory failure in children. *Crit Care Med* 1996; 24:1316–1322
32. Willson DF, Bauman LA, Zaritsky A, et al: Instillation of calf's lung surfactant extract (Infasurf) is beneficial in pediatric acute hypoxemic respiratory failure. *Crit Care Med* 1999; 27:188–195
33. Pollack MM, Ruttimann UE, Getson PR: Pediatric risk of mortality (PRISM) score. *Crit Care Med* 1988; 16:1110–1116
34. Pollack MM, Patel KM, Ruttimann UE: The Pediatric Risk of Mortality III-Acute Physiology Score (PRISM III-APS): A method of assessing physiologic instability for pediatric intensive care unit patients. *J Pediatr* 1997; 131:575–581
35. Shann F, Pearson G, Slater A, et al: Paediatric index of mortality (PIM): A mortality prediction model for children in intensive care. *Intensive Care Med* 1997; 23:201–207
36. Slater A, Shann F, Pearson G: PIM2: A revised version of the Paediatric Index of Mortality. *Intensive Care Med* 2003; 29: 278–285
37. Quasney MW, Goodman DM, Billow M, et al: Routine chest radiographs in pediatric intensive care units. *Pediatrics* 2001; 107:241–248
38. Kurachek SC, Newth CJ, Quasney MW, et al: Extubation failure in pediatric intensive care: A multiple-center study of risk factors and outcomes. *Crit Care Med* 2003; 31: 2657–2664
39. Randolph AG, Wypij D, Venkataraman ST, et al: Effect of mechanical ventilator weaning protocols on respiratory outcomes in infants and children: A randomized controlled trial. *JAMA* 2002; 288:2561–2568
40. Willson DF, Thomas NJ, Markovitz BM, et al: Effect of exogenous surfactant in pediatric acute lung injury: A randomized, controlled trial. *JAMA* 2005; 293:470–476
41. Curley MAQ, Hibberd PL, Fineman LD, et al: Effect of prone positioning on clinical outcomes in children with acute lung injury. A randomized, controlled trial. *JAMA* 2005; 294:229–237
42. RFA-HD-04-004 (Clinical Centers) http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-04-004.html; and RFA-HD-04-015 (Data Coordinating Center) http://grants1.nih.gov/grants/guide/rfa-files/RFA-HD-04-015.html; National Institute of Child Health and Human Development, Department of Health and Human Service, April 2004
43. Naclerio AL, Gardner JW, Pollack MM: Socioeconomic factors and emergency pediatric ICU admissions. *Ann N Y Acad Sci* 1999; 896:379–382
44. Suruda A, Burns TJ, Knight S, et al: Health insurance, neighborhood income, and emergency department usage by Utah children 1996–1998. *BMC Health Serv Res* 2005; 5:29

APPENDIX

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  - Research coordinator: A. Abraham
  - Data administrator: K. Bongiorni
- Seattle Children's Hospital
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  - Alternate investigator: T. Brogan, MD
  - Research coordinator: R. Barker, RN
  - Data administrator: S. Craig
- Data Coordinating Center, University of Utah
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  - Biostatistician: R. Holubkov, PhD
  - Program manager: J. Burr
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- University of Virginia Children's Hospital
  - Network Chairman: D. Willson, MD