

END OF LIFE ISSUES IN CLINICAL RESEARCH

Pamela Hinds, PhD, RN, CS
Director of Nursing Research
St. Jude Children's Research Hospital,
Memphis, Tennessee

Abstract: *A September 2002 Institute of Medicine report states that 53,000 children and adolescents die each year in the United States. The literature shows that participating in end-of-life decision-making is life altering for the patient, family members, and healthcare providers. This article highlights end-of-life research, including three studies conducted at St. Jude Children's Research Hospital. End-of-life research can help decrease the suffering of the dying child or adolescent, his/her survivors, and perhaps, the healthcare providers who care for the dying child or adolescent.*

St. Jude Children's Research Hospital is a pediatric research and care facility that strives to find cures for childhood catastrophic illnesses. This article highlights what we have learned about conducting end-of-life research, particularly the perspectives of adolescents who chose to end treatment for incurable cancers, and the perspectives of their parents and healthcare providers. Examples from the literature and three end-of-life studies conducted at St. Jude's demonstrate the issues that confront end-of-life researchers. The St. Jude's studies were funded by the Project on Death in America, Oncology Nursing Foundation, Critical Care Nurses Association, National Cancer Institute, and American Lebanese Syrian Associated Charities.

Why would anyone conduct end-of-life research on dying children and adolescents? It is very clear from a September 2002 Institute of Medicine report that 53,000 children and adolescents die in the United States each year. They suffer as they die. It is equally clear from more limited research that the health of their parents, siblings, neighbors, and classmates suffers as a result of this child or adolescent dying. Even healthcare teams that are functioning well experience discord and tension

when they must make end-of-life decisions for patients whom they have been actively caring for. Table 1 provides several quotations from parents and a nurse who participated in St. Jude's end-of-life studies that depict these issues.

Table 2 shows the desired outcomes of end-of-life research. There are many challenges in conducting end-

of-life research. There is an ethical question: by studying end of life, are you causing harm to the patients and their parents from whom you are so boldly asking these questions?

There are also feasibility challenges. How do you know when an end-of-life decision has been made? Do you know it promptly enough to honor design points?

TABLE 1

Quotes from Participants in St. Jude's End-of-Life Research

"I wanted to do the phase 1 study. I understood that the drug would not help my son. But I knew that if we stopped all treatment, my son would ask me why. And I knew that I could not tell him the truth, that he was dying."

The mother of a 6-year-old child with stage 4 neuroblastoma

"We work well as a team until we get to an end-of-life decision. And then we just fall apart. We don't see it the same."

A senior nurse on an inpatient unit

"I made the do not resuscitate (DNR) status decision for my son. Then, for the next three shifts, I asked every staff member who entered his ICU room what their definition of a DNR might be. Not one of those members had the same definition of a DNR. So at the end of those shifts, I rescinded the DNR order. If staff don't know, I'll be the one to decide. I am his father. And I'm going to be a good father to the end."

The father of a 16-year-old youth dying in intensive care

Table 2

The Desired Outcomes of End of Life Research

- More competent healthcare professionals
- Patients and family members who are more certain about end-of-life decisions
- Patients and parents who are better prepared for the symptoms of dying
- Less suffering for patients, families, and healthcare professionals

There are structural issues related to medical records. Individual styles dictate how much is documented in medical records, and the quality and comprehensiveness of the information. Painfully important for me as a clinical investigator was whether I would produce anything from these studies that would be useful and would in some way make end of life better for patients, their families, and their healthcare providers.

The End-of-Life Literature

We paid careful attention to the literature before beginning our studies and were able to draw some conclusions from this work. Participating in end-of-life decision-making is life altering for the patient, family members, and healthcare providers. Yet, very few healthcare providers have any formal training in how to make a decision about ending a child or adolescent's life and there are no empirically-based guidelines.

The greatest body of literature is about dying infants, who comprise the majority of the 53,000 American infants and children who die each year. They are born with overwhelming congenital abnormalities and their parents must make a very quick decision about how much effort to put into prolonging life.

One concept from this body of literature has also emerged from our end-of-life studies: the good parent. Even parents who are giving birth for the first time have a fixed notion of what constitutes a good parent. Surely a good parent would decide in a very definite way. That same definition of the good parent could lead one set of parents to choose to prolong life and another set to decide to end life as quickly as possible. Another major factor in helping parents of neonates make an end-of-life decision is the prognostic information that healthcare providers give them.

Methodology in End-of-Life Research

By far the most frequent methodology used in end-of-life research has been medical record review. However, 22% to 62% of potentially eligible medical records cannot be used for end-of-life research because missing information is extensive.

The second most common methodology is contacting survivors of the deceased child or adolescent. We have used that methodology.

There are about a dozen studies of adolescents participating in health-related decisions. We have also studied this literature and found a conclusion that is relevant to our work: chronically ill adolescents far prefer to be involved with health-related decision-making than not to be included. This is a startling finding for parents. Parents and adolescents do not agree about the importance and the burden of adolescents participating in decision-making. Adolescents report great satisfaction in participating in health-related decisions, whereas their parents describe it as being far too burdensome and inappropriate for them to be involved.

Healthcare providers are uncomfortable with routinely including adolescents in health-related decisions, much less end-of-life decisions. Interviews have shown that healthcare providers believe that adolescents: (1) are developmentally unable to honestly and accurately identify all options; and (2) may not be able to identify all consequences to those options.

Healthcare providers have special responsibilities when trying to include, to the extent desired, adolescents in health-related decisions. We must be very clear in our explanations of options and the consequences of those options. It is painful to do that with an adolescent who is dying.

A few clinical reports in the literature also help inform end-of-life research. In 1982, Dr. R. Nitsctke (R. Nitsctke, et al, *The Choices Made By End Stage Cancer Patients*, The Journal of Pediatrics, Vol. 10, Issue 3, pp 471-476) at the University of Oklahoma conducted a study in which the healthcare team interviewed more than 43 families when it was clear that curative efforts to address the child or adolescent's cancer were no longer possible. The children (as young as age 6) and adolescents participated in these end-of-life discussions. More than 83% of the decisions were made by the child/adolescent. Allowing an adolescent to make his/her own end-of-life decision is defined in three ways:

- Whether the adolescent chooses to enroll in a phase 1 study.
- Whether the adolescent wishes all treatment efforts to be ended, at times even supportive care efforts.
- Whether the adolescent wants to become a do not resuscitate status.

End-of-Life Studies at St. Jude's DECIDE 1, DECIDE 2, and DECIDE 3 were about end-of-life decision-making. DECIDE 1 was a retrospective review in which we contacted parents six months to two years after their child had died. We contacted them first through a letter, which included a return response card for them to check off whether or not they wanted to know more about the study. At the end of DECIDE 1, we knew that we were missing the patient's voice. We began DECIDE 2, a prospective study where we interviewed adolescents, their parents, and their physicians about an end-of-life decision. Toward the end of DECIDE 2, we wanted to know whether end-of-life factors were the same in other parts of the globe. We started a small feasibility study—DECIDE 3—in hospitals in Hong Kong and Sydney, Australia, and at St. Jude's.

TABLE 3
Study Interview Questions

Recently, you made a serious decision about your treatment (DESCRIPTION OF DECISION).

- Would you please describe that decision for me?
- What did you consider to be your choices at the time?
- What did you consider to be the likely outcome of each of your choices?
- What kind of factors did you think about when you were trying to make this decision?
- What kinds of things did your doctor, nurse, or chaplain say or do that helped you to make this decision or that made it harder to make this decision?

What helps you now to feel all right about this decision, or not all right?

We asked six questions across all three studies (Table 3) and a modified version of these questions with the adolescents in the second and third studies. We did a semantic content analysis across all responses. We had at least six coders for every interview and scored inter-rater agreement of 92% to 96% across all studies.

Thirty-seven families participated in DECIDE 1. We interviewed the families and the healthcare provider who, according to the families, was most involved with the patient (30 physicians, 5 nurses, and 2 chaplains). Thirty-three of the families said the end-of-life decision was the most difficult decision they made. Parents were most influenced in choosing an end-of-life option by: information from healthcare providers about the child's prognosis and the likelihood of survival, being supported by the staff (this was critically important), being seen as the good parent (by healthcare providers), and believing that their child would have made the same decision they made. Healthcare professionals' end-of-life decision-making was most influenced by: respect for the patient's and family's preferences, and concluding that the patient could not survive.

In DECIDE 2, we interviewed 52 families within hours to one week of their having made an end-of-life decision and 10 adolescents between the age of 10 and 19. Those factors

that were identified retrospectively as being most important in end-of-life decisions came forward again prospectively: staff support, being the good parent and being seen as the good parent, religious beliefs, information from the healthcare team, and doing what was necessary (pursuing options that would be seen as honorable by relatives and neighbors).

Physicians said that in caring for children and adolescents in oncology, they had to seek input from healthcare providers on the team. Most care in pediatric oncology is protocol driven. There are few controversial decisions to make until end of life. Physicians said that the most influential factors in their decision to choose an end-of-life option were: respecting family preferences, knowing that the patient could not continue to live, the severity of the diagnosis and the prognosis, and feeling as if there were no therapeutic (curative) options left.

In DECIDE 3, we interviewed 48 families, 23 of whom had made an end-of-life decision, in Hong Kong and Sydney, Australia, and at St. Jude's. We interviewed 20 adolescents, 10 from the United States and 10 from Australia.

We found some universal factors and some unique factors. For the parents, the most important influences were: information from

the healthcare team, trusting the staff to have done everything that they could do and to have done it well, and wanting to minimize the suffering of their child. Only the American families talked about needing to know and consider their child's preference in the end-of-life decision-making, and reported that it was important that the staff supported them and viewed them as good parents. The Australian parents and adolescents talked a great deal about alternative therapies and their belief in alternative therapies.

Among the adolescents, six chose to become do not resuscitate status, seven considered a phase 1 study (four opted against the study and three opted for it), and seven decided to end all treatment efforts as of that day. The number one reason why adolescents (19 out of 20) chose to end their lives when they had an incurable cancer was relationships with others (parents, siblings, and healthcare providers); they made the decision to honor others either because they had become too burdensome or they trusted what they were told. Eleven adolescents identified other people who they did not know, such as other patients.

A 15-year old with incurable Hodgkin's disease said, "My mom has taken good care of me for two years. The best thing I can do for her now is to die and die quickly. Her second marriage is falling apart. She needs to go home now and be with my step-dad."

Avoiding adverse effects was another reason for an end-of-life decision. Several adolescents said, "I would do a phase 1 because my mom needs me to live longer. But I really don't want to be in the hospital longer. I really want to go home. I really don't want the toxicities." The adolescents felt that they had done their best and now they wanted to die and go to heaven.

BOOK REVIEW

Several adolescents chose a phase I study in the hope that it would lead to a cure. One said, "I suspect this isn't true, but maybe it is my one chance. If I can stay alive a little bit longer, maybe the real cure will come soon." Seeing others die and feeling that treatment was futile were other reasons that adolescents made an end-of-life decision.

In both studies, the adolescents conveyed the importance of their being informed and involved in end-of-life decision-making. They gave clear weight to the opinions and preferences of their healthcare team members, parents, and siblings. They made it clear that they want to know that all possible curative efforts have been attempted, that there is no other acceptable option, and that survival is no longer possible.

Conclusion

We have a very strong commitment to facilitating end-of-life decision-making research. We want to have a trusting relationship that includes and respects the personhood of the patient and the parents. We want to honor the adolescent's desire for relationships and to recognize that sometimes, an adolescent makes an end-of-life decision out of regard for others. We want to assist parents in achieving their definition of the good parent. We want to provide the information adolescents, families, and other members of the healthcare team want. We want to document end-of-life decisions well so that members of the healthcare team are less likely to have discord.

All of us are diminished when a child or adolescent dies. We are diminished by the loss itself, by the suffering we have witnessed, and by the sense that we, as healthcare providers, could not do enough. End-of-life research can help us decrease the suffering of the child or adolescent, of the survivors, and of ourselves. Perhaps we can become more competent and contribute in some way to protecting the health of survivors.

From Test Tube to Patient: Improving Health Through Human Drugs

Book review provided by
Carolyn E. Rugloski
President, Fairplay Consultants, Inc.

This publication by the FDA Center for Drug Evaluation and Research (CDER) presents, in easy-to-understand articles, the new drug development process in the United States. The 1999 edition provides a great overview of clinical trials as well as explaining current changes and reforms stemming from the 1997 FDA Modernization Act (FDAMA). Covering a realm of topics from the consumer perspective to the more scientific evaluation of benefit versus risk decisions related to the approval of new drugs, this collection of articles provides a general coverage of the regulation of new drugs from discovery to post-marketing surveillance.

If you're making a career transition into the world of pharmaceutical research and development, these articles provide a great overview of the industry! Articles discuss the USA drug development process including pre-clinical drug testing, FDA regulations, testing in people, protecting human subjects, the advisory committee role, the role of the FDA inspector, prescription drug labeling, generic drugs, and protecting vulnerable populations in clinical trials. If you're training new employees at your company, consider this inexpensive collection of interesting articles as part of your new employee curriculum! I recommend using this source along with a mandatory visit to <http://www.fda.gov/cder/handbook/> to secure a perfect balance of CDER's educational resources (including several interactive charts) and the "latest and greatest" news regarding drug development in the USA.

Copies can be secured through the Government Printing Office (Order Processing Code *8307) **Test Tube to Patient: Improving Health Through Human Drugs** (017-012-00400-8) for \$9.00 each or \$11.25 foreign.