Research on Informed Consent in Pediatric Cancer: Reflections on Methods and Lessons Learned

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Goals of Presentation

• To identify practical and methodological lessons learned in 16 years of programmatic research on informed consent in pediatric cancer
• To describe the implications for research in bioethics and relevant training more broadly
Relevance of Interdisciplinary and Transdisciplinary Approaches To Research on Bioethics

- Need for multiple perspectives (Baker, 2009)
- Importance of interdisciplinary collaboration in decision making in ethics (Beauchamp, 1982)
- Need to integrate multiple methods (Sugarman et al., 2010)
- Need to create new models of research that transform methods and available scientific knowledge
Importance of Informed Consent in Pediatric Research

- **Ubiquitous issue:** requires close attention in every study
- Investigators can experience conflict / tension between the need to enhance consent / assent in ways that address ethical principles **versus** the need to recruit a sufficient number of participants to achieve study goals
- Consent raises challenges for investigators and families that vary with specific research studies
- Complexity of process that involves parents, children, and investigators in decision making
- Evidence that the consent process is not ideal in a range of pediatric studies
Dimensions of Informed Consent in Pediatric Research

• Parental permission or consent
• Assent of the child
• Family level informed and empowered research participation
Significance of Research on Informed Consent in Pediatric Cancer

- Prevalence and impact of pediatric cancer
- Importance and evolution of clinical trials in treatment of pediatric cancer
- High percentages of children enrolled in clinical trials
- Complexity of the consent process and specific context: constraints and impact on the quality of consent
- Need for empirical research to understand and improve the process
Back to the Beginning of the Research and Collaboration

- The initial collaborators and context:
  - An invitation to review and help with a colleague’s research proposal on informed consent
  - A challenging, interesting topic leads to stimulating dialogue and the development of shared intellectual interest, collaboration, and respect
  - “Good timing” and readiness to collaborate
  - Collaboration leads to successful R01
History and Overview of the Research Collaboration (1998-Present)

• Initial proposal submitted on a descriptive study: revised based on collaborative process
• Revised proposal was funded: Descriptive study of informed consent in phase 3 treatment of pediatric cancer
• Second NIH grant funded based on findings of the first study: investigator-directed intervention to improve the informed consent process
• Third NIH grant funded: Descriptive study of consent process in phase 1 treatment of pediatric cancer has been completed: analyses in process
Initial Study of Informed Consent in Pediatric Cancer (Kodish et al., 2004)

- Multisite study (N = 140)
- Observed audiotaped consent conferences, interviews with parents, other validated measures
- Quantitative and qualitative data
- Parents participated in Phase III RCT of treatment for leukemia (Children’s Oncology Group Protocols)
  - 85% consented to RCT for treatment of leukemia
Data Collection: Informed Consent Study

**Clinical Event**
- Diagnosis of cancer
- Informed consent conference for clinical trial
- 6 months in treatment
- Treatment Ends

**Research Event**
- Consent for observational study
- Observed/taped conferences and parent interviews
- Telephone Interviews
- Focus Groups
- Parent advisory group feedback
Primary Findings: Parental Understanding of Key Dimensions of Informed Consent (Kodish et al., 2004)

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<thead>
<tr>
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<th>Explained by Investigators:</th>
<th>Understood by Parents:</th>
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<tbody>
<tr>
<td>Choice</td>
<td>89%</td>
<td>67%</td>
</tr>
<tr>
<td>Randomization</td>
<td>83%</td>
<td>49%</td>
</tr>
</tbody>
</table>

- Parents of racial minority status and low SES: less likely to understand choice and randomization
- 34% demonstrated evidence that they did not understand the distinction between study participation vs. treatment outside the RCT
Correlates of Parental Participation in Informed Consent Conference  (Drotar, Miller, Willard, Anthony, & Kodish, 2004)

• Physician rapport building (e.g., statements of concern/empathy) and Physician partnership building (e.g., checking for understanding, eliciting questions)
  • Correlated with parental participation in the conference
  • Information giving did not
• An index of parental participation (e.g., asking questions) correlated with parental understanding of randomization
Implications (Kodish et al., 2004)

- Significant gap between what investigators communicated about the study, and what was understood by participants
- Some participants were more vulnerable to misunderstanding than others
- Gaps may relate to the way information was presented, the content, or both
- Need for interventions to enhance quality of investigator-parent communication to enhance parental understanding of research
Physician-Directed Intervention to Improve Consent in Pediatric Leukemia Trials (Yap et al., 2009)

• Multisite intervention (RCT) (N=59)
• Intervention was based on study findings and recommendations from parents
• Physicians trained in seminars that included: review of research on informed consent; Audiotapes of process of consent; and, sequential approach
• Examples of good versus problematic communication
• How to elicit parental questions and participation
• Sequential approach:
  1. What is leukemia?
  2. Current medical treatment
  3. What is the RCT?
   [Check for understanding at each step]
PAGIC Model of Informed Consent

What is Leukemia?

- Yes
- No

Current Treatment

- Yes
- No

Randomized Clinical Trial

- Yes
- No

Decision

1st Meeting

1st or 2nd Meeting

Depending Upon Parents

2nd Meeting

Project on Informed Consent
Eric Kodish, MD  Principal Investigator
Improving Informed Consent: **Parents’ Suggestions** for Leukemia Trials (Eder et al., 2007)

| Additional material: E.g., “Road Maps” that describe key concepts |
| Simpler explanation |
| Change timing and sequence of presentation |
| More organization and repetition |
| Check for understanding |
| Facilitate dialogue / questions |
| Anticipatory guidance: What is going to happen next? |
| More time for decision: Conduct dialogue in stages |
| Translational materials and qualified interpreters (Spanish speaking parents) |
Results of Intervention Based on Audiotapes of the Consent Conference and Parental Interview (Yap et al., 2009)

In the intervention group:

• Physician-investigators were more likely to use recommended sequenced approach
• Parents asked more questions
• Parents showed greater understanding of choice (but not randomization) compared with controls
Improving Physician-Parent Communication during Informed Consent in Pediatric Leukemia (Cousino et al., 2011)

- Secondary analysis of impact of physician-directed intervention on physician behavior (Yap et al., 2009)
- Coding of audiotapes with the Roter Interaction Analysis System: Rapport building, empathic statements, partnership building (e.g., asking for opinions) and study related communication (parents)
- Intervention associated with more frequent physician rapport building, but no difference in partnership building
- Parents in the intervention group engaged in more study related communication
Lessons Learned About the Process of Research on Bioethics

# 1: Leadership

• Importance of leadership in facilitating interdisciplinary collaboration and communication
• Need for consensus
• Facilitating mutual learning
• Managing differences in perspective
Lessons Learned About the Process of Research on Bioethics

#2 Building and Nurturing an Interdisciplinary Team and Culture of Ideas

• Pediatric Oncology
• Bioethics
• Clinical Psychology
• Anthropology
• Biostatistics
• Nursing
• Sociology
### Peer Reviewed Journals of the Team’s Publications (N = 32) (2003-2012)

<table>
<thead>
<tr>
<th>Professional Discipline/Topic</th>
<th>Example of Journal</th>
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<tbody>
<tr>
<td>Medicine/Pediatrics:</td>
<td>JAMA, Pediatrics</td>
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<tr>
<td>Oncology:</td>
<td>Pediatric Blood and Cancer</td>
</tr>
<tr>
<td>Nursing:</td>
<td>Journal of Pediatric Oncology Nursing</td>
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<tr>
<td>Ethics:</td>
<td>American Journal of Bioethics; Journal of Medical Ethics</td>
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<tr>
<td>Education:</td>
<td>Academic Medicine</td>
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<td>Health Communication:</td>
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Lessons Learned About the Process of Research on Bioethics

#3: Mentorship of Next Generation of Researchers in Bioethics

- Openness to interdisciplinary trainees
- Generosity in opportunity for authorship for investigators at multiple levels: graduate students, fellows, and junior faculty
- Facilitating career development
Lessons Learned About Methods of Research on Bioethics

#1 Importance of Using and Integrating Multiple Methods

- Direct observation of informed consent conference as a cornerstone
- Measures of perceptions of participants (parents and oncologists)
- Qualitative and quantitative methods
- Integration of data across methods
Lessons Learned about the Methods of Research On Bioethics

• #2 Importance of Involving Participants In Planning, Implementation, and Understanding of Research on Bioethics
Prevalent Model of Involving Participants in Research

Investigators:
• Plan and implement the study
• Inform the participants of findings

Participants:
• Complete procedures
• Receive results
Model of Involving Research Participants is Well Suited for Research on Bioethics

- Planning/Implementing Study
- Reviewing findings and identifying implications
- Participating in research implementation and design going forward
Process of Involving Parents in Research on Informed Consent in Pediatric Cancer

• Focus Groups: Framing the Question
• Parent Advisory Groups: Understanding the data
• Making recommendations to improve the informed consent process in phase 3 and phase 1 trials in pediatric cancer
• Collaborating in interventions to improve the process of informed consent
• Mutual feedback and support
Broader Implications: Applying These Lessons Learned To:

- Training investigators to enhance the quality of informed consent
- Involving participants in planning, implementing, and understanding the findings of research on bioethics
- Implementing quality improvement methods to informed consent: norms/benchmarks of quality of investigator-parent communication and parental understanding
- Training researchers in bioethics research (e.g., study design, multiple methods, developing research teams)
Several Unanswered Questions

• What are the most effective methods to train investigators to enhance the quality of their communications with research participants to improve their understanding of research?
• What are the most important, potentially modifiable factors that differentiate between good versus problematic understanding among research participants?
• What do children/adolescents understand about research participation? And how can we enhance the quality of their assent and participation?
Study Team & Authors (1998 – Present)

- **Eric Kodish, MD (PI)**
  - Steve Zyzanski, PhD
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