Article:
Bergstraesser, Eva, Thienprayoon, Rachel, Brook, Lynda et al. (9 more authors) (2021) Top ten tips palliative care clinicians should know about prognostication in children. Journal of Palliative Medicine. pp. 1725-1731. ISSN: 1557-7740

https://doi.org/10.1089/jpm.2021.0439

JOURNAL OF
Palliative Medicine

Journal of Palliative Medicine: http://mc.manuscriptcentral.com/palliative

Top Ten Tips Palliative Care Clinicians Should Know About Prognostication in Children

Journal:	*Journal of Palliative Medicine*
Manuscript ID	JPM-2021-0439
Manuscript Type:	Palliative Care Specialists Series (by Invitation Only)
Keyword:	Prognostication, Pediatric Communication Issues, Pediatric Palliative Care
Manuscript Keywords (Search Terms):	Prognostication in Children, Neonatology, Pediatric Communication issues, Adolescent/Young Adult cancer patients, Pediatric chronic conditions, Pediatric Palliative Care

Top Ten Tips Palliative Care Clinicians Should Know About Prognostication in Children

Eva Bergstraesser; MD, MSc Palliative Medicine;
Department of Pediatric Palliative Care, University Children's Hospital Zurich, Zurich, Switzerland.

Rachel Thienprayoon; MD, MSCS
Division of Palliative Care, Department of Anesthesia, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA.

Lynda Brook; MBChB, MSc;
Alder Hey Children's NHS Foundation Trust, Liverpool, UK.

Lorna K. Fraser; MBChB Phd;
Martin House Research Centre, University of York, Helington, UK.

Jenny L. Hynson; MBBS, PhD;
Department of Paediatrics, University of Melbourne, Melbourne;
Victorian Pediatric Palliative Care Program, The Royal Children's Hospital Melbourne, Meldbourne, Australia.

Abby R. Rosenberg; MD, MS, MA;
Palliative Care and Resilience Lab, Seattle Children's Research Institute, Seattle;
Department of Pediatrics, Division of Hematology/Oncology, University of Washington School of Medicine, Seattle;
Cambia Palliative Care Center of Excellence at the University of Washington, Seattle, WA USA.

Jennifer M. Snaman; MD, MS;
Department of Psychosocial Oncology and Palliative Care, Dana-Farber Cancer Institute, Boston, MA;
Department of Pediatrics, Boston Children's Hospital, Boston, MA, USA.

Meaghann S. Weaver; MD, MPH, PhD;
Division of Pediatric Palliative Care, Department of Pediatrics, Children's Hospital and Medical Center, Omaha, NE;
National Center for Ethics in Healthcare, Washington DC, USA.

Kimberley Widger; RN, PhD;
Lawrence S. Bloomberg Faculty of Nursing, Univeristy of Toronto;
Pediatric Advanced Care Team, Research Institute, Hospital for Sick Children, Toronto, Canada.

Boris Zernikow; MD, PhD;
Pediatric Palliative Care Centre, Children's and Adolescents' Hospital Datteln;
Department of Children's Pain Therapy and Pediatric Palliative Care, Datteln;
Faculty of Health – School of Medicine, Witten/Herdecke University, Witten, Germany.

Christopher A. Jones; MD, MBA;
Department of Medicine, Duke University School of Medicine, Durham, NC, USA.

Mathias Schlögl; MD, MPH;

Centre on Aging and Mobility, University Hospital Zurich and City Hospital Waid Zurich, Zurich; Universtiy Clinic for Acute Geriatric Care, City Hospital Waid Zurich, Zurich, Switzerland.

Corresponding author:
Bergstraesser Eva; MD, MSc Palliative Medicine
Department of Pediatric Palliative Care
University Children's Hospital Zurich
Steinwiesstrasse 75
8032 Zurich, Switzerland
eva.bergstraesser@kispi.uzh.ch

Abstract word count: 101

Word count: 3388 (not including abstract)

Tables/Figures: 0/0

Abstract (100-150 words) 101

Pediatric palliative care (PPC) is different from palliative care for adults. However, conceptualizing PPC remains cumbersome due to the high heterogeneity of often rare diseases, the high diversity of disease trajectories, and the particular difficulty to predict the future of an individual, severely ill child. This article aims to provide an overview and critical reflection of different aspects of prognostication in children with palliative care needs. This includes different diseases from neurology to oncology, from the unborn baby to the young adult, new approaches in treatment, advance care planning, and, most important, communication with the affected child as well as parents.

Introduction:

Prognostication is probably the most demanding task physicians have to learn. Patients and families desire comprehensive information around a life-limiting or life-threatening condition (LL/LTC), which should include a consideration of prognosis. Prognostication in this regard should not be reduced to simply considering the question of "how long" but should include many other factors important to children with serious illnesses and their families. Paul Glare and Christian Sinclair provided important background in their hallmark article on prognostication in medicine;[1] important both for physicians working with adults and for pediatricians, particularly those working with children suffering from LL/LTCs and their families.

Prognostication should be recognized as an important component of care planning, decision-making, and defining goals of care. Uncertainty is an integral part of prognostication, particularly in pediatrics, and should be acknowledged as such. This uncertainty, though, complicates the timing around when to involve palliative care (PC) services, especially in institutions where PC predominantly cares only for those at end-of-life (EOL). Though PC providers understand that PC should be provided independent of prognosis, referring clinicians and parents may conflate PC and EOL care, delaying potentially beneficial support. Whether as an entre to referrals or as a tool to create care plans that align with patient/family values, as accurate an understanding of prognosis as possible is crucial to good care for pediatric patients with LL/LTCs and their families. These top 10 tips for PC physicians aim to illuminate the broad spectrum of prognostication and its impact on the affected child or adolescent, and their family.

Tip 1: Prognostication is difficult for patients of any age but is particularly difficult in children; its domains include likelihood of cure, anticipated quality of life, feasibility of survival, and length of life.

Clinicians may best support communication about prognostication by understanding and appreciating the multi-layered dimensions of prognostication.[2] The word "prognosis" carries vastly different meaning for different people. This diversity of definitions warrants clarity of meaning prior to delving into prognostic disclosures.

Clinicians are wise to seek parent and patient preferences for the forecasting domains of prognosis (cure, quality of life (QOL), survival feasibility, length of life). If a parent thinks prognosis describes *curability* and the provider thinks prognosis means *timeline*, then an announcement about "weeks to months prior to death" would represent alarming information for an unbraced parent simply seeking to understand whether their child's cancer remains curable with chemotherapy. Conversations about prognosis warrant pacing according to family and patient readiness,[1] recognizing opportunities to explore additional prognostic domains and build upon information-sharing during subsequent encounters and growth of the therapeutic relationship.

More complex than a binary "cure" or "unable to cure", prognostication represents the opportunity to discuss both the current time and the future. Attempts at cure may require travel or family relocation, extreme symptom burden to the child, or cumulative impact to the child's childhood experience of play and relationships. Conversations about prognosis should include more than physical or body domains and more comprehensively cover topics such ability to play (known as the work of childhood), to interact with peers and siblings, to engage in developmentally-relevant tasks, and foster spiritual/existential meaning. While parents often desire quantification of prognosis in terms of timelines, expanding the conversation to include additional dimensions of prognosis such as QOL allows clinicians to commit to continued support beyond a binary "curable/incurable" prognostic content.

Tip 2: Prognostication for neonates with LL/LTCs is exceedingly difficult and can inadvertently focus more on function than on infant and family quality of life, reinforcing the value of parallel planning's 'hope for the best and prepare for the worst' approach.

Mortality rates are highest for babies around the time of birth and in the first year of life with 75% of child deaths occurring in this time period.[3] There are also growing numbers of babies and infants with LL/LTCs with uncertain short and long term prognoses in both high[4] and low to middle income countries.[5] Diagnoses in this realm include congenital anomalies, sequelae of prematurity, and birth trauma.[4,5]

Although there are some diagnoses in babies which will have an inevitable fatal outcome,[6] there are many more where the disease trajectory and prognoses are uncertain. Even for those with an expected fatal outcome, defining prognosis in terms of weeks or months, can be challenging given variability within individual diagnoses. This uncertainty highlights the need for a more integrative approach to health care including parallel planning[7] where PC and advance care planning (ACP) are introduced alongside disease-directed care when there is concern for a LL/ LTC.

There is a growing understanding of the need for specialty perinatal or neonatal PC services to work with the existing obstetric and neonatal services in caring for high-risk infants. Involvement of these PC subspecialists shows some evidence of practice change including more family centred care[8] but we lack any consensus on the best model of providing this care.[9] There is also a recognition that this care may require professional education and training specific to this age group.[10]

Tip 3: When discussing prognosis, clinicians should begin by exploring a family's cultural needs and norms, and end with honest, complete, and equitable information delivery.

While racial, cultural, and social disparities in prognostic understanding are well-described among adults with serious illness,[11-14] less is known about pediatric experiences.[15] This data gap is important because non-white children tend to have potentially inferior EOL experiences, including increased pain, symptom distress, and intensity of care.[16-19] A 2007 review of PPC studies attributed these disparities to contextual factors (e.g., access to care and poverty), patient-specific factors (e.g., medical diagnosis), and patient-clinician factors (e.g., clinician bias, trust, and quality of information exchange).[15]

Fortunately, patient-clinician factors are immediately actionable. A study of pediatric oncologists and parents suggested that ~90% of parents wanted comprehensive prognostic information, regardless of their race/ethnicity.[20] However, physicians assumed that <33% of Black and Hispanic parents would want such detail. In a study of parents of children with advanced neuroblastoma (a disease that is rarely curable), non-white parents were 81% less likely to understand their child's poor prognosis than white parents.[21]

These two findings are related; if pediatric clinicians assume diverse families want less information, they likely will communicate less, in turn limiting the family's opportunity to understand. Indeed, established barriers to communication among children with serious illness include foreign language and foreign culture.[19,22,23] Emerging guidelines suggest clinicians must approach all prognostic communication first with curiosity: assume nothing and deliberately explore a family's cultural needs, norms, and style.[23] When families are non-English speaking, communication must be done with a certified medical interpreter. Next, clinicians should deliver comprehensive prognostic information compassionately and honestly. Variations in approach should be tailored to the family's endorsed preferences to improve prognostic understanding for all patients and families.

Tip 4: Though adolescent and young adult patients with cancer desire high-quality prognostic communication from the time of diagnosis, mutual protectionism between

child and parent may delay external prognostic discussions independent of internal prognostic awareness.

Adolescent and young adult (AYA) patients with cancer consider prognostic information important and more extensive prognostic disclosure is associated with improved patient well-being and higher trust in the oncologist.[24] Three-quarters of AYAs expressed that having a precise, numeric understanding of prognosis was important at the time of diagnosis and this percentage increased over the first year.[25] Honest communication about prognosis in advanced cancer, including near the EOL, allows for open exploration of patient and family hopes, worries, and decisions about medical care.[26]

Unfortunately, open prognostic discussions and associated larger goals of care may be hindered by mutual pretense, wherein both parties know information but do not openly acknowledge it with each other.[27] Parents may seek to avoid open discussions about prognosis with their child to protect or shield them from harm and conversely some children may avoid this open communication to similarly protect their parents.[28,29] However, inadequate prognostic communication in AYAs with cancer may result in anxiety and fear at the EOL[30] and lingering regret in parents following the child's death.[31] In a large study of bereaved parents, over one-quarter of those that did not discuss prognosis with their child regretted this decision; parents were more than three times as likely to express regret if the child was a teenager.[32] Clinicians must consider personal, familial, and cultural differences in prognostic disclosure, while engaging in longitudinal, compassionate exploration of both parent and AYA preferences.[26]

Tip 5: Prognostication in advanced pediatric cancer remains difficult and, unlike in adult medical oncology, prognostic and functional scales offer little to no useful guidance.

While several prognostic scales have been developed and tested in adult populations (e.g., Glasgow Prognostic Score, Palliative Performance Scale, Palliative Prognostic Score, Palliative Prognostic Index, Prognosis in Palliative Care Study (PiPS)), similar scales in the

pediatric cancer population are lacking.[33] Some pediatric scales were developed or tested across a variety of LLCs so performance in oncology may be unknown. As well, some scales focus on when to refer a child and family to PC services rather than on prognostication, though the two are related.

In adults, a common prognostic approach is the surprise question: would you be surprised if this person died in the next 12 months.[33] In pediatrics, the surprise question may be more accurate than has been demonstrated in adult populations.[34] For children with cancer, sensitivity of the surprise question was 100% but specificity was 33%, while specificity was 81% and 70% for children with neurological or congenital illnesses respectively.[34] The Paediatric Palliative Screening Scale (PaPaS) was developed and validated to determine the need for PC in children with any LLC, but incorporates the surprise question with a six-month window.[35] The PaPaS has demonstrated feasibility and utility in a mixed population to identify PC needs.[36] Finally, specific to children who received an allogeneic hematopoietic cell transplant (HCT) and required intensive care unit (ICU) admission, risk of mortality during the admission increased when there was pre-existing renal comorbidity, cytomegalovirus seropositivity, less than 100 days from HCT to ICU admission, acute myelogenous leukemia as the underlying condition, and a high Pediatric Risk of Mortality 3 (PRISM-3) score.[37] Outside of the specific situation of HCT, the surprise question and PaPaS may offer some guidance for prognostication in pediatric cancer, but more research is needed.

Tip 6: Several chronic conditions, including Trisomy 13/18, can have wide variations in prognosis depending on the aggressiveness of treatments utilized.

Trisomy 13 (T13) and 18 (T18) are genetic diagnoses that confer multiorgan system anomalies including cardiac malformations and neurologic impairment. T13, also called Patau syndrome, occurs in approximately 1.68 per 10,000 live births and T18 (Edwards syndrome) occurs in approximately 4.08 per 10,000 live births.[38] Despite historic teaching that these

conditions are “uniformly fatal” or “incompatible with life”, multiple large-scale studies have recently demonstrated that a proportion of children with T13 and T18 will live for years. One large international cohort study found that for infants with T13 born live, median first-week mortality was 48%, median first-year mortality was 87%, and cumulative 5-year survival was 7%.[38] That same study found a median first-week mortality of 42% for T18, median first-year mortality of 88%, and cumulative 5-year survival of 7.7%. In a study of patients born in Ontario, Canada over 21 years, Nelson et al. found a one-year survival rate of 19.8% in T13 and 12.6% in T18 and that among those infants with T13 and T18 alive at 6 months, 50.5% and 60% respectively survived to 10 years.[39] Importantly, cardiac and neurologic diagnoses or congenital anomalies in more than one organ system did not confer worse survival in T13 or T18.[39]

Evidence is mounting that surgical and medical interventions may further improve survival rates in children with these conditions.[40] Yet despite an improved understanding of long-term survival in T13 and T18, parents continue to report poor quality medical communication regarding prognosis and decision making for these children.[41] An interdisciplinary approach is warranted in the care of children with T13 and T18, integrating PPC clinicians prenatally and continuing longitudinally, in order to ensure parental counseling that is accurate and attentive to each family’s unique goals and values for the child’s entire length of life.[42]

Tip 7: In children with spinal muscular atrophy (SMA) and other genetically determined life-limiting conditions, gene therapy is a game changer in pediatric palliative care since it prolongs life substantially and leads to new questions regarding ethics, health care costs, and uncertainty of life expectancy.

Not all rare conditions are life-limiting, but a large majority of children receiving PPC suffer rare diseases. The Food and Drug Administration (USA) and the European Medicines Agency (EUROPE) implemented strategies like the Orphan Products Development to enable

development of drugs for rare diseases. These drugs, biological products and techniques will change care for children with LLCs and raise ethical questions. However, it remains unclear when to stop the treatment if gains have not been achieved. Nusinersen and the other gene therapies will change the way of care.[43] They provide palliation but no cure. In parallel, re-imbursement may challenge healthcare systems as well as families.

SMA, an autosomal recessive disorder, is the most common genetic cause of infant mortality in the USA (Carrier rate 1:50; incidence 1 in 10,000 births). SMA type I counts for 60% of all cases. Typically, newborns show muscle weakness (never able to sit independently) and respiratory impairment. Without extensive treatment 70% die before their second birthday. Children with SMA type II can sit without support, but cannot stand or walk independently. The majority of patients live into early adulthood.

Patients with SMA have a mutation in the survival motor neuron (SMN) 1 gene that leads to motor neuron loss; nusinersen (Spinraza, Biogen), a breakthrough gene-therapy treatment approved in late-2016, increases SMN protein production leading to near normal motor development. In the USA, direct medical treatment costs are about $ 324,410/year[44] and reimbursement in Europe depends on the country. Meanwhile, universal newborn screening tests are available in several countries that allow treatment with gene therapies before symptoms occur.

While celebrating the medical breakthrough, modern medicine transforms many serious diseases into chronic conditions requiring people to remain a “patient” forever (e.g. HIV disease; organ-allo-transplantation). That leads to a lifelong balancing act between desired and undesired treatment effects, burdens, and gain of therapy. New challenges are lifelong need for (financial) support, the desire to live independently, to participate in the workforce, and to have an own family. In SMA I/II patients receiving gene therapy, several new uncertainties remain unanswered: Who benefits and for how long? What are the long-term sequelae of treatment? Will the treatment improve language acquisition and cognitive outcomes?[45]

Tip 8: Markers of declining prognosis include failure of the gastrointestinal system (feeding intolerance, retching, and pain), increasing hospital admissions without the return to baseline level of functioning, and a diminishing quality of life as defined by the family.

Severe neurologic impairment (SNI) describes a group of disorders of the central nervous system arising in childhood, resulting in motor and cognitive impairment and medical complexity, typically requiring much assistance with activities in daily living.[46] Up to 40% of children cared for by PPC teams have SNI.[47] The vast majority live with medical technology. Because SNI comprises myriad disease states, patterns of decline and length of life are highly variable; prognostic uncertainty and limited empirical evidence complicate how to best counsel their families.[47,48]

Although many children with SNI have static encephalopathy, physical decline across SNI conditions can mirror that observed in adult neurologic disorders such as dementia or following traumatic brain injury. Feeding intolerance manifested by retching, vomiting or pain with feeds may occur, prompting reassessment of feeding goals.[49] Worsening seizures, central or obstructive apnea, autonomic dysfunction and neurogenic bowels and bladder; increased global pain and discomfort; and changes in consciousness may also occur over time.[49] Restrictive lung disease due to neuromuscular weakness and scoliosis is generally progressive, with rate of decline accelerated by recurrent pneumonia and slowed by the use of positive pressure ventilation and aggressive respiratory care.

Physical changes may be gradual or occur abruptly and then be followed by a period of stability for years, complicating prognostication. Additionally, children with SNI are at risk for cascading symptoms—feeding intolerance may lead to increased visceral hyperalgesia and autonomic dysfunction, worsening seizures and exacerbating hypertonicity, for example—and careful attention must be paid when assessing symptoms in order to treat perceived

suffering.[47,49] For these reasons, children with SNI and their families benefit from ongoing comprehensive PC across all phases of their lives.[47]

Tip 9: There are times when the most accurate prognostic approach simply acknowledges uncertainty; rather than offering a specific prognosis, PPC teams should support parents and children as they journey through the proverbial wilderness.

Prognostication is difficult in PPC. Many of the conditions encountered are rare or even one-of-a-kind. Even in conditions in which there is considerable knowledge about the group as a whole, there can be great phenotypic variability. Technological advances create additional challenges. In this setting, predicting any individual child's lifespan can be fraught and there is evidence to suggest that clinicians are often wrong when making predictions about how long a patient may have to live.[50]

Parents often report that uncertainty is one of the most challenging aspects of caring for a child with a LLC.[51] Clinicians can feel an overwhelming need to help provide some certainty by attempting to predict the future. Even if the certainty is of a bad outcome or a short lifespan, there is a sense that knowing this can help families prepare and make important decisions about how to spend the time they have left together.[51] However, a life of suffering that continues for longer than anticipated or a life cut suddenly short can create a great deal of distress.
It may that the real task for those who work in PC is to work with humility and to acknowledge and help families navigate uncertainty. Parallel planning may be a helpful approach,[52] with various potential scenarios are explored and plans put in place for each of these.

Tip 10: Anticipatory and post-death grief varies widely for children and parents; the dual process model of loss-oriented and restoration-oriented tasks can provide a cognitive framework for clinicians' understanding of the family's perspective or actions.

Anticipatory grief starts from diagnosis or recognition of a LL/LTC[53] as the family adjusts to a different future than the one they had previously envisioned for their child. However the experience and expression of anticipatory and post-death grief varies widely. One proposed approach to deal with grief is called the 'dual process model'.[54] In this schema, loss-oriented stressors and restoration-oriented stressors are held simultaneously by families. These stressors are confronted or avoided as needed given the situation at hand. For example, in the context of anticipatory grief, a parent might at times focus on planning for their child's return to school, whilst at other times focus on planning their funeral.

From time to time patients' and/or their families' words and actions suggest that perhaps they have not understood or accepted prognostic information given to them. However this is not necessarily the case. Misinterpreting these cues can lead to misplaced emphasis on cure directed therapy, prolonging the child's life at all costs or inappropriate emphasis on "getting the message home". Either of these approaches are likely to increase distress for the patient, parent, and clinician.

Awareness of the dual process of grief can help the clinician explore and understand better the thoughts and feelings of the family member. The clinician is then able to better pace the provision of prognostic information in response to cues from the family member with benefits including mutual understanding, increased trust and satisfaction with communication,[55] and reduced symptom burden.[56] Awareness of the dual process model can also be helpful when facilitating ACP discussions: allowing exploration of hopes as well as fears, supporting the family to anticipate and plan for both positive and negative events, and naming the inherent uncertainty to facilitate coping.[57]

Conclusion:

Prognostication has many different dimensions. In PPC, this is of particular relevance. Discussing prognosis with patients and families may provide the opportunity to support patients

and families as they actively participate in the process of defining goals of care and treatment, allowing autonomy and ideally enhancing resilience for everyone involved.

References:

1. Glare P, Sinclair C. Palliative medicine review: prognostication. *J Palliat Med.* 2008;11(1):84-103.
2. Lamont EB, Christakis NA. Complexities in prognostication in advanced cancer: "to help them live their lives the way they want to". *Jama.* 2003;290(1):98-104.
3. United Nations Inter-agency group for Child Mortality Estimation (UN IGME). *Levels and Trends in Child Mortality: Report 2017, Estimates Developed by the UN Inter-agency Group for Child Mortality Estimation'.* New York2017.
4. Fraser LK, Gibson-Smith D, Jarvis S, et al. Estimating the current and future prevalence of life-limiting conditions in children in England. *Palliat Med.* 2020:269216320975308.
5. Knaul FM, Farmer PE, Krakauer EL, et al. Alleviating the access abyss in palliative care and pain relief-an imperative of universal health coverage: the Lancet Commission report. *Lancet.* 2018;391(10128):1391-1454.
6. Breeze AC, Lees CC, Kumar A, et al. Palliative care for prenatally diagnosed lethal fetal abnormality. *Arch Dis Child Fetal Neonatal Ed.* 2007;92(1):F56-58.
7. Milstein J. A paradigm of integrative care: healing with curing throughout life, "being with" and "doing to". *J Perinatol.* 2005;25(9):563-568.
8. Younge N, Smith PB, Goldberg RN, et al. Impact of a palliative care program on end-of-life care in a neonatal intensive care unit. *J Perinatol.* 2015;35(3):218-222.
9. Balaguer A, Martín-Ancel A, Ortigoza-Escobar D, et al. The model of palliative care in the perinatal setting: a review of the literature. *BMC Pediatrics.* 2012;12(1):25.
10. Mancini A, Kelly P, Bluebond-Langner M. Training neonatal staff for the future in neonatal palliative care. *Semin Fetal Neonatal Med.* 2013;18(2):111-115.
11. Weeks JC, Catalano PJ, Cronin A, et al. Patients' expectations about effects of chemotherapy for advanced cancer. *N Engl J Med.* 2012;367(17):1616-1625.
12. Gramling R, Fiscella K, Xing G, et al. Determinants of Patient-Oncologist Prognostic Discordance in Advanced Cancer. *JAMA Oncol.* 2016;2(11):1421-1426.
13. Enzinger AC, Zhang B, Schrag D, Prigerson HG. Outcomes of Prognostic Disclosure: Associations With Prognostic Understanding, Distress, and Relationship With Physician Among Patients With Advanced Cancer. *J Clin Oncol.* 2015;33(32):3809-3816.
14. Ingersoll LT, Alexander SC, Priest J, et al. Racial/ethnic differences in prognosis communication during initial inpatient palliative care consultations among people with advanced cancer. *Patient Educ Couns.* 2019;102(6):1098-1103.
15. Linton JM, Feudtner C. What accounts for differences or disparities in pediatric palliative and end-of-life care? A systematic review focusing on possible multilevel mechanisms. *Pediatrics.* 2008;122(3):574-582.
16. Johnston EE, Alvarez E, Saynina O, et al. Disparities in the Intensity of End-of-Life Care for Children With Cancer. *Pediatrics.* 2017;140(4).
17. Johnston EE, Alvarez E, Saynina O, et al. Inpatient utilization and disparities: The last year of life of adolescent and young adult oncology patients in California. *Cancer.* 2018;124(8):1819-1827.
18. Johnston EE, Bogetz J, Saynina O, et al. Disparities in Inpatient Intensity of End-of-Life Care for Complex Chronic Conditions. *Pediatrics.* 2019;143(5).

19. Ilowite MF, Al-Sayegh H, Ma C, et al. The relationship between household income and patient-reported symptom distress and quality of life in children with advanced cancer: A report from the PediQUEST study. *Cancer.* 2018;124(19):3934-3941.
20. Ilowite MF, Cronin AM, Kang TI, Mack JW. Disparities in prognosis communication among parents of children with cancer: The impact of race and ethnicity. *Cancer.* 2017;123(20):3995-4003.
21. Mack JW, Uno H, Twist CJ, et al. Racial and Ethnic Differences in Communication and Care for Children With Advanced Cancer. *J Pain Symptom Manage.* 2020;60(4):782-789.
22. Contro N, Davies B, Larson J, Sourkes B. Away from home: experiences of Mexican American families in pediatric palliative care. *J Soc Work End Life Palliat Care.* 2010;6(3-4):185-204.
23. Rosenberg AR, Bona K, Coker T, et al. Pediatric Palliative Care in the Multicultural Context: Findings From a Workshop Conference. *J Pain Symptom Manage.* 2019;57(4):846-855 e842.
24. Mack JW, Fasciano KM, Block SD. Communication About Prognosis With Adolescent and Young Adult Patients With Cancer: Information Needs, Prognostic Awareness, and Outcomes of Disclosure. *J Clin Oncol.* 2018;36(18):1861-1867.
25. Sisk BA, Fasciano K, Block SD, Mack JW. Longitudinal prognostic communication needs of adolescents and young adults with cancer. *Cancer.* 2020;126(2):400-407.
26. Rosenberg AR, Wolfe J, Wiener L, et al. Ethics, Emotions, and the Skills of Talking About Progressing Disease With Terminally Ill Adolescents: A Review. *JAMA pediatrics.* 2016;170(12):1216-1223.
27. Glaser BG, Strauss AL. In: *Awareness of dying.* London: Weidenfeld & Nicolson; 1966:82-96.
28. Bluebond-Langner M. Mutual pretense: causes and consequences. In: *The private worlds of dying children.* Princeton, N.J.: Princeton University Press; 1978:210-230.
29. Bluebond-Langner M, Belasco JB, DeMesquita Wander M. "I want to live, until I don't want to live anymore": involving children with life-threatening and life-shortening illnesses in decision making about care and treatment. *Nurs Clin North Am.* 2010;45(3):329-343.
30. Mack JW, Joffe S. Communicating about prognosis: ethical responsibilities of pediatricians and parents. *Pediatrics.* 2014;133 Suppl 1:S24-30.
31. Mack JW, Currie ER, Martello V, et al. Barriers to Optimal End-of-Life Care for Adolescents and Young Adults With Cancer: Bereaved Caregiver Perspectives. *J Natl Compr Canc Netw.* 2021;19(5):528-533.
32. Kreicbergs U, Valdimarsdottir U, Onelov E, et al. Talking about death with children who have severe malignant disease. *N Engl J Med.* 2004;351(12):1175-1186.
33. Hui D, Paiva CE, Del Fabbro EG, et al. Prognostication in advanced cancer: update and directions for future research. *Support Care Cancer.* 2019;27(6):1973-1984.
34. Burke K, Coombes LH, Menezes A, Anderson AK. The 'surprise' question in paediatric palliative care: A prospective cohort study. *Palliat Med.* 2018;32(2):535-542.
35. Bergstraesser E, Paul M, Rufibach K, et al. The Paediatric Palliative Screening Scale: Further validity testing. *Palliat Med.* 2013;28(6):530-533.
36. Chong PH, Soo J, Yeo ZZ, et al. Who needs and continues to need paediatric palliative care? An evaluation of utility and feasibility of the Paediatric Palliative Screening scale (PaPaS). *BMC Palliat Care.* 2020;19(1):18.
37. Zinter MS, Logan BR, Fretham C, et al. Comprehensive Prognostication in Critically Ill Pediatric Hematopoietic Cell Transplant Patients: Results from Merging the Center for International Blood and Marrow Transplant Research (CIBMTR) and Virtual Pediatric Systems (VPS) Registries. *Biol Blood Marrow Transplant.* 2020;26(2):333-342.
38. Goel N, Morris JK, Tucker D, et al. Trisomy 13 and 18-Prevalence and mortality-A multi-registry population based analysis. *Am J Med Genet A.* 2019;179(12):2382-2392.

39. Nelson KE, Rosella LC, Mahant S, Guttmann A. Survival and Surgical Interventions for Children With Trisomy 13 and 18. *Jama.* 2016;316(4):420-428.
40. Carey JC. Emerging evidence that medical and surgical interventions improve the survival and outcome in the trisomy 13 and 18 syndromes. *Am J Med Genet A.* 2020;182(1):13-14.
41. Janvier A, Farlow B, Wilfond BS. The experience of families with children with trisomy 13 and 18 in social networks. *Pediatrics.* 2012;130(2):293-298.
42. Weaver MS, Anderson V, Beck J, et al. Interdisciplinary care of children with trisomy 13 and 18. *Am J Med Genet A.* 2021;185(3):966-977.
43. Ojala KS, Reedich EJ, DiDonato CJ, Meriney SD. In Search of a Cure: The Development of Therapeutics to Alter the Progression of Spinal Muscular Atrophy. *Brain Sci.* 2021;11(2).
44. Dean R, Jensen I, Cyr P, et al. An updated cost-utility model for onasemnogene abeparvovec (Zolgensma(R)) in spinal muscular atrophy type 1 patients and comparison with evaluation by the Institute for Clinical and Effectiveness Review (ICER). *J Mark Access Health Policy.* 2021;9(1):1889841.
45. Abreu NJ, Waldrop MA. Overview of gene therapy in spinal muscular atrophy and Duchenne muscular dystrophy. *Pediatr Pulmonol.* 2021;56(4):710-720.
46. Allen J, Brenner M, Hauer J, et al. Severe Neurological Impairment: A delphi consensus-based definition. *Eur J Paediatr Neurol.* 2020;29:81-86.
47. Bogetz JF, Lemmon ME. Pediatric Palliative Care for Children With Severe Neurological Impairment and Their Families. *J Pain Symptom Manage.* 2021.
48. DeCourcey DD, Silverman M, Oladunjoye A, et al. Patterns of Care at the End of Life for Children and Young Adults with Life-Threatening Complex Chronic Conditions. *J Pediatr.* 2018;193:196-203 e192.
49. Hauer JM. Gastrointestinal problems: retching, vomiting, feeding intolerance, and other problems. In: *Caring for children who have severe neurological impaiment: a life with grace.* Baltimore: The John Hopkins University Press; 2013:131-177.
50. White N, Reid F, Harris A, et al. A Systematic Review of Predictions of Survival in Palliative Care: How Accurate Are Clinicians and Who Are the Experts? *PLoS One.* 2016;11(8):e0161407.
51. Verberne LM, Kars MC, Schouten-van Meeteren AYN, et al. Parental experiences and coping strategies when caring for a child receiving paediatric palliative care: a qualitative study. *Eur J Pediatr.* 2019;178(7):1075-1085.
52. Sidgwick P, Fraser J, Fortune PM, McCulloch R. Parallel planning and the paediatric critical care patient. *Arch Dis Child.* 2019;104(10):994-997.
53. Al-Gamal E, Long T. Anticipatory grieving among parents living with a child with cancer. *J Adv Nurs.* 2010;66(9):1980-1990.
54. Stroebe M, Schut H. The dual process model of coping with bereavement: rationale and description. *Death Stud.* 1999;23(3):197-224.
55. Brouwer MA, Maeckelberghe ELM, van der Heide A, et al. Breaking bad news: what parents would like you to know. *Arch Dis Child.* 2021;106(3):276-281.
56. Levine DR, Mandrell BN, Sykes A, et al. Patients' and Parents' Needs, Attitudes, and Perceptions About Early Palliative Care Integration in Pediatric Oncology. *JAMA Oncol.* 2017;3(9):1214-1220.
57. Lotz JD, Daxer M, Jox RJ, et al. "Hope for the best, prepare for the worst": A qualitative interview study on parents' needs and fears in pediatric advance care planning. *Palliat Med.* 2017;31(8):764-771.

Dr Weaver contributed to this paper in a private capacity. No official support or endorsement by the U.S. Department of Veterans Affairs is intended, nor should be inferred.