

Pediatric Palliative Care Research Comes of Age: What We Stand To Learn from Children with Life-Threatening Illness

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THIS ISSUE OF THE *JOURNAL OF PALLIATIVE MEDICINE* includes three publications providing evidence to inform the provision of palliative care for children with life-threatening illness (LTI) and their families. The authors of these pieces are to be commended for sharing their experience with the larger palliative care community in an effort to advance knowledge and understanding in the field. These works highlight innovative strategies to reduce suffering and improve the well-being of seriously ill children and families. Nevertheless, it is worthwhile noting the nature of these studies: they are case studies or reports. Such descriptive studies, based on a limited sample, are emblematic of the current state of the science in pediatric palliative care research.

Whereas the numbers of children living with serious illness are notably smaller than those of adults, they are still considerable. In 2010, 45,000 children died in the United States; over 25,000 children are living with a serious illness at any given time; and nearly 17 million adults are serving as caregivers to a seriously ill child.¹ In the absence of evidence on which to base pediatric palliative care practice, too often decisions are made based upon anecdote; and experience or knowledge gleaned from the study of adult populations is extrapolated and applied to children. Whereas in a few instances the latter strategy may be acceptable (e.g., opioids for dyspnea, strategies for treatment of chemotherapy induced nausea), in most it is unacceptable, and research focusing specifically on children is imperative. Reasons for this are many, and include the distinct patterns of pediatric life-threatening conditions and developmental and physiologic considerations specific to children. In sum, as trainees entering pediatrics learn early on, “children are not small adults.”

The Way Forward: Priorities in Pediatric Palliative Care Research

The next steps forward must address important clinical questions of interest. They must also build on existing evidence, fill in gaps in knowledge and practice, and lay a strong foundation on which to build future research. This translates into moving beyond the current status of early-phase descriptive studies and focusing on the identification of impor-

tant outcomes, development of methodologies to evaluate these outcomes, and design of interventions targeting the outcomes of interest.

There is much to be learned about the care of children with LTI, rendering the identification of pediatric palliative care research priorities a challenge. However, the research priorities established should fall into one of two categories. They should be either 1) issues related specifically to children, from which lessons learned from adult research cannot be extrapolated, or 2) unique opportunities for pediatric palliative care research to inform the provision of palliative care for people of all ages.

Pediatric-Specific Issues

Developmental considerations are of considerable import in pediatrics, since neonates, children, and adolescents constitute a broad developmental spectrum. Important questions relating to the intersection of developmental pediatrics and pediatric palliative care exist. Developmental considerations may reflect the child’s chronological age, but also the direct effects from the underlying condition and the child’s experience with being ill. Developmental considerations impact a variety of key elements of palliative care, such as ability to self-report one’s experience, communication of preferences and values, and participation in decision making.

Insight into how children with serious illness perceive and understand their experience, and participate in their care, is needed. While it is appreciated that children can conceptualize death in ways that are influenced by their stage of development, more remains to be learned about how the experience of LTI further shapes their conceptualization of death and other concepts. Even relatively young children with advanced cancer can express their values, goals, and preferences, and participate in decision making.² Development and evaluation of age-appropriate strategies to support these processes, such as the recent development of the My Thoughts, My Wishes, My Voice advance care planning tool for adolescents,³ is needed. How to support parents holding the responsibility of making the best possible decisions on behalf of their child also requires attention.

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Developmental considerations include physiologic processes in children that do not necessarily parallel those of adults. For example, pharmacodynamics and pharmacokinetics as well as the suitability of medication formulations may be quite different for children, and these differences must be considered in the development of safe and efficacious therapeutics for children. Recognizing this, and the dearth of scientifically sound, rigorously designed studies of therapeutic agents and devices for children, the Food and Drug Administration (FDA) has implemented several regulatory initiatives. These include the voluntary pediatric exclusivity provision of the FDA Modernization Act of 1997, subsequently reauthorized in 2002 and extended through 2007 as the Best Pharmaceuticals for Children Act, and more recently, the Pediatric Research Equity Act, which permits the FDA to require studies in children. Research stemming from these initiatives has yielded important information relating to the safety and efficacy of drugs such as midazolam, gabapentin, and fentanyl.

Special populations

The extremes of the pediatric age spectrum, the perinatal and the adolescent and young adult populations, merit special attention. About one half of childhood deaths are in neonates and infants, yet these youngest of children are markedly underserved, representing only 19% of pediatric hospice admissions⁴ and 17% of children receiving inpatient pediatric palliative care consultation.⁵ Advances in the ability to detect life-threatening condition in utero have created a particular need for pediatric palliative care to support families in the perinatal period.

As life-extending interventions postpone childhood deaths, the population of adolescents and young adults with LTI is also growing in magnitude. Adolescents and young adults grapple with issues around independence, peer acceptance, and self-image, all of which are likely to be complicated by LTI. Evidence addressing these adolescent and young adult issues is needed to guide their care.

Symptom patterns

Numerous studies from around the globe document uncontrolled symptoms experienced by children at end of life. However these studies are limited in scope, focusing on children with cancer, at the very end of life, with data gathered retrospectively from bereaved parents or the medical record, and usually from a single institution. A recent study published by the North American based Pediatric Palliative Care Research Network⁵ has deepened our understanding of the symptom experience of children with noncancer diagnoses through a multicenter, prospective approach. Symptoms related to neurologic conditions, including cognitive impairment, speech difficulties, fatigue/sleep disturbance, enteral intake problems and seizures were found to be most prevalent. These findings have important implications. First, patterns of symptoms experienced by children with a nonmalignant LTI may differ significantly from symptoms experienced by children with cancer. Second, the development of instruments to accurately assess symptoms in a developmentally appropriate manner (i.e., children with neurocognitive impairment who may have a limited ability to self-report) is imperative. Third, while about 20% of children experienced somatic pain, they endured a high burden of nonpain symptoms. Improved un-

derstanding of nonpain symptoms and rigorous testing of interventions to relieve them is an essential next step in ameliorating the suffering of children with LTI.

Family as the unit of care

The experience of children with LTI cannot be considered in isolation, but rather in the context of their familial relationships and in conjunction with the experience of members of the family. For this reason, in pediatric palliative care the family is regarded as the unit of care. Parents often struggle to keep the family together while caring for their ill child or in the wake of the child's death. As children with serious illness are surviving longer and are increasingly receiving care outside the hospital, often in the face of limited community-based support, the burden experienced by parents and other family members will only grow. While studies examining the experience of such parents exist, research samples often exhibit a marked gender imbalance, with little representation of fathers.⁶ A more complete understanding of the experience of family members is needed to devise supportive interventions that will benefit a child's entire family.

Research with Broad Applications

Blended goals of care

A distinctive feature of pediatrics is a strong focus on cure/life extension and therefore frequent use of disease-directed treatment or life-extending treatments until the very latest phases of life. This phenomenon likely stems from a combination of factors, including difficult prognostication in the setting of rare pediatric conditions and the fact that the death of a child is frequently felt to be at odds with the natural course of life. Recognition that treatments to cure or extend life up until the moment of death form and will continue to form the standard of care requires the development and study of strategies for supporting families who hold multiple, concomitant goals of care involving curative or life-prolonging therapies in the face of uncertainty. Improved understanding is needed of how families come to hold multiple goals and the ways in which intensive or invasive efforts may inadvertently contribute to suffering in children with advanced illness. Evidence-based strategies are needed to effectively explore goals of care and implement curative or life-prolonging treatments in line with the stated goals, to promote living as well as possible without prolonging dying or increasing suffering. These issues so commonly encountered in the care of children with LTI provide a rich opportunity to answer questions that are also relevant to the care of adults with advanced illness. The pediatric palliative care population is small, but study of it may reveal findings generalizable to the care of adults with LTI.

Linked to this approach is the need to develop models of palliative care delivery that recognize these blended goals. Recent examples of these models include the Patient Protection and Affordable Care Act's Concurrent Care for Children Requirement (CCCR), that requires state Medicaid programs to cover hospice services for children with an estimated prognosis of six months or less, without obligating these children to forego curative treatment or other medically necessary services. Individual states (e.g., Florida, California) have utilized strategies such as a Medicaid Waiver or State Plan Amendment to extend palliative care to all children with LTI, irrespective of

prognostic certainty. Study of the effects of the federal CCCR and state-level initiatives to promote delivery of pediatric palliative care likely will yield important findings that are relevant to provision of palliative care across the entire age spectrum.

Early implementation of palliative care

Because prognostication in the setting of rare and heterogeneous pediatric conditions is complex, estimation of a child's prognosis is often fraught with uncertainty. For this reason and others, early provision of palliative care, even at the time of diagnosis, receives particular emphasis in pediatrics. With early implementation, even before prognosis is established with certainty, the duration of pediatric palliative care provision may be long. Indeed, in the aforementioned Pediatric Palliative Care Research Network study, 70% of children were alive one year after their initial pediatric palliative care consultation.⁵ Study of pediatric palliative care delivery patterns may afford a unique opportunity to inform efforts to deliver palliative care earlier in the course of illness, before prognosis is established, over a longer time horizon.

Community-based palliative care

Many children with LTI receive considerable care at home in the last year of life, and they live predominantly outside the hospital.⁷ There is considerable experience with providing community-based hospice care for adults at the end of life, but the experience of providing a growing population of medically fragile children with palliative care in the community may require different resources and entail different challenges.⁸ Investigation of the models of effective palliative care provision in the community and related outcomes will have important implications for the care of children and adults alike.

Design and conduct of palliative care research

High quality pediatric palliative care research faces many potential barriers, including rarity and heterogeneity of conditions, developmental concerns, low subject enrollment rates, attrition, ethical issues, and the highly emotionally charged nature of caring for children with LTI. While many of these challenges are not unique to pediatric palliative care, they may be particularly problematic in the pediatric population. Lessons learned while surmounting these logistical, ethical, and other barriers are yet another way in which pediatric palliative care research may advance the field of palliative care research as a whole.

Reframing research in children

Through history, biomedical research has often overlooked pediatric-specific issues, leaving clinicians with little evidence on which to base care for their young patients. In other instances, children have been a "special case," requiring study only to benefit the very few children with a given condition.

Palliative care offers a unique opportunity in that pediatric research has the potential to generate knowledge and understanding with broad applications across the age spectrum to persons living with serious illness and their families. As palliative care research priorities are established and the limited resources supporting such research are distributed, we should bear in mind the ways in which pediatric palliative care research can, in fact, afford unparalleled opportunities to advance the frontiers of palliative care innovation and discovery. At the same time, however, we cannot lose sight of the singular importance of pediatric palliative care research irrespective of its application to adult medicine. As Vice President Hubert Humphrey said in his last speech, "The moral test of government is how that government treats those who are in the dawn of life, the children; those who are in the twilight of life, the elderly; and those who are in the shadows of life; the sick, the needy and the handicapped." It is our obligation to ensure adequate federal funding and conduct of high quality research in pediatric palliative care so that publication of case series becomes the exception rather than the norm.

Acknowledgments

Dr. Ullrich is a recipient of a Career Development Award (5K23HL107452-02) from the National Heart, Lung, and Blood Institute. Dr. Morrison is a recipient of a Midcareer Investigator Award in Patient-Oriented Research (5K24AG022345-10) from the National Institute on Aging. This work was also supported by the National Palliative Care Research Center.

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