PARENTAL DECISION-MAKING ABOUT CHILDREN'S
PARTICIPATION IN CLINICAL RESEARCH

by

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# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>List of Tables</td>
<td>2</td>
</tr>
<tr>
<td>List of Figures</td>
<td>4</td>
</tr>
<tr>
<td>Acknowledgments</td>
<td>5</td>
</tr>
<tr>
<td>Abstract</td>
<td>8</td>
</tr>
<tr>
<td>Chapters:</td>
<td></td>
</tr>
<tr>
<td>1. Background and Introduction</td>
<td>10</td>
</tr>
<tr>
<td>2. Methodology</td>
<td>34</td>
</tr>
<tr>
<td>3. Parent Decision-Making</td>
<td>52</td>
</tr>
<tr>
<td>4. Patient and Parent Factors</td>
<td>71</td>
</tr>
<tr>
<td>5. Social Network Factors</td>
<td>96</td>
</tr>
<tr>
<td>6. Clinician Factors: Doctor/Parent Relationship</td>
<td>114</td>
</tr>
<tr>
<td>7. Clinician Factors: Physician Recommendation</td>
<td>128</td>
</tr>
<tr>
<td>8. Clinician Factors: Presentation of Benefits</td>
<td>151</td>
</tr>
<tr>
<td>9. Clinician Factors: Presentation of Risks</td>
<td>168</td>
</tr>
<tr>
<td>10. Testing the Model</td>
<td>199</td>
</tr>
<tr>
<td>11. Discussion and Conclusions</td>
<td>229</td>
</tr>
<tr>
<td>References</td>
<td>265</td>
</tr>
</tbody>
</table>
# List of Tables

<table>
<thead>
<tr>
<th>Number</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Measurement of Variables</td>
<td>43</td>
</tr>
<tr>
<td>2</td>
<td>Reasons for Declining Trial</td>
<td>55</td>
</tr>
<tr>
<td>3</td>
<td>Reasons for Participating in Trial</td>
<td>59</td>
</tr>
<tr>
<td>4</td>
<td>Combinations of Reasons for Participating in Trial</td>
<td>68</td>
</tr>
<tr>
<td>5</td>
<td>Illness Severity</td>
<td>75</td>
</tr>
<tr>
<td>6</td>
<td>Prognosis</td>
<td>81</td>
</tr>
<tr>
<td>7</td>
<td>Parent Demographics</td>
<td>89</td>
</tr>
<tr>
<td>8</td>
<td>Network Members Present</td>
<td>97</td>
</tr>
<tr>
<td>9</td>
<td>Social Network Questions and Comments During ICC</td>
<td>99</td>
</tr>
<tr>
<td>10</td>
<td>Most Helpful Sources of Information During Decision-Making</td>
<td>107</td>
</tr>
<tr>
<td>11</td>
<td>Doctor and Parent Views of Who Directed the Trial Decision</td>
<td>117</td>
</tr>
<tr>
<td>12</td>
<td>Shared Decision-Making During ICC</td>
<td>118</td>
</tr>
<tr>
<td>13</td>
<td>Parent and Physician Views of the Most Strongly Recommended Treatment Option</td>
<td>128</td>
</tr>
<tr>
<td>14</td>
<td>Strength of the Physician's Recommendation</td>
<td>129</td>
</tr>
<tr>
<td>15</td>
<td>Neutral Presentations of Trial</td>
<td>131</td>
</tr>
<tr>
<td>16</td>
<td>Implicit Recommendations of Trial</td>
<td>134</td>
</tr>
<tr>
<td>17</td>
<td>Explicit Recommendations of Trial</td>
<td>137</td>
</tr>
<tr>
<td>18</td>
<td>Clinician Self-Report of Approach to Informed Consent</td>
<td>144</td>
</tr>
<tr>
<td>19</td>
<td>Direct Benefit – This Child</td>
<td>152</td>
</tr>
<tr>
<td>20</td>
<td>Direct Benefit – General</td>
<td>155</td>
</tr>
<tr>
<td>21</td>
<td>Recipient Categories</td>
<td>159</td>
</tr>
</tbody>
</table>
22. Increased Toxicity Discussions ......................................................... 169
23. Decreased Cure Rate Discussions .................................................. 172
24. Uncertainty Discussions ................................................................. 175
25. Types of Oversight/Control Mechanisms ....................................... 182
26. Experiment Subgroups ................................................................. 186
27. Prior Use Statements .................................................................... 190
28. Factors Related to the On/Off Trial Decision ................................. 201
29. Factors Related to Citing Direct Benefit as a Reason for Participation in the Trial ................................................................. 205
30. Factors Related to Citing Altruism as a Reason for Participation in the Trial ................................................................. 209
31. Factors Related to Citing the Right to Withdraw as a Reason for Participation in the Trial ................................................................. 211
32. Factors Related to Citing Comparison to Standard as a Reason for Participation in the Trial ................................................................. 214
33. Factors Related to Citing Safety as a Reason for Participation in the Trial ................................................................. 217
34. Factors Related to Citing the Doctor as a Reason for Participation in the Trial ................................................................. 220
35. Factors Related to Citing Better Monitoring as a Reason for Participation in the Trial ................................................................. 224
36. Results of Logistic Regression Analyses ......................................... 227
List of Figures

1. Model of Parental Decision-Making About Trial Participation... 33
2. Research Methodology Overview................................. 37
3. Decision-Making Preference Questionnaire...................... 115
4. Total Oversight/Control Mechanisms............................. 181
5. Relationships Between Independent Variables and On/Off Trial Decision.......................................................... 200
6. Relationships Between Independent Variables and Direct Benefit as a Reason for Participation in the Trial.............. 204
7. Relationships Between Independent Variables and Altruism as a Reason for Participation in the Trial.......................... 208
8. Relationships Between Independent Variables and the Right to Withdraw as a Reason for Participation in the Trial........... 210
9. Relationships Between Independent Variables and Comparison to Standard as a Reason for Participation in the Trial.......................................................... 213
10. Relationships Between Independent Variables and Safety as a Reason for Participation in the Trial............................ 216
11. Relationships Between Independent Variables and the Doctor as a Reason for Participation in the Trial............................. 219
12. Relationships Between Independent Variables and Better Monitoring as a Reason for Participation in the Trial........ 223

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Parental Decision-Making About Children's Participation in Clinical Research

Abstract

By

MICHELLE EDER

Decisions about participation in clinical research are becoming a common part of treatment seeking for many diseases, yet little is known about how these decisions are made. The purpose of this research was to enhance understanding of parental decision-making regarding their child's participation in a clinical trial for the treatment of acute leukemia by: 1) describing the reasons parents give for enrolling their child in a clinical trial, and 2) examining the factors that influence parental decision-making, including patient, parent, clinician, and social network factors. Informed consent conferences between doctors and the families of 108 children with leukemia were observed and audiotaped. Parent interviews conducted after the informed consent conference were designed to elicit information regarding parents' understanding of the informed consent information as well as factors related to their decision to participate (or not) in a clinical trial for the treatment of their child's leukemia.

In-depth analysis of the informed consent conferences and parent interviews indicates that parental decision-making in this context is quite complex. Although the majority (82%) of parents did decide to participate in the trial, these parents reported many different reasons for their decision. The two
most frequently cited reasons for participation in the trial were direct benefit to
their child and altruism, but parents also listed the right to withdraw, comparison
to standard, safety, the doctor, and better monitoring as reasons. All four
factors that were hypothesized to impact decision-making (patient, parent,
clinician, and social network factors) were found to shape parental decision-
making in some manner.

Two findings in particular have important implications for decision-
making and communication research. First, this study provides evidence that
the language used by the physician in recommending the trial and presenting
the risks and benefits of the trial, including positive/negative and
specific/general framing of issues, impacted parental decision-making in many
ways. Second, parental decision-making was affected by the significant roles
played by social network members both during and after the informed consent
conferences. Physician sensitivity to the influence that they and social network
members have on parental decision-making can improve doctor-family
interactions and aid parents in making this difficult decision.
Chapter 1: Background and Introduction

Anthropologists have long been interested in describing health and illness behavior, including decision-making about treatment (Coreil, et al. 1994; Curry, et al. 2002; Frank, et al. 1998; Garro 1998; Oths 1994; Pelto and Pelto 1997; Ryan 1998; Sargent 1989; Schoenberg, et al. 2003; Yoder and Hornik 1996; Young 1981b). Decisions about participation in clinical research are becoming a common part of treatment seeking for many diseases, yet little is known about how these decisions are made. There has been a great deal written, especially in the bioethics literature, about how decisions regarding participation in clinical research should be made (American Academy of Pediatrics Committee on Bioethics 1995; Edwards, et al. 1998; Faden and Beauchamp 1986; Levine 1986; Markman 1998; U.S. Department of Health and Human Services 1983), but few studies have been conducted to determine how they are actually made. An in-depth study of this decision-making process is needed to improve our understanding of this increasingly important aspect of illness behavior, and an anthropological approach is well-suited to this endeavor.

When patients are presented with the option of participating in a clinical trial, they experience a specific kind of encounter with physicians called the informed consent process. The doctrine of informed consent is a product of the Declaration of Helsinki that was drafted by the World Medical Association in 1964 in an effort to ensure the protection of human research subjects (Faden and Beauchamp 1986; Levine 1986). This informed consent process consists of four essential elements: disclosure of information about the research, subject
understanding of the information, voluntary consent, and subject competence to consent (Faden and Beauchamp 1986; Levine 1986). Children under the age of 18 are not considered competent to give informed consent, so their participation in research requires the proxy consent of their parents or legal guardians. In pediatric research, the protection of the patient-subject becomes particularly critical because someone other than the patient is making the decision about participation, and this decision is expected to be made in the patient’s best interests (Zupancic, et al. 1997).

The majority of children with cancer are treated on a randomized clinical trial (Bleyer 1997; Hirschfeld, et al. 2000; Murphy 1995; Pediatric Oncology Group 1992), therefore it is important to explore the process of parental consent in this context. Because most parents decide to enroll their children in cancer clinical trials (between 51% and 92% reported in literature), the reasons for the decision to participate become as interesting as the decision itself.

Much has been written about what kinds of information clinicians are required to give to prospective research subjects (Faden and Beauchamp 1986; Levine 1986). Researchers have also looked at why people accept or decline participation in a trial, but these studies suffer from many methodological limitations, such as the use of hypothetical situations instead of actual decision-making, reliance on closed-ended survey questions, and exclusive focus on rational decision-making processes (Harth and Thong 1990; Penman, et al. 1984; Ruccione, et al. 1991; Tabak 1995; Verheggen, et al. 1998; Zupancic, et al. 1997). In addition, there has been no link made between research in
informed consent communication and patient decision-making. Empirical studies of informed consent must resolve this limitation by examining both the communication that occurs during informed consent as well as its link to patient decision-making.

The overall goal of this dissertation is to enhance understanding of parental decision-making regarding their child's participation in a randomized clinical trial (RCT) for the treatment of acute leukemia. In order to achieve this goal, this research aims to: 1) describe the reasons parents give for their decision about their child's participation in a clinical trial for the treatment of acute leukemia, and 2) examine the factors that influence parental decision-making regarding their child's participation in a trial, including patient, parent, clinician, and social network factors. The aim of this study is not to predict behavior, but to provide a descriptive analysis of how the factors of interest influence decision-making.

Literature on Clinical Trial Decision-Making
There are a growing number of studies that look at people's decision-making regarding clinical trial participation, however few of these focus on parental decision-making on behalf of their minor children. The literature review below includes research on adults making decisions for themselves as well as parents making decisions for their minor children. First, studies that have examined the reasons given by patients and parents for their decision to participate in a
clinical trial are reviewed. Next, the results of previous research focusing on factors that potentially influence decision-making are outlined.

**Reasons Given by Patients and Parents for Participation in a Clinical Trial**

A review of studies which have investigated patients' and parents' reasons for participation in a clinical trial shows that altruism (advancing science, helping children in the future), the hope of better care on a trial, and trust in the physician are the most common reasons given for participation. For instance, van Stuijvenberg's study of parental consent to their child's participation in a clinical trial found that 32% of consenting parents listed "benefit for their own child" as a major reason for participation, and 54% of consenting parents listed "contributions to clinical science" or "benefit for other children in the future" as important (van Stuijvenberg, et al. 1998). Ninety-four percent of the parents surveyed by Zupancic regarding their decision to enroll their newborn on a clinical trial cited altruistic motives for participating (Zupancic, et al. 1997). In addition, the results of Harth and Thong's study showed that "to benefit my own child" and "to benefit others" were the two most common reasons given by parents for volunteering their child for trial participation, with 61 out of 68 parents listing the former reason and 67 out of 68 listing the latter (Harth and Thong 1990). Parents of children with cancer who participated in a focus group about trial participation discussed helping other children as well as better care and monitoring for their child as the primary reasons for trial participation (Caldwell, et al. 2003).
In Dehlinger’s study of adult cancer patients, the most common reason for patients’ decision to participate was perceived direct benefit followed by the fact that the physician recommended the research trial (Dehlinger 1986). Bevan found that the three main reasons given by adult patients for participating in a clinical trial were to help others, improve their own treatment, and because the doctor asked them to participate (Bevan, et al. 1993). Jenkins and Fallowfield also found that altruism and trust were the most important reasons given for entry onto a cancer trial (Jenkins and Fallowfield 2000).

Another reason given for participating in a clinical trial is a feeling of obligation to society because other people have participated in the past. For example, one-third of the adult subjects in Madsen’s study felt a moral obligation to participate in research because of benefits they received from former trial participants (Madsen, et al. 1999). Kass also found that many adults viewed participation in research as a “civic responsibility” (Kass, et al. 1996).

**Factors that Influence Decision-Making**

Many studies have examined factors that may influence decision-making regarding trial participation. The factors that emerge from the literature can be broadly grouped into four types: 1) patient factors, 2) parent factors, 3) clinician factors, and 4) social network factors. These four types of factors are briefly outlined below and provide the major categories of independent variables used in this dissertation.
**Patient Factors**

The patient's illness severity may impact the decision-making process. Schaeffer found that illness severity influenced the reasons for participating in clinical research in adults making a decision for themselves (Schaeffer, et al. 1996), but Zupancic's research showed illness severity was not a significant predictor of parents' decisions to enroll their newborn in a clinical trial (Zupancic, et al. 1997). In focus groups, parents of healthy children and parents of children with cancer expressed the belief that their child's illness severity influenced their willingness to participate in a trial (Caldwell, et al. 2003). Other related patient factors that may influence parental reasons for participating in a trial include the child's prognosis and the way it is presented to the family. Negative framing of the patient's prognosis may be associated with acceptance of riskier treatments such as RCTs (O'Connor 1989; Siminoff and Fetting 1989; Tversky and Kahneman 1981).

**Parent Factors**

Parent factors that can influence the reasons given for participating in a clinical trial include understanding, sociodemographic variables, and general attitudes toward research. Cox and Avis suggest that understanding is an important variable because people may make decisions based on unrealistic expectations of the benefits of trial participation (Cox and Avis 1996). Certain sociodemographic variables are also likely to be associated with decision-making. Levin and Schiller point out that social class can affect ethical
decision-making because people of different social classes have different values as a result of their different life experiences (Levin and Schiller 1998). These lived experiences vary according to people’s place in the “social organization of production” and influence what matters to individuals, which in turn affects the way people look at their treatment options. People’s religious backgrounds can also influence their medical and ethical decision-making (Wind 1990). People of different ethnic or cultural groups may place more or less emphasis on autonomous decision-making, the significance of obligations to the larger society, the doctor/patient relationship, and trust in physicians (Fox and Swazey 1984; Kaufert and O’Neil 1990).

A parent’s general attitude about clinical research will influence their decision about their child’s participation in a clinical trial. There have been several studies of public attitudes toward clinical trials, all of which show that the majority of people have a positive outlook on research (Cassileth, et al. 1982; Fallowfield, et al. 1998; Ganz 1990; Madsen, et al. 1999). For example, 71% of respondents to Cassileth’s questionnaire answered “I believe that people should serve as research subjects” (Cassileth, et al. 1982). In another study, 90% of subjects asked about their general attitude toward clinical trials chose “very positive” or “positive” as their response (Madsen, et al. 1999).

There may be some groups of people, however, who are more likely to hold negative views of research. For example, several studies show barriers to the participation of African Americans in clinical trials due to such issues as a lack of trust in researchers because of past research abuses (Corbie-Smith, et
Corbie-Smith asked a sample of African-American outpatients about their concerns regarding participation in medical research (Corbie-Smith, et al. 1999). These patients expressed a generally negative attitude toward participation in clinical research, related concerns about physician honesty, and expressed the belief that there is a fundamental lack of trust between physician-researchers and patients. In another study, African Americans, Hispanics, and Native Americans all expressed mistrust of research and those who conduct research (Roberson 1994).

Clinician Factors

The literature on decision-making suggests that there are three major ways in which clinicians influence the decision-making process. First, the manner in which information about the trial is presented by physicians can play a major role in parents' views of participation. For example, disclosure of uncertainty surrounding the risks and benefits of the clinical trial could give parents a negative view of the trial (Katz 1984). The framing of the risks associated with the trial can shape the meaning of participation in the trial for parents by altering their assessment of risks and benefits. For example, O'Connor et al. suggest that the choice between treatment alternatives with uncertain risks and benefits can be influenced by whether the outcomes are framed positively or negatively (O'Connor 1989).
During informed consent meetings, doctors may discuss trial participation in terms of the benefit to future children and/or in terms of a better chance of cure for the individual child. Clinician choice of how to present the benefits of participation will impact parents’ determination of the risks and benefits of participation. In this sense, Daugherty suggests that patients’ perceptions of chance for benefit in trials “may merely be a reflection of the beliefs of the physicians who explain the trials and obtain a patient’s informed consent” (Daugherty, et al. 1995).

Evidence for variability in clinicians’ views of the benefits of participation can be found in the literature, and it is likely that these differences translate into diverse approaches to presenting a trial. For example, some recent studies have reported evidence that patients who are treated on a clinical trial do better than patients given the same treatment outside of a trial (Lantos 1999; Stiller 1989). Several reasons for this “inclusion benefit” have been postulated, including bias in trial recruitment, placebo effects, and increased medical attention, such as monitoring of side effects. Lantos concludes from this evidence of an inclusion benefit that “perhaps we should include, as part of the informed consent process for clinical research, a statement to the effect that participation in a research protocol has been shown to lead to better outcomes than nonparticipation” (Lantos 1999). Several other authors agree with Lantos and recommend providing patients with this information to use during decision-making (Gelber and Goldhirsch 1988; Kaufman 1993; Markman 1998; Murphy 1999). On the other hand, Edwards stresses that personal gain is not a realistic
hope in these trials, and decisions based on self-interest can not be considered informed choices (Edwards, et al. 1998). Debates such as these point to the complexity of issues like the presentation of the benefits of participation in clinical trials.

Second, the physician's recommendation of the trial can influence parents' decision-making because, as Schain suggests, "a patient's expectations about how the physician's behavior is likely to be affected by participation in a clinical trial are likely to motivate trial enrollment" (Schain 1994). For example, Siminoff and Fetting found the physician's recommendation to have the greatest effect on the treatment decision-making of women with breast cancer (Siminoff and Fetting 1989). Bevan found that 38% of patients consented to participate in a clinical trial out of a desire to comply with the doctor's request (Bevan, et al. 1993). In the Subject Interview Study conducted by the Advisory Committee on Human Radiation Experiments, 100 of the patients who reported having personal experience in medical research were interviewed in depth about their reasons for participating (Kass, et al. 1996). The physician's recommendation was cited as a powerful factor influencing the research decision, indicating a high level of trust in the physician. Many other researchers found high levels of trust in the clinician to be related to participation in clinical trials (Bujorian 1988; Zupancic, et al. 1997). As Kass advises, "The current emphasis in research ethics on analyses of benefits and risks and on subjects' autonomous decisionmaking is insufficient. The paradigm must be enriched with a sensitivity to the profound trust
Third, the parent’s relationship with the clinician offering the clinical trial clearly plays an important role in parental decision-making. High levels of trust can lead to a desire to follow doctors’ treatment recommendations, but trust can also be related to a preference to leave decision-making about treatment to the doctor. Many studies concerned with decision-making have looked at how involved patients want to be in making decisions regarding their treatment (Blanchard, et al. 1988; Cassileth, et al. 1980; Strull, et al. 1984; Sutherland, et al. 1989). Research has shown that the degree to which patients wish to rely on their doctor’s advice about research participation varies, but is generally quite high. For example, Strull’s survey of adult hypertensive outpatients showed that only 53% of patients desired to participate in treatment decisions (Strull, et al. 1984). Similarly, Sutherland et al. found that 63% of adult cancer patients felt the physician should be the primary decision-maker (Sutherland, et al. 1989).

Pyke-Grimm asked parents of children with cancer about their desired role in treatment decision-making and found that 52% of parents preferred a collaborative role, 34% a passive role, and 14% an active role (Pyke-Grimm, et al. 1999). Zupancic found that 32% of parents would prefer to have the doctor advise them about enrolling their newborn on a trial rather than deciding themselves (Zupancic, et al. 1997). Snowden reports that some parents who consented to their child’s participation in a clinical trial viewed the responsibility
for making the decision as burdensome and anxiety provoking (Snowdon, et al. 2002).

Patients’ and parents’ preferences for involvement in the decision-making process can be influenced by several things. Butow found significant differences in preferences for decision-making control between the patients of two doctors, and suggests that the doctor’s behavior can influence patient’s decision-making preferences by sending messages of their preferences for involving patients in decision-making (Butow, et al. 1997). Butow also found a significant influence of religion on attitudes toward decision-making, with those believing God controlled the outcome of disease desiring less decision-making responsibility. Bujorian proposes that illness severity may influence patients’ level of participation in decision-making, and it may be true that the child’s illness severity will affect parental decision-making preferences as well (Bujorian 1988). In addition, there may be cultural differences in how patients view the doctor/patient relationship. For example, Kaufert and O’Neil studied informed consent interactions between biomedical doctors and Native Canadian patients and found problems due to different expectations of the doctor/patient relationship (Kaufert and O’Neil 1990). Native Canadians used a cultural model of the doctor/patient relationship that expects doctors to prescribe ONE treatment and patients to follow instructions without question. The degree to which decision-making is shared with the physician is an important measure to include in studies of the clinical trial decision-making process.
Social Network Factors

Studies of decision-making about trial participation are primarily concerned with individual decision-making and downplay the important influence of social network members. Anthropological research has shown that social networks, often referred to as the "lay referral network", influence many aspects of the illness career. Beginning with the classic works of Chrisman and McKinlay, anthropologists and sociologists have described the role of social networks in the labeling of symptoms, decisions about when to take action and what type of action to take, and adherence to treatment regimens (Chrisman 1977; McKinlay 1973; McKinlay 1980). More recently, Mathews has stressed the fact that treatment decision-making is rarely limited to the patient, but often involves the social network (Mathews 1987). Hampshire's study of pastoralist women in Chad showed how the availability of social networks influences treatment options (Hampshire 2002).

It is likely that the lay referral network plays a significant role in decision-making about trial participation, as it does for treatment seeking in general. McKinlay's work describes the ways in which social networks influence what actually goes on during doctor/patient encounters (McKinlay 1973; McKinlay 1980), and these influences are likely to occur during informed consent conferences as well. For example, family members are involved in shaping the patient's expectations of the relationship. In addition, the presence of family members during the encounter influences the content of the conversation. Family members often help in the relay of information both to the doctor and the
patient, and they also work with the patient to evaluate the interaction with the
doctor and the relationship. Janzen describes the role of the "therapy
management group" in Zaire—a group of the patient's kin who make decisions
regarding the cause and appropriate treatment for the patient's illness (Janzen
1978). People may turn over responsibility for decision-making to their kin, as
in Zaire, when faced with a decision about research participation.

The few studies which have looked at the role of social networks in
people's decisions regarding trial participation suggest that social networks are
influential. For instance, 27 of 28 parents in a study by Ruccione said they had
discussed the consent form for their child's participation in a cancer trial with
someone else before they signed it (Ruccione, et al. 1991). The majority of
parents reported spouse, grandparents, other patients' parents, and friends as
sources of information that they utilized in making their decision, and they rated
the information received from these sources as helpful. Dehlinger found that
almost all of the cancer patients in her study consulted with someone in their
social network regarding participation in a clinical trial, and the majority of these
patients reported a strong influence of the social network's input on their
decision (Dehlinger 1986). Penman et al. found that most of their 144 subjects
discussed a chemotherapy trial with family and friends to get more information
or help in the decision-making process (Penman, et al. 1984). Rodenhuis et al.
found that all patients said relatives and friends were of great importance in
their decision to participate in a chemotherapy trial (Rodenhuis, et al. 1984),
and Tabak reports 70% of patients in his study consulted with other people
before making their decision (Tabak 1995). Finally, Daugherty et al. looked at a cancer clinical trial and found that 85% of patients discussed participation with their family and 48% discussed participation with friends (Daugherty, et al. 1995).

Sutherland et al. asked patients to identify people who would most likely want them to participate in research and those whose recommendations they would most want to comply with (Sutherland, et al. 1998). These social norms proved to be a significant contributing factor to patients' decisions. Penman's results also showed that 61% of patients cited “family wants it” as a major reason for their acceptance to participate in a clinical trial (Penman, et al. 1984). DeLuca et al. looked at patients' decision-making regarding participation in cardiovascular clinical trials and found that 97% of those who had the approval of their spouse to participate did consent and 96% of those whose spouse was opposed to participation declined (DeLuca, et al. 1995). Approval of other family members proved to be equally influential to patients' decision-making. In addition, 30% of patients in Daugherty's research said that a major reason for consenting to the trial was that family members wanted them to (Daugherty, et al. 1995). This suggests the importance of network approval for decisions made regarding trial participation.

The studies described above lend credence to the conclusion of Daugherty et al. that “family members and community physicians...should be viewed as important as the research oncologist...in playing a role in patients' decisions to participate in...trials.” Unfortunately, none of these studies have
looked at what kind of information or advice was sought or received by patients, leaving a significant gap in knowledge regarding decision-making about trial participation (Daugherty, et al. 1995).

Limitations of Current Decision-Making Research

In summarizing his research, Kass stated, "Patients conceptualize research participation in quite complex ways. On the one hand, patients described themselves as sincerely motivated to help others, while, on the other, they suggested that they would not have participated on that basis alone...[They] must have belief in some personal benefit as well" (Kass, et al. 1996). This complexity has not been explored in decision-making research to date. The studies cited above present many variables that influence participation in clinical research. What these studies fail to do is explain why some patients say altruistic motives influenced their decisions, but others that were offered the same trial say their decision was driven by the desire to benefit directly from participation. In other words, they do not provide an explanation for the variability in reasons given for participating, nor do they suggest how the various reasons are weighed by individuals in making a decision.

The lack of such explanations is likely related to the fact that many decision-making studies are conducted and reported from the perspective of trying to increase patient accrual to clinical trials by uncovering barriers to participation rather than understanding the decision-making process.
Many of these studies are also limited by their use of hypothetical situations rather than actual decision-making. Surveys, the predominate methodology used by clinicians and ethicists, may give quite different answers to how people view ethical issues than direct observation and interviewing with regard to particular behaviors. What people say they will do and what they do are often two different things, so responses to hypothetical situations are not an accurate reflection of actual decision-making (Fox and Swazey 1984; Lambert and McKeivitt 2002). As stated by Muller “To understand the ‘rumpled reality’ of moral decision making, it is critical to examine how people actually behave in problematic situations and the reasons or justifications they give for their behavior” (Muller 1994).

Another methodological pitfall that hinders these studies is the use of closed-ended questions that force people to choose from a limited list of options that reflect the interests of the researchers rather than allowing them to answer in their own words. Daugherty suggests that specifically asking if altruistic motivations influenced a person’s decision biases the results because people are reluctant to say that they wouldn’t want to help others (Daugherty, et al. 1995). Semi-structured interviews with open-ended questions offer some flexibility that allows parents the opportunity to provide spontaneous answers, speak in their own terms, and expand on issues that are relevant to them without being biased or led by ideas expressed by the researchers (Lambert and McKeivitt 2002).
Most studies of decision-making are also limited by their nearly exclusive emphasis on rational decision-making, such as weighing the costs and benefits of participation in research. For instance, both Zupancic and Verheggen found that participation in the research trial was associated with a lower assessment of risk and a higher assessment of benefit (Verheggen, et al. 1998; Zupancic, et al. 1997). Both of these authors conclude that people make a decision about participation in a clinical trial by weighing the risks and benefits of participation, but the results of these studies may merely be a reflection of the restricted set of variables that were examined.

There is evidence to suggest that many nonrational elements of decision-making are important as well, and should be included in studies to get an accurate picture of the decision-making process. Allan Young made a strong argument against this assumption of decision-makers as “rational men” (Young 1981a). He provided examples of many types of nonrational influences on decision-making, including reference to a particular sickness episode experienced in the past as a “prototype” for understanding later episodes. Bujorian suggests that patients often have either a positive or negative bias toward research, and they may make hasty, irrational decisions based on these biases (Bujorian 1988). Harth and Thong discuss “attitudinal and psychological” factors that may militate against a rational approach to decision making, such as a high level of trust in doctors or the medical system (Harth and Thong 1995). Huizinga found that many patients offered the option of participating in a cancer trial did not use a rational decision-making approach,
but rather decided about participation immediately after receiving information
about the trial (Huizinga, et al. 1999).

Kahneman and Tversky point out many ways in which people make
choices in nonrational ways (Kahneman and Tversky 1982; McKean 1985). For
example, their studies showed that the threat of a loss has a greater impact on
people's decisions than the possibility of an equivalent gain. Eraker and
Politser discuss many nonrational influences on treatment decision-making,
such as framing (positive versus negative), vividness (the fact that emotionally
stimulating information may have more impact on decision-making than other
information), and fear of regret, which can cause people to minimize their
involvement in decision-making (Eraker and Politser 1982). Janis and Mann
describe how the stress of the situation and decision-making itself can limit a
person's ability to think rationally (Janis and Mann 1977). Brock and Wartman
explore other forms of irrational decision-making, such as a bias toward the
present and near future, and the fear of pain (Brock and Wartman 1990).

Perhaps the biggest problem with decision-making research to date is
the failure to study the interaction between patients and doctors and how this
interaction influences decision-making (Kuczewski and Marshall 2002). As
Renee Anspach argues, "Until we know about the social dynamics of
communication between parents and professionals, informed consent is likely to
remain an elusive ideal rather than a practical reality" (Anspach 1993). Kaufert
and O'Neil's work is one of the few examples of research that actually examines
the process of interaction in consent (Kaufert and O'Neil 1990). In their
investigation of interactions between Native Canadians and biomedical doctors, they focused on what happened during the informed consent encounter and how the participants influenced each other's perception of the situation, but this study did not look at the patients' decision-making process. Jenkins audiotaped consent discussions for cancer RCTs and surveyed patients regarding their reasons for accepting or declining (Jenkins, et al. 1999). They examined patients' remarks during the consent conference about reasons to participate in the RCT, and compared these comments to the reasons they gave after they made their decision. They stopped short, though, of including an analysis of what the physicians said during the consent conference and how this influenced patient decision-making.

An Anthropological Approach to the Study of Trial Decision-Making

Anthropologists have long been interested in medical decision-making. Many anthropologists have focused on decision-making in medically pluralistic settings in developing countries. In many such settings, people are faced with a choice between Western biomedicine and traditional forms of medicine, and anthropologists have played a key role in increasing our understanding of how people make these choices. Some well-known examples of this type of research include John Janzen's research on treatment seeking in Zaire (Janzen 1978), Carolyn Sargent's study of obstetrical choices made by Bariba women (Sargent 1989), Young and Garro's work on decision-making in Mexico (Young
1981b), and Kathryn Oths' study of a change in patterns of resort made by families in Peru during an economic crisis (Oths 1994).

Anthropological research has also extended to the study of medically pluralistic settings in developed countries. For example, some researchers have conducted studies to explain people's choices between biomedical treatment versus "alternative" or "unconventional" therapies (Kelner and Wellman 1997; McGregor and Peay 1996; McGuire 1988). Others have concentrated on describing how U.S. immigrants choose between Western biomedical treatment and folk treatment of their country of origin (Chavez, et al. 1992; Guo 2000; Leclere, et al. 1994; Markides, et al. 1985; Pang 1989).

The choice faced by the parents in this study represents a relatively new situation of medical pluralism that exists in the developed world. These parents were asked to make a decision between standard leukemia treatment for their child and treatment on a clinical research trial. Participation in a clinical trial is becoming an increasingly common treatment option available to patients, and is thus an important part of the contemporary context of medical decision making. Many of the lessons learned from anthropological work in developing countries mentioned above may apply to this newer context. For example, Sargent's description of Bariba women's decision-making as "juggling" conflicting goals and priorities may fit the decision-making process of parents who are asked to choose between standard treatment and participation in a clinical trial (Sargent 1989). Like treatment options such as indigenous healing and alternative medicine, people's decisions to participate in a clinical trial for treatment need to
be studied in order to fill out our understanding of medical decision-making as it occurs today.

The use of ethnographic methods, such as observation, open-ended and in-depth interviewing, and qualitative analyses, to explore bioethical issues is a major contribution that anthropology can make to decision-making studies (Marshall 1992; Marshall and Koenig 1996; Muller 1994). There are several examples of decision-making studies that have utilized an ethnographic approach (Anspach 1993; Rapp 1999; Zussman 1992). The major advantage of ethnography as a methodology is that it provides crucial information on actual behavior. Hoffmaster points out the importance of describing how people actually “muddle through” ethical problems (Hoffmaster 1992). Conrad articulates the difference between social science and bioethics by saying that bioethicists write about how they think medical decisions ought to be made, while social scientists try to describe the way they actually are made in practice (Conrad 1994). Some of the ethnographies of medical decision-making have shown that participants in ethical problem-solving rarely make decisions in a manner consistent with the guidelines set by bioethicists (Rapp 1999; Zussman 1992).

In medical anthropology, the idea that illness has meaning to people is central. That idea can be extended to this context by saying that participating in research has meaning to people. Using a meaning-centered approach to studying decision-making about trials, it is possible that people give different reasons for participating in research because participating means something
different to each of them. In this setting, the informed consent conference (ICC) is the primary communicative event that influences parental conceptions of the trial, but what each participant brings with them into the ICC also influences the outcome. Siminoff and Fetting summarize the state of decision-making research by saying, “Much of the research in this area has, to date, been based on retrospective surveys or presentation of hypothetical clinical situations to subjects. Further studies should concentrate on the actual information preferences expressed by patients during the decision-making process and on the impact of information disclosure on decision-making” (Siminoff and Fetting 1991).

Model
This study will attempt to respond to this call for more robust research with a methodology and analysis that includes all the individuals involved in the decision-making process, an expanded list of potential influences on decision-making, and a link between the actual doctor-parent informed consent interaction and parental decision-making. The independent variables of the study are based on the decision-making literature and studies of doctor-patient communication cited above, and are grouped into four types of factors: patient, parent, clinician, and social network factors. The model in Figure 1 below depicts the hypothesized relationships between the four sets of factors and parental decision-making.
Figure 1: Model of Parental Decision-Making About Trial Participation

**Patient Factors**
- Prognosis
- Illness Severity at Time of Decision
- Risk Level
- Sociodemographics

**Parent Factors**
- Sociodemographics
- Understanding of Trial

**Social Network Factors**
- Support Given During ICC
- Support Sought and Given During Decision-Making

**Clinician Factors**
- Doctor/Parent Relationship
- Physician’s Recommendation
- Description of Trial

**Parental Decision about Participation in Trial**

**Parental Reasons for Participation in Trial**
Chapter 2: Methodology

Data Collection

This dissertation is based on a multi-site, NCI-funded study entitled Informed Consent in the Children’s Cancer Group (R01 CA083267, PI: Eric Kodish, MD). This study examined the informed consent process for participation in clinical trials for treatment of pediatric leukemia. We recruited a total of 140 parent subjects from six Children’s Cancer Group (CCG) institutions that routinely treat children with acute leukemia: Rainbow Babies & Children’s Hospital of University Hospitals of Cleveland in Cleveland, Ohio; Children’s Hospital of Philadelphia in Philadelphia, Pennsylvania; Children’s Hospital Medical Center in Cincinnati, Ohio; Children’s Hospital of Los Angeles in Los Angeles, California; MD Anderson Cancer Center in Houston, Texas; and Children’s National Medical Center in Washington, D.C. Eligible parents included all those whose children were diagnosed with acute leukemia and were offered participation in a front-line CCG acute leukemia RCT. The study was approved by the Institutional Review Board at each site.

We obtained the informed consent of the parents, physicians, and patient (as age appropriate) shortly after the patient’s diagnosis with either acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML). Trained researchers observed and tape recorded the informed consent conference(s) (ICCs) that clinicians convened for the purposes of discussing treatment options including participation in a clinical trial. Each taped conference was later coded using the Observer Checklist (OC), an instrument developed to code the
occurrence of behaviors specific to clinical discussions related to cancer (Siminoff and Fetting 1991). The Observer Checklist allowed us to document whether certain information about the trial was disclosed to parents. Three independent coders listened to each tape and recorded data on the checklist, and variations were reconciled according to established policy rules.

Parents were interviewed within 48 hours of their informed consent conference with their child's clinician(s), and then interviewed again once they had made a decision about whether or not to participate in the trial. Whenever possible, the parent who was most active during the informed consent conference was interviewed. We designed the parent interviews, available in English and Spanish, to elicit information regarding parents' understanding of the informed consent information as well as factors related to their decision to participate (or not) in the clinical trial for the treatment of their child's leukemia. Many of the questions were open-ended to allow parents to speak freely and respond in their own words rather than being forced to choose between a list of items. A Decision-Making Preference Questionnaire (Pyke-Grimm, et al. 1999) and a Trust Scale (Wheeless 1978) were also administered. Demographic information was collected, including patient age and gender, and parent age, gender, education, socioeconomic status, race, and religion. Follow up interviews were conducted over the telephone 6-8 months after diagnosis, and included items to assess long-term understanding of issues related to clinical trial participation.
Clinicians involved in the taped informed consent conference(s) were asked to complete a self-administered questionnaire. The clinician questionnaire included items relating to the information that was given to parents/patients and the clinician's recommendations regarding treatment options. In addition to this Case Specific Questionnaire, we asked clinicians at all six institutions to fill out a general clinician questionnaire about their attitudes toward informed consent.

After the observation and interview phase of the study was complete, focus groups were held at each of the participating sites with a sample of parents who had participated in our research previously. These focus groups were designed to elicit more in-depth parent perspectives on aspects of the informed consent process using a more open-ended, interactive methodology. A professional facilitator with a background in education and unknown to the participants facilitated the discussions, with an observer taking notes. Each session lasted 2 hours and was audiotaped.

In October of 2002, nine of the parents who were involved in the focus groups attended a two day meeting in Cleveland. During the meeting, members of this Parent Advisory Group on Informed Consent (PAGIC) were asked to provide their perspectives on the data we had collected during observation of ICCs, parent interviews, and focus groups. They also worked together to develop recommendations for how to improve the informed consent process. An overview of the research methodology is shown in Figure 2 below.
Role of Dissertation in Larger Research Project

This dissertation project is part of the NCI-funded study discussed above. I have been involved in this study since its inception in 1999, acting as a Research Associate during data collection, and as the Project Director since 2002. I assisted the Principal Investigator of the project (Eric Kodish, MD) and the original Project Director (Christian Simon, PhD) with the development of the study instruments (interviews and Observer Checklist), including pilot testing. During the data collection period, I was responsible for recruiting new parent-subjects, observing informed consent conferences, coding audiotaped

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conferences using the Observer Checklist, and administering parent interviews for all cases in Cleveland. I also served as an independent coder of all cases from the other five research centers, entered all data for the project into our Access database, and maintained data tracking systems. In order to gather more information regarding parental decision-making for the purposes of this dissertation, I wrote several questions to include in the follow-up interviews, focus groups, and PAGIC seminar. I attended five of the eleven focus group sessions, acting as a silent observer and note taker.

My interest in this topic, and my initial formulations of the variables that influence parental decision-making, came directly from my experience with direct observation, coding of conferences, parent interviews, focus groups, and the PAGIC meeting. More specifically, during data collection, I made two significant observations. First, I came to appreciate the diversity of ways physicians presented a clinical trial as a treatment option. At the same time, I recognized that although most parents consented to enroll their child in a trial, their reasons for consenting varied, but the reason for this variability was not readily apparent. The goal of this dissertation is to bring these two observations together to describe in detail the process of decision-making in this context. None of the decision-making data from the project has been previously analyzed or published.
Sample

The larger project described above had a total sample of 140 cases. For this dissertation, 32 cases involving parents who had no understanding of choice between participation in a clinical trial or receiving treatment outside of the trial were excluded, leaving a sample of 108 cases (see Chapter 4 for more information).

Context

Clinical features that determine the child's prognosis include the diagnosis (type of leukemia), the white blood cell count (WBC) at diagnosis, and whether or not there was Central Nervous System (CNS) disease at diagnosis. One hundred (92.6%) of the 108 patients were diagnosed with Acute Lymphoblastic Leukemia (ALL) and 8 (7.4%) with Acute Myelogenous Leukemia (AML). The two types of leukemia differ in their treatment and cure rate, with the treatment for ALL being longer (2-3 years vs. 6 months), less intense, and associated with a higher chance of cure (70-90% vs. 50-60%). The WBC at diagnosis is an important prognostic feature of leukemia, and is used to separate ALL into standard risk (WBC<50,000) and high risk types (WBC>50,000). The mean WBC at diagnosis for the sample of 108 patients was 43,424 (SD = 72,896), with a range of 700 to 459,000. Children with leukemia in the CNS at diagnosis are considered higher risk and automatically receive intensified therapy. Only two patients out of the 108 had CNS disease at diagnosis.
Cure is defined as disease-free survival at least 5 years beyond the completion of therapy. The mean chance of cure given at diagnosis for the 108 patients in this sample was 76.5, with a fairly wide range of 50-90. While the cure rate for pediatric leukemia has improved vastly in the past few decades, many children still die from the various forms of the disease. This fact looms large in parents’ minds and is coupled with the negative connotations associated with a diagnosis of cancer. Thus, the context of decision-making about trial participation may be perceived and experienced quite differently by parents as compared to physicians.

Children in this study all had some type of acute leukemia, which is characterized by rapid onset. Presenting symptoms are the result of the growing number of immature lymphocytes (blast cells) that crowd out the normal blood cells throughout the body. These symptoms can include fatigue, fever, bone pain, anemia, bruising or bleeding, swollen lymph nodes, and hepatosplenomegaly (enlarged liver and spleen). Some patients are diagnosed from a blood test during a routine visit to the pediatrician and have no noticeable symptoms at diagnosis.

The 108 children in this sample were offered participation in one of four different Children’s Cancer Group (CCG) Phase III randomized clinical trials depending on their type of leukemia. Twenty (18.5%) were offered CCG-1952 for standard risk ALL, 33 (30.6%) were offered CCG-1991 for standard risk ALL, 47 (43.5%) were offered CCG-1961 for high risk ALL, and 8 (7.4%) were offered CCG-2961 for AML. These four trials are all randomized and include
standard therapy as one of the arms of the trial. Because they are Phase III trials, the research questions in these trials are limited to minor modifications from standard therapy.

The informed consent conference typically takes place within several hours of the diagnosis, and presentation of the clinical trial is embedded in a larger discussion of the diagnosis and general treatment issues. The 108 ICCs included in this study were conducted in English in 92 cases, and 15 non-English cases included translators. The 108 ICCs were led by 59 different physicians, making it unlikely that physician style unduly influenced conference characteristics. The time allowed for decision-making about trial participation varies according to the trial offered. In this study, 69% of patients were offered participation in a trial that required a decision within 72 hours of the child receiving their first chemotherapy. The CCG-1991 study that was offered to 31% of the families incorporated a staged consent process which allowed parents to consent up front to the first 28 days of therapy which is the same on or off the trial, and then make a decision about the randomized portion of the trial by the 28th day.

All of the families included in this analysis were treated at a large pediatric research institution, so the hospital environment is similar for all 108 informed consent conferences. Because the setting is held constant across cases, it does not need to be included in the model as a potential confounding variable. Additionally, it is estimated that 95% of children with cancer in the U.S. are treated at a large research hospital belonging to a national cooperative
group (Bleyer 1997; Hirschfeld, et al. 2000; Murphy 1995; Pediatric Oncology Group 1992), therefore the findings from this study are likely to be representative of what occurs in the majority of pediatric cancer cases.

Measures

Table 1 below shows the variables that were measured, and the instrument used to assess each. The diversity of instruments used for the dissertation allows for 1) incorporation of perspectives from all groups involved (clinicians, parents, network members), and 2) triangulation of data by comparing results from different methods of data collection (Mays and Pope 2000). In addition to the instruments listed in the table, the transcripts of the Focus Groups and PAGIC meeting were searched for illustrative examples, but were not used for coding or measurement of any of the variables. Inclusion of examples from the Focus Groups and PAGIC meeting provides depth to the analysis by presenting parent perspectives of the decision-making process at three different time points and using three different methodologies: 1) Year 1-2 of project (Parent Interviews), 2) Year 3 of project (Focus Groups), and 3) Year 4 of project (PAGIC meeting).
<table>
<thead>
<tr>
<th>Variables</th>
<th>Instrument</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dependent Variables</td>
<td></td>
</tr>
<tr>
<td>On or Off Trial</td>
<td>Parent Interview</td>
</tr>
<tr>
<td>Reasons for Participation in Trial</td>
<td>Parent Interview</td>
</tr>
<tr>
<td>Independent Variables: Patient Factors</td>
<td></td>
</tr>
<tr>
<td>Prognosis</td>
<td>Transcript of ICC</td>
</tr>
<tr>
<td>Illness Severity</td>
<td>Transcript of ICC</td>
</tr>
<tr>
<td>Risk Level</td>
<td>Observer Checklist</td>
</tr>
<tr>
<td>Sociodemographics</td>
<td>Parent Interview</td>
</tr>
<tr>
<td>Independent Variables: Parent Factors</td>
<td></td>
</tr>
<tr>
<td>Sociodemographics</td>
<td>Parent Interview</td>
</tr>
<tr>
<td>Understanding of Trial</td>
<td>Parent Interview</td>
</tr>
<tr>
<td>Risk Analog</td>
<td>Parent Interview</td>
</tr>
<tr>
<td>Trust Scale</td>
<td>Parent Interview</td>
</tr>
<tr>
<td>Decision Making Preference Questionnaire</td>
<td>Parent Interview</td>
</tr>
<tr>
<td>Who was most important in decision</td>
<td>Parent Interview &amp; Clinician Questionnaire</td>
</tr>
<tr>
<td>Shared Decision Making During ICC</td>
<td>Transcript of ICC</td>
</tr>
<tr>
<td>Recommendation of Trial</td>
<td>Transcript of ICC</td>
</tr>
<tr>
<td>Physician's Recommendation</td>
<td></td>
</tr>
<tr>
<td>Strength of Recommendation</td>
<td>Parent Interview, Observer Checklist &amp; Clinician Questionnaire</td>
</tr>
<tr>
<td>Trial Most Strongly Recommended Option?</td>
<td>Parent Interview &amp; Clinician Questionnaire</td>
</tr>
<tr>
<td>Perceived Pressure</td>
<td>Parent Interview</td>
</tr>
<tr>
<td>Description of Trial</td>
<td></td>
</tr>
<tr>
<td>Presentation of Risks</td>
<td>Transcript of ICC</td>
</tr>
<tr>
<td>Presentation of Benefits</td>
<td>Transcript of ICC</td>
</tr>
<tr>
<td>Independent Variables: Social Network Factors</td>
<td></td>
</tr>
<tr>
<td>Support Given During ICC</td>
<td></td>
</tr>
<tr>
<td>Network Presence</td>
<td>Observer Checklist</td>
</tr>
<tr>
<td>Network Questions &amp; Comments</td>
<td>Transcript of ICC</td>
</tr>
<tr>
<td>Support Sought and Given During Decision-Making</td>
<td></td>
</tr>
<tr>
<td>Network Helpful in Decision</td>
<td>Follow Up Interview</td>
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<td>Network Helpful in Understanding</td>
<td>Follow Up Interview</td>
</tr>
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Dependent variables:

The dependent variables are: 1) the parents' decision to participate in the clinical trial or not, and 2) the reason(s) given by parents for their decision about enrolling their child in a clinical trial. First, each of the 108 parents was classified as "on" or "off" trial, based on their decision about whether to participate in the trial.

Besides the decision about whether or not to participate in the trial, the reasons parents gave for participating in the trial are also the focus of this dissertation. The reasons were measured by analyzing parents' answers to the following two questions during the interviews: Could you tell me why you have decided to participate (not to participate) in the clinical research study? and What three things were most important to your decision about the clinical research study? A list of reasons was developed from the analysis of the above items. Subsequently, each of the cases was examined for the presence/absence of each of the reasons. Measuring the dependent variable in this way allowed for using individual reasons in the analyses, which was necessary because most parents gave more than one reason for their decision.

Independent variables:

The independent variables are based on the decision-making literature and studies of doctor-patient communication cited above, and are grouped into four types of factors: patient, parent, clinician, and social network factors. More
specific information on the operationalization of the variables is described in the appropriate chapter devoted to that factor.

**Patient factors**

1. *Prognosis*. This variable was measured by the prognosis given by the clinician to parents during the ICC.

2. *Illness severity*. This comes from the physician's discussion during the ICC of the patient's presenting symptoms and general condition as compared to other patients with leukemia.

3. *Risk Level*. This variable encompasses risk factors such as age, white blood cell count, and diagnosis type.

4. *Sociodemographic variables*. These include age and gender.

**Parent factors**

1. *Sociodemographic variables*. These include age, gender, ethnicity, education, religion, and social class, which were collected during the parent interviews.

2. *Understanding of the clinical trial*. Cases involving parents who did not understand choice were excluded, so understanding of choice is held constant. Parental understanding was measured by a) whether or not a parent comprehends randomization, and b) their answer, on a scale of 0-10, to the question: *How risky is therapy in the clinical research study compared to standard therapy?*
Clinician factors

1. **Doctor/parent relationship.** This is characterized by two aspects of the doctor/parent relationship: trust and level of shared decision-making. A standardized instrument called The Individualized Trust Scale was used to measure trust (Wheeless 1978). In order to characterize the doctor/parent relationship further, the ICCs were analyzed for evidence of shared decision-making, including a) parents sharing their opinions about the trial or decision-making process, b) parents requesting the physician's recommendation about the trial, c) physician eliciting the opinions or decision of parents regarding the trial, d) discussion of parent and physician decision-making roles, and e) discussion of how the decision about participation in the trial should be made. Another standardized instrument, The Decision Making Preference Questionnaire, directly assessed parental preferences regarding decision-making responsibility (Pyke-Grimm, et al. 1999). In addition, we asked both parents and clinicians the question: Who was most important in directing this decision?

2. **Physician's recommendation.** Informed consent conferences were evaluated for recommendation of the trial by the physician. In addition, the particular language used by the physician in introducing the trial as a treatment option during the ICC was analyzed. The strength of the physician's recommendation of the trial was measured using a scale of 0-10, and was rated by parents, clinicians, and the research team. Two
parent interview questions relate to this factor: *Which treatment option did the doctor most strongly recommend for your child?* and *Did you feel that you were under any pressure to permit your child to enroll in the clinical research study?* We also asked the physicians the following question: *What treatment options did you recommend most strongly for this patient?*

3. **Description of Trial.** This includes the physician’s presentation of the risks and benefits of participating in the trial. The measurement of this factor relied heavily on a qualitative analysis of the informed consent conferences to uncover the actual language used by clinicians when describing the trial.

**Social network factors**

1. **Support given during ICC.** This was characterized by looking at whether social network members were present at the informed consent conference, and analyzing any questions or comments made by social network members during the ICC.

2. **Support sought and given during decision-making.** This was primarily assessed by examining responses to the following questions from the follow-up interview: *What sources of information were most helpful to you in making your decision about whether or not to participate in this clinical research study?* and *Since the time your child was diagnosed, have any of the following helped you better understand what*
Data Analysis

The approach to data analysis for this dissertation utilized a combination of qualitative and quantitative techniques, and an examination of the differences between cases was complemented by an exploration of their similarities.

**Qualitative Analysis:**

The audiotaped ICCs and the open-ended items from the interviews were transcribed and the transcripts were imported into a NUD*IST Vivo (NVivo) program for qualitative analysis. Dialogue in Spanish was translated into English for the analysis. The Spanish-English translation was then verified by a second bilingual person to ensure accuracy and attention to language subtleties.

While the qualitative analysis and coding of the transcripts reflect the actual language used during the informed consent conference and parent interviews, this does not represent a linguistic or discourse analysis. Rather, the analytic approach for the textual data is based on grounded theory, an inductive process that identifies important themes in the data through multiple readings of the transcripts (Strauss and Corbin 1990). The analysis began with a process of familiarization with the data by reading ten transcripts and listing key ideas and recurrent themes. The content of all ICC transcripts was then
grouped into categories following the factors of interest: patient, parent, clinician, and social network factors. Next, the content was further coded within each of these categories, using themes that emerged from the data. This was accomplished by reading and re-reading the text coded in each category, using the constant comparison method to establish further subcategories (Pope, et al. 2000). Therefore, the final coding scheme includes key issues laid out a priori in the objectives of the dissertation (the four factors), as well as topics discovered in the transcripts themselves. Strict inclusion and exclusion criteria were developed for every category to prevent the need for subjective judgments while coding. Particularly illustrative examples were flagged during coding for later use in description of the variable and its subcategories. A detailed account of how each variable’s coding structure was developed and refined is found in the appropriate chapter below.

Quantitative Analysis:
The quantitative analyses were based on coded observer checklist and closed-ended interview items as well as categories discovered in the qualitative analysis. Quantitative data from the coding of audiotaped ICCs, parent interviews, and clinician questionnaires were entered into a Microsoft Access database. These data, along with the results of the categorized qualitative analysis, were loaded into SPSS for statistical analysis.

First, frequencies for every category of each variable were run. Most of the continuous variables were not normally distributed, so they were recoded
into dichotomous variables using the median value as a cutoff. Standard
descriptive statistics (frequencies, means, standard deviations) were used to
describe all variables.

The aim of this study is not to predict behavior, but to provide a
descriptive analysis of how the independent variables of interest influence
decision-making. The rich data set that forms the basis for the analyses
provides an infinite number of potential relationships to test. The purpose of the
analyses conducted for this dissertation is exploratory, and is not meant to be
an exhaustive examination of all possible influences on decision-making. The
analyses conducted focus specifically on the relationships shown in Figure 1
between the 4 types of independent variables (patient, parent, clinician, and
social network) and the dependent variables (decision-making). Therefore,
statistical procedures were used to: 1) test for differences between on and off
trial cases regarding the independent variables, and 2) test for differences
between the different reasons given for the decision to participate with respect
to the independent variables.

Chi-square analyses were used to assess which independent variables
were significantly related to the dependent variables. The reported chi-square
is based on the Yates Continuity Correction if any cell sizes were 5 or smaller.
Variables found to be significantly associated with the decision itself or the
reasons for participation were subsequently entered into a logistic regression
model to determine whether they remained significant after controlling for the
effects of the other variables. It was necessary to run separate logistic
regressions for each category of the dependent variable since they are not
discrete (parents could give multiple reasons for their decision).

For all quantitative analyses, relationships significant at the p<.05 level
are reported, as well as relationships that approach significance (p<.10). The
analyses were broadened to include relationships significant at the p<.10 level
because of the relatively small sample size, the complexity of the concepts
being measured, and the possibility that the concepts are not fully assessed by
the methods employed here.

Layout of Chapters

The remaining chapters of the dissertation are arranged by the factors in the
model shown in Figure 1 and begin with a full explanation of how the variables
related to the factor were measured. In the following chapters, all variable
names are shown in bold italics for clarity. Descriptive statistics for each
variable are reported, followed by a rich description of each of the categories of
the variable using examples from the transcripts. Examples from the focus
groups are also presented to further illuminate each variable by providing
parental perspectives on decision-making from at least 6 months after the
decision was made. Each chapter concludes with an account of how the
continuous variables were recoded for use in analyses conducted to test the
model in Chapter 10. All discussion of the variables and results of the analyses
is found in Chapter 11.
Chapter 3: Parent Decision-Making

The dependent variables of this study are: 1) the parents' decision to participate in the clinical trial or not, and 2) the reason(s) given by parents for their decision to enroll their child in the trial.

The Decision

First, each of the 108 parents was classified as "on" or "off" trial, based on their decision about whether to participate in the clinical trial. Eighty-nine (82.4%) of parents decided to enroll their child in the clinical trial they were offered. In Chapter 10, the relationship between the On/Off Trial Decision and each of the independent variables discussed in Chapters 4-9 will be examined.

During the informed consent conferences, physicians often brought up the difficulty of the decision, saying things like, "I know it's a big decision to make", "It's a very big thing to think about", and "It's a heavy decision". While no interview questions prompted specifically for parents' perceived difficulty of the decision about trial participation, the topic did come up during the focus groups and PAGIC meeting. During focus groups, parents made the following comments about the difficulty of the decision:

- "That decision was the hardest decision I have ever faced in my whole life." (2nd Philadelphia focus group)
- "It was a pretty intense decision." (2nd Cleveland focus group)
- "Again, it just all came down to the grueling part was making the decision, at least for me." (2nd Cleveland focus group)
"It took us awhile to decide. That was a hard decision to make." (2nd Cincinnati focus group)

One parent comment during a focus group discussion about decision-making pointed to the effect of the horrible context on the informed consent process:

"In the [informed consent] meeting, you could talk about any and everything, and all I'm thinking about is my son's in another room dying." (2nd Philadelphia focus group)

The following conversation about the difficulty of the decision occurred among several participants at the PAGIC meeting:

"I think it was big."

"I was thinking about it every minute."

"Whether to be in the study?"

"Oh, yeah."

"Yeah, I couldn't make it up."

"Because you don't know...."

"It's an unknown, what would happen?..."

"It's always the study, the study, the study. There's no way to get that out of your head."

"But when you look back at...to me, at the time you're thinking you have to make this big decision. But I look back and through all of it, it kind of, the importance diminishes."

"But back then, it was an important decision because you didn't know what, you know, there are so many unknowns."

"And now we are so used to it."
These parent and physician comments suggest that parents and physicians alike view the decision as difficult, which underscores the need to more clearly understand the decision-making process.

Reasons for the Decision

The reasons parents reported for their decision were measured by analyzing parents' answers to the following two questions during face-to-face, semi-structured interviews: 1) Could you tell me why you have decided to participate (not to participate) in the clinical research study? and 2) What three things were most important to your decision about the clinical research study? This open-ended manner of eliciting reasons is infrequently used in published studies of clinical trial decision-making, and offers many advantages to the more common practice of ranking a pre-established list of reasons developed by the researchers. By allowing respondents to develop their own list of reasons, this methodology is more likely to give a true picture of actual decision-making instead of merely a reflection of the researchers' interests.

A list of reasons was developed from the analysis of the above items by reading all parents' responses. Subsequently, each of the cases was examined for the presence/absence of each of the reasons. Reasons for agreeing to participate in the clinical trial were separated from reasons for declining the trial.
Reasons for Declining:

The reasons for declining participation in the trial fell into 5 categories: risks, standard treatment is good enough, randomization, uncertainty, and other. The majority (73.7%) of parents who declined participation gave reasons from more than one category. Multiple reasons given in a particular category were counted only once. The 19 parents who did not put their child on the trial gave 2.2 reasons on average (SD = .9), with a range of 1 to 4.

The frequencies with which parents reported each of the five decline reason categories are shown in Table 2 below. Because parents often gave more than one reason, the percentages do not add up to 100.

<table>
<thead>
<tr>
<th>Reasons for Declining Trial</th>
<th>Frequency</th>
<th>Percent of Parents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks</td>
<td>15</td>
<td>78.9%</td>
</tr>
<tr>
<td>Standard Good Enough</td>
<td>7</td>
<td>36.8%</td>
</tr>
<tr>
<td>Uncertainty</td>
<td>5</td>
<td>26.3%</td>
</tr>
<tr>
<td>Randomization</td>
<td>4</td>
<td>21.1%</td>
</tr>
<tr>
<td>Other</td>
<td>11</td>
<td>57.9%</td>
</tr>
</tbody>
</table>

The most frequently cited reason for declining participation in a clinical trial related to the risks of the trial, with 80% of the 19 parents giving this reason for their decision. These parents reported that the increased chance for side effects on the trial was a primary motivator for their decision. Several examples from the parent interviews include:

- “I guess I would also say the fear of any complications.” (CIN-16)
o "The symptoms could possibly be worse – the side effects." (CL-14)

o "But they never talked about the negative part. Sometimes too much medicine is bad for the health, and we thought it could be bad for her, maybe it could cause damage to her." (HO-01)

o "The most important is my child’s life – that he won’t suffer from side effects." (LA-19)

o "It just seemed you might be endangering your child just a little bit more than maybe, I don’t know, you needed to." (PH-25)

Seven parents said that they decided against participating in the trial because the **standard treatment was good enough**. These parents were more comfortable with giving their child the standard therapy which is proven to have a good success rate. For instance:

o "I just think that we’re so overwhelmed, and I think a lot of it was that we didn’t want any more options. You’re so overwhelmed. And here you have this standard treatment that they have been doing for years and years that has shown to be very successful. And you’re so overloaded and you don’t even...if you’ve got that, why consider other options? is kind of the attitude that you get." (CIN-16)

o "I looked at it like his condition was treatable by the standard, so I didn’t see no sense in experimenting around if the standard was going to work." (CL-07)

o "Because the cure rate on the standard was 85%." (DC-03)

The third most often listed reason for declining the trial was the **uncertainty** inherent in the trial, including a lack of information about the
effects of the trial treatments and the absence of a guarantee that their child
would benefit from the trial. For example:

- “Not enough background on the study’s drugs. We wanted to go with what we knew had proven results.” (CL-01)
- “No guarantee that she was going to do any better on it as opposed to being on the regular.” (CL-19)

Only 4 parents mentioned randomization as a reason why they decided
not to enroll their child in the trial, including one parent who stated:

- “The fact that it was an unknown...I like to have the control as to what my treatment options are going to be. Basically, I don’t want the control taken away from me. We want to be able to select the mode of treatment as opposed to having something randomly selected.” (PH-22)

The 11 parents who gave reasons not included in the above categories
made reference to the doctor’s lack of recommendation, the advice of someone
in their social network, and other reasons. Two parents declined the trial
because their child’s doctor did not explicitly recommend it when asked:

- “I asked the doctor – well, he doesn’t have any kids but he said he had a dog – I said, ‘If you had a child with leukemia would you put that child on the study?’ And he said he couldn’t answer that. You know? I mean, if I was a doctor, I would have put my input on it.” (CIN-09)

Two parents said they were advised against participating by someone:
We also talked to a number of...by happenstance we have a member of the family...who is a pediatrician who did some of her own research. We talked to oncologist friends...and while no one said 'don't do it,' enough people said that they wouldn't do it with their own children. Enough people said that at the least it wouldn't be a mistake not to do it, that we finally decided not to do it.” (PH-34)

Reasons for Participating:
The main focus of the dissertation is description and preliminary explanation of the variety of reasons parents give for deciding to enroll their child with leukemia in a clinical trial. Analysis of the reasons given for participating in the trial resulted in 8 major categories of reasons: direct benefit, altruism, the right to withdraw, comparison to standard, safety, the doctor, better monitoring, and other. The majority (86.5%) of parents who decided to participate in the trial gave reasons from more than one category. Multiple reasons given in a particular category were counted only once. For the 89 parents who enrolled their child on the trial, the mean number of reasons given was 2.8 (SD = 1.2), with a range of 1 to 6.

The frequencies with which parents reported each of the eight participation reason categories are shown in Table 3 below. Because parents often gave more than one reason, the percentages do not add up to 100.
Table 3: Reasons for Participating in Trial (N = 89 cases)

<table>
<thead>
<tr>
<th>Reasons for Participating in Trial</th>
<th>Frequency</th>
<th>Percent of Parents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Benefit</td>
<td>71</td>
<td>79.8%</td>
</tr>
<tr>
<td>Altruism</td>
<td>60</td>
<td>67.4%</td>
</tr>
<tr>
<td>Right to Withdraw</td>
<td>25</td>
<td>28.1%</td>
</tr>
<tr>
<td>Comparison to Standard</td>
<td>24</td>
<td>27.0%</td>
</tr>
<tr>
<td>Safety</td>
<td>21</td>
<td>23.6%</td>
</tr>
<tr>
<td>Doctor</td>
<td>14</td>
<td>15.7%</td>
</tr>
<tr>
<td>Better Monitoring</td>
<td>13</td>
<td>14.6%</td>
</tr>
<tr>
<td>Other</td>
<td>20</td>
<td>22.5%</td>
</tr>
</tbody>
</table>

Direct Benefit

The most frequent reason given by parents for participating in the trial is Direct Benefit to their child. For descriptive purposes, this category was further divided into parent reference to “chance” for benefit, versus unqualified statements that their child would benefit from the trial. Of the 71 parents who listed Direct Benefit as a reason, 23 (32.4%) mentioned a “chance” for benefit, 43 (60.6%) suggested their child would benefit unconditionally, and 5 (7.0%) made reference to both subcategories of Direct Benefit. In the “chance” for benefit category, parents’ statements often reflected feelings of hope, but also the realization that there was no guarantee that the trial would be better for their child than standard therapy. Examples include:

- “Well, I decided because it might help him.” (CIN-03)
- “Maybe the new medication is better...I hope it is better.” (LA-03)
"I decided because if there is any chance that this treatment could be even a little better than the standard treatment, then I want the best for my child...For me, all I needed was to hear the doctor say that he could have a better chance." (LA-07)

"Because I think there might be...we don't know, but there might be, since there are more drugs involved, a slight edge as far as the curing of the cancer or the treatment of the cancer." (PH-04)

In contrast, the “unconditional” benefit category includes parent responses that indicate absolute conviction that their child will benefit from participation in the trial. For instance:

"...it does nothing but give me another opportunity to save my son's life." (CIN-01)

"Him getting the best treatment." (DC-05)

"Because it looks like there's a higher percentage when she participates." (DC-13)

"We simply think this is the best option for L. It is as simple as that – thinking about her." (HO-04)

"To keep him alive." (LA-24)

"Our child, our child, and our child. What I'm trying to suggest is that in the abstract, the notion of moving science forward is very important, but when you're facing it with your own child, I could give a flying hoot about that." (PH-34)

**Altruism**

The second most common answer given by parents when asked why they decided to enroll their child in a trial was *Altruism*. These responses all concern benefit to others (not the child-patient) from the child’s participation in
the trial. In order to flesh out this variable, it was further categorized according to who was mentioned as the beneficiary or recipient of benefit from their participation. The "others" mentioned by parents fell into two groups: 1) other/future patients or children, and 2) science, knowledge, or treatment in general. Of the 60 parents who listed *Altruism* as a reason, 35 (58.3%) cited "other/future patients or children" as the recipient, 14 (23.3%) cited "science, knowledge, or treatment in general" as the recipient, and 11 (18.3%) cited both subcategories of *Altruism*.

In the "other/future patients or children" category, parents expressed a desire to help children and families like theirs. For example:

- "They presented it as helping. To us, that was a key factor. We're helping somebody not be as sick as J. is somewhere down the line." (CIN-07)
- [relayed through Spanish interpreter] "In the future it's going to help other children. She [the mother] would feel good knowing that her daughter is going to help other children." (DC-15)
- "For the benefit of other children which might have the same type of sickness or illness that he has." (LA-13)
- "The other thing is you're trying to do the right thing by your child, but there's some type of ethical responsibility to do the right thing with other people who might be in the same situation." (PH-07)

Altruistic reasons in the "science/knowledge/treatment" category do not refer to a person as recipient, and focus more on the cancer research enterprise as the beneficiary. For instance:
“Another 10 to 15 years down the road, we could have this whipped if people keep caring. It takes one person at a time to care.” (CIN-07)

“Just to be able to help science to figure this stuff out.” (CIN-13)

“So we might as will give them this knowledge to help assist them. That’s what they’re looking for.” (CL-04)

“The fact that we were assisting the research.” (LA-18)

A separate, but related category has to do with the sense of obligation to repay the past altruistic behavior of others who enrolled their child in previous leukemia trials. Mention of “past altruism” as a reason for participation was found in 9 of the interviews, such as the following parent comment:

“The past 20 years of leukemia victims and survivors – their tests have come to help N. now, so it’s sort of like passing the torch. So what comes around, goes around kind of thing.” (CIN-08)

**Right to Withdraw**

Twenty-five parents listed the **Right to Withdraw** as one of the reasons they consented to the trial. Most of these parents spoke specifically about the right for the family to stop participation in the trial at any time, as in the following statements:

“I think just being able to get out of it if we have to...that sort of makes us feel like he’s not being sort of a guinea pig, you know? That you have that option. So I think that’s really the major one.” (CIN-13)
"If we’re not comfortable with it, we can cancel at any time." (CL-03)

"If I don’t think this is going right, I have every opportunity to say ‘whoa, hold it up’, and I like that." (PH-05)

Three of these parents explained that the right to withdraw gave them time to seek the advice of others, as exemplified in this response:

"What makes it acceptable is that at any point during the process you can change your mind and decide you didn’t want to be a part of it. So it gives you a few days after...because everyone goes through the initial standard operating procedure, and they’re going to follow the same regimen. So you have a time cushion to ask other people if you have questions. That’s why we’re comfortable with it.” (LA-32)

Less commonly, parents discussed the doctor’s right to either take their child off the trial or adjust the treatment according to the patient’s best interests. For example:

"The doctor still has the ability to say it’s too much." (CL-09)

"And the other thing is the fact that he’s going to be monitored so closely so if they see that his body can’t respond to something, they’re not gonna continue going forward for the sake of the study. So I think that’s J.’s best interest.” (CL-10)

Comparison to Standard

Twenty-four parents gave reasons for their decision that involved comparison of the trial to treatment they would receive off the trial. One way parents articulated this reason was by discussing how similar the trial is to standard
treatment. In the context of Phase III clinical trials, there are only small
differences in the various arms of the trial, and one of the arms that a child
could be randomized to is the standard treatment. Many parents were
reassured by this similarity:

- “It’s not too dissimilar to what the standardization
  is.” (DC-01)

- “I think on one hand because it’s not that different
  from the regular treatment...I guess the
  comparison of the drugs that would be
  randomized – it was important that I understand
  the level of variance between them. You know, if
  we were talking about substituting vanilla for
  chocolate, then I would think it would be more of a
  problem. But it was pretty clear that they were
  very similar drugs, just maybe a little different
  strength. That was real important to try to get a
  grasp of that.” (PH-07)

Parents also discussed the trial as offering at least what they would get if they
didn’t participate in the trial. For instance:

- “The main concern was that he wasn’t going to
  get inferior treatment. That was basically it. As
  long as he was getting the best treatment that he
  could, that was my concern. Anything above that
  was just a plus.” (CIN-02)

- “By going on study, it’s not going to be worse, it’s
  going to better. My chances won’t be lower than
  85%.” (LA-34)

**Safety**

Twenty-one parents cited the lack of risk or **Safety** of the trial as a reason for
their participation, often making specific reference to what the doctor told them.

For instance:
- "And they said it was safe." (CIN-07)
- "It was presented as relatively low risk compared to the standard treatment." (LA-26)
- "Because they guaranteed me that there was no more of a risk of harming her." (PH-05)
- "Even if it doesn't turn out to help her, I don't think it would hurt her." (PH-18)

**Doctor**

Fourteen parents reported the **Doctor** as a reason for their decision. This category includes both the doctor's recommendation of the trial and trust in the doctor. Parent responses relating to the doctor's recommendation include:

- "Dr. M. said 'If it was my child, I would enroll. I would participate in that study.' She said it has great benefits. Knowing that, not knowing much about the study except the literature that I got, some people's feelings about it can influence my decision. It's coming from somebody who has seen and experienced and treated children with all these diseases." (DC-10)

- "The doctor's approval, you know. She suggested it." (DC-13)

- "I guess our reason is the doctors really, really, really wanted her to do it." (PH-42)

Examples of parent answers regarding trust in the doctor include:

- "Well, when I was reading it I thought it was a good thing, you know, to do. Cuz I know so little and, you know, these doctors know more. I put my whole trust in the doctors now, and they tell me what to do." (CIN-03)
The truth? The confidence that I have in the doctors, the hospital, and the system in general.” (LA-36)

“I put all my faith in God, and if I have to put all my faith in a human being, it has to be the physician. And I have to trust her unconditionally, so I am!” (LA-07)

Better Monitoring

Thirteen parents responded that they enrolled their child in the trial because they believed their child would be watched more closely in the trial. For instance:

“I think if you’re in a program like this that you get to see the doctors more often than you would...you know, keep a better eye on him. Because I’m new at this and I need all the help I can get.” (CIN-03)

“He’ll maybe be monitored more closely because of the study.” (PH-20)

Other Reasons

Twenty parents listed a reason that did not fall in any of the above categories. Eight parents stated that advice from a member of their social network was a reason for their decision, with mention of their pediatrician, another doctor, a doctor in the family, a friend who is a doctor, and a family member. For example:
"I didn't feel that I was really qualified to decide, you know what I mean? That's the sort of thing you'd rather someone decide for you. I really, I don't really believe that it was my decision. Had our pediatrician decided against it, I would have gone against it because I'm not qualified to make that decision. I don't know anything about these chemotherapies, you know, other than that they practically have to poison you to save you. I basically went by her judgment, not my own." (CIN-11)

"And we talked to his [the father's] mom, and his mom said in her gut feeling she feels doing the study is the best way to go." (PH-01)

Other reasons given included the fact that they were given the power to decide, belief in the research enterprise, the design of the trial, and that it's used worldwide.

Relationships Between Reasons for Participating:

Because most parents cite more than one reason for their decision, the most commonly paired reasons were explored. Chi-square analyses were used to assess which dependent variables were significantly related to each other. The reported chi-square is based on the Yates Continuity Correction if any cell sizes were 5 or smaller. The matrix in Table 4 below shows the frequency of each of the 21 possible pairs of reasons out of the 89 "on trial" cases, as well as the p value from the chi-square test. The "other" category has been excluded from this and all future analyses because the responses in this category are not conceptually similar.
Table 4: Combinations of Reasons for Participating in Trial

<table>
<thead>
<tr>
<th></th>
<th>Direct Benefit</th>
<th>Altruism</th>
<th>Right to Withdraw</th>
<th>Comparison to Standard</th>
<th>Safety</th>
<th>Doctor</th>
<th>Better Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Benefit</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Altruism</td>
<td>46 (.01)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right to Withdraw</td>
<td>17 (.79)</td>
<td>16 (.33)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comparison to Standard</td>
<td>16 (.91)</td>
<td>17 (.09)</td>
<td>10 (.02)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Safety</td>
<td>14 (.92)</td>
<td>18 (.00)*</td>
<td>10 (.01)*</td>
<td>10 (.01)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doctor</td>
<td>12 (.17)</td>
<td>8 (.90)</td>
<td>1 (.24)</td>
<td>5 (.34)</td>
<td>4 (.57)</td>
<td></td>
<td>3 (.47)</td>
</tr>
<tr>
<td>Better Monitoring</td>
<td>11 (.22)</td>
<td>10 (.10)</td>
<td>4 (.73)</td>
<td>3 (1.00)</td>
<td>5 (.14)</td>
<td></td>
<td>3 (.47)</td>
</tr>
</tbody>
</table>

*p<.05

The most frequent pairing of reasons was Altruism and Direct Benefit, with 46 of the 89 parents who decided to participate in the trial citing both (p < .01). Although both benefits to others and to their child are cited together, the priority of Direct Benefit is often clearly articulated. For instance:

- “A couple of different reasons. One, the first reason you do anything in this situation, I would think it would be, is looking out for the best interests of your child...And the possibility of hopefully helping out in the future is just an added benefit.” (CIN-08)

- “So my son can benefit from it all, and maybe other children too.” (LA-23)

The second most common pairing of reasons is Altruism and Safety, with 18 parents listing both (p < .01). This combination is typically presented by parents as a willingness to help others as long as there is no risk to their child, as in the following statement:
"I would love to be able to advance the methods of treatment and bump the success rates up higher as long as it's not going to be any kind of detriment to my child, I would participate. But if there was any? That he was going to get any less good therapy? I would not do it, and I still feel that way." (PH-13)

The relationship between the Right to Withdraw and Comparison to Standard was also significant (p < .02), with 10 parents mentioning both of these reasons. The responses of these 10 parents reflect their view that the trial poses little risk to the child because it is at least as good as standard therapy and can be stopped at any time if deemed necessary by the parents or physician. For instance:

- "...Even if you got chosen to do the standard treatment [randomized to the standard arm within the trial], you'd never get less than what the best benchmark is at this point – you wouldn't lose anything there. And also, you wouldn't waste anytime at all in withdrawing from, you know, the program, either by our decision or the doctor's decision, if you see anything going wrong. So it did seem like virtually zero risk." (CIN-08)

Those parents listing Safety as a reason for their decision were more likely to also cite Comparison to Standard as a reason (p < .01). This pairing seems to represent parents' view that the trial is safe because it is similar to standard therapy. For example:

- "The treatment seemed to be very similar so there would be no different side effects." (CL-04)

- I think on one hand because it's not that different from the regular treatment...if, you know, if we accept this as fact, everything that was given to us, it doesn't seem like it's any type of a risk" (PH-07)
Finally, **Safety** and the **Right to Withdraw** are significantly related to each other, with 10 parents giving both reasons for their decision to participate (p < .01). These parents articulated their belief that the trial wasn’t risky, and if they ever decided that it was harming their child, they could withdraw from the trial. For instance:

- “I think probably because we know, you know, that it’s not going to hurt him to do it, and that we have the decision, the ability to be able to, if it gets to be too much stress on his body or whatever, that we can always just say, ‘You know what? This is too much,’ and sort of get out of it.”

(CIN-13)

This chapter has focused on describing the reasons parents gave for their decision about participating in a clinical trial. Although most parents did ultimately decide to participate in the clinical trial, this analysis illustrates the variability in the reasons parents gave for this decision. The following chapters will explore the four factors hypothesized to influence both the decision to participate in the trial or not as well as the reasons given for participating in the trial: patient factors, parent factors, clinician factors, and social network factors. The variables comprising these four factors will be described and their relationship to parental decision-making will be assessed.
Patient Factors

The four patient factors analyzed were sociodemographic variables, risk level, prognosis, and illness severity. Patient sociodemographic variables were limited to age and gender. Patients were 6.7 years old on average, with a range of 1 to 17, and 42.6% of patients were girls.

Risk level was computed by assigning patients into a low or high risk group according to the trial they were offered. Patients offered one of the two trials for standard risk ALL were placed in the low risk group, and patients offered either the high risk ALL or AML trial were put in the high risk group. This grouping also distinguishes between trials that are more or less risky for participants. The risks are higher in the trials for high risk ALL and AML because the treatment is more intense. Also, because the cure rate for high risk ALL and AML is lower, the focus of these trials is more on increasing the cure rate rather than decreasing side effects, so experimental arms with intensified treatment may result in more toxicity. Fifty-three (49.1%) patients were in the low risk group, and 55 (50.9%) were in the high risk group. This risk level variable was used in the analyses in Chapter 10 to represent both the risk level of the disease and the trial.
Illness Severity:

Several statements made by parents during the PAGIC meeting point to the potential influence of illness severity at the time of diagnosis on decision-making. For instance:

- "It depends on how sick they are too because our daughter was perfectly fine until we started treatment."

- "See, one of the key words that I heard was 'high risk'. My daughter was at high risk because she was 10 years old. And I knew how sick she looked to me. It was like, 'why are we waiting? Let's do it!'"

- "For me, it was that E. was going to die unless I do something. Should I save him with going to study and taking that way? Because he wasn't really sick at that time, so I was more worried about what the chemotherapy was going to do to him. And should I just go with the normal...treatment?"

Illness severity was measured by analyzing the physician’s discussion during the ICC of the patient’s presenting symptoms and general condition as compared to other patients with leukemia. By using the transcripts to code what the physician actually said about the patient’s illness severity, this examination goes beyond the suboptimal methods used by many other researchers, such as mere speculation about what the family was told or reliance on clinical measures recorded in the patient’s chart (i.e., WBC) that may or may not be communicated to parents.

Based on previous research that has shown strong influences of framing on decision-making (O'Connor 1989; Siminoff and Fetting 1989), this analysis
also includes assessment of physicians’ positive and negative framing of the patient’s illness severity. Positively framed physician comments about the child’s condition might affect decision-making via their effect on how parents perceive the risks and benefits of treatment. For example, parents may be less inclined to participate in a trial involving stronger therapies if they’ve been told that their child is in relatively good shape to begin with. Parents who do participate in a trial may have different reasons for doing so depending on how their child’s illness severity was presented to them. Negatively framed physician comments about their child’s presentation or condition could impact parents’ decision-making about participation in the opposite way. For instance, the following physician’s remark about a patient’s illness severity stresses the need for intensified treatment:

- “...we found that there were patients who survived more often, and patients who survived less often. And we learned that patients who have a high white blood cell count, for example, survive less often, survived less often than patients who had low white blood cell counts, and teenagers survived less often than younger children did. So we were able to split the patients with ALL into a standard risk group and a high risk group. Then what we did was we made the treatment for the high risk patients more intense. What has happened over the last 10 years is that low risk patients and high risk patients survive roughly equally often. The high risk patients just have a harder time getting there. They have more chemotherapy and it’s more intense. So we’re not going to use gentle treatment with H.” (PH-19)

First, all physician comments about the severity of the illness were extracted from the transcripts of the ICCs, including only statements of
comparison to other children with leukemia that indicate this patient is worse or better off than could be the case for leukemia. This analysis does not, therefore, include general discussion of presenting symptoms as they relate to making the diagnosis or prognostic characteristics like age or WBC unless they are comparative. Almost all parents enter the informed consent process with no knowledge of leukemia, so a discussion of features like WBC are meaningless without an explanation of where it places their child on the spectrum of illness severity for patients with leukemia.

Eighteen (16.7%) ICCs had no discussion of illness severity as defined by the above criteria. The discussions of illness severity found in the other 90 ICCs were then categorized as either positively or negatively framed. In general, positively framed physician comments relate to the child’s presentation or condition being typical for leukemia or better than other children with leukemia, while negatively framed comments have to do with the child’s presentation being unusual or worse than other children with leukemia. Both positively and negatively framed illness severity discussions were further coded into subcategories for in-depth description of this variable. Frequencies for each of subcategories are shown in Table 5 below, and examples follow. As shown in Table 5 below, there were more than twice as many positively framed statements about illness severity than negatively framed statements.
Table 5: Illness Severity  
(Number and Percent of Comments Within Positive/Negative Categories)

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical</td>
<td>21</td>
</tr>
<tr>
<td>Good Features Present</td>
<td>106</td>
</tr>
<tr>
<td>Could Be Worse</td>
<td>89</td>
</tr>
<tr>
<td>Total</td>
<td>216</td>
</tr>
</tbody>
</table>

9.7% 49.1% 41.2% 7.9% 81.2% 10.9%

Positive Illness Severity

Three subcategories of positively framed comments developed out of the data. The positive subcategories include 1) Typical: statements that the child’s presentation or condition is common or typical for leukemia, 2) Good Features Present: discussion of positive features or symptoms the patient has that puts him/her at lower risk relative to other children with leukemia, and 3) Could Be Worse: comments about features or symptoms that other patients have, but this patient does NOT have, that would have increased his/her risk. Every instance of each of the 3 categories was counted for each ICC. Across all 108 ICCs, there were a total of 21 statements in the “typical” category, 106 in the “good features present” category, and 89 in the “could be worse” category. The total number of Positive Illness Severity comments for all 108 ICCs was 216.

Examples of physician comments coded in the “typical” category include:

- “And his presentation with this is nothing unusual to how a lot of kids come in when they have this illness. They often come in with swollen lymph nodes, with big livers, big spleens.” (CIN-02)
Statements coded in the "good features present" category are from physicians who said things such as:

- "His age is good. Children who are from 1 to 9 years of age do better than kids who are younger or older." (CIN-12)

- "And he has certain factors that make it even better for him in terms of the type he has...in terms of his age, in terms of how much of his bad cells or normal cells he had." (LA-34)

- "She has a lowish white count...And when you look at the history of how children do with leukemia that puts her in the standard risk group. Meaning the most responsive group. Some doctors used to use the term 'good risk', but we would never want to imply that any cancer is good. However, it's just the kind of group that's most responsive to our treatments, okay?" (PH-25)

The "could be worse" category includes statements indicating that this child's situation could be worse because s/he does not have some bad features that other children have. For example:

- "And like I mentioned to you yesterday, I don't see much of any lymph nodes or liver or spleen being massively enlarged, which is also a very good sign...And the spinal tap we did today does not show any leukemia, so that's another very good thing...So these factors, although they are small things, add up to a major thing because it really means that we are starting off in a much better place as opposed to a much worse place." (CIN-16)
“Okay, so he does not have CNS disease, and his testicles feel normal. So he really, I mean, with his age, his white count, which was low...because we've seen children, if their white count is over 50,000 they become high risk. If his age was less than a year or over ten years, he would be extremely high risk. Those leukemias are very hard to treat, even if they are pre-B ALL. So he is basically a good risk ALL. I know that you don’t feel that it’s a good risk to begin with, but of all the leukemias that we see in childhood, this is probably the best that we can treat.” (LA-14)

**Negative Illness Severity**

Three subcategories of negatively framed comments were also formed and utilized for further coding, including 1) **Unusual**: statements that the child’s presentation or condition is unusual for leukemia, 2) **Bad Features Present**: discussion of negative features or symptoms the patient has that puts him/her at higher risk relative to other children with leukemia, and 3) **Urgency**: discussion of the need to start treatment right away because of the child’s illness severity. Every instance of each of the 3 categories was counted for each ICC. Across all 108 ICCs, there were a total of 8 statements in the “unusual” category, 82 in the “bad features present” category, and 11 in the “urgency” category. The total number of **Negative Illness Severity** comments for all 108 ICCs was 101.

Examples of physician comments coded in the “unusual” category include:

- “Most kids, fortunately, don’t come in with as much leukemia as W.” (CIN-01)
"But most kids who have standard risk ALL, acute lymphoblastic leukemia, usually don’t have such big swollen glands...So his is not a typical case.” (LA-06)

Statements coded in the “bad features present” category are from physicians who said things such as:

- "We also know based from all the studies that we have done that some patients are lower risk patients than other patients...He’s in a higher risk group, and that’s because of his age – he’s older. And that’s also because he has such a lot of involvement in his liver and spleen. It puts him at a slightly higher risk. And that means that the treatment we’re talking about is going to be a little more intensive than some of our other patients.” (CIN-06)

- "Because her white blood cell count was on the high side and because she has the mass in her chest, she is what we call high risk ALL, which means that we have to treat her with more chemotherapy than we would with someone whose white count was lower.” (PH-15)

Statements in the “urgency” category included:

- "What’s really important, I think, is that we get started on his treatment...And the reason we’re pushing a little harder today is because of his high white count. It’s gonna keep going up...Okay? Otherwise, you know, normally we’d say ‘Take tonight and think about it’, but it's really important that we get going.” (DC-04)

- "And we thought it was important on Friday to start treatment as soon as we could given the size of the mass that was in his chest.” (PH-02)

Thirty-one (28.7%) of the ICCs include both positively and negatively framed comments about illness severity, and are typically characterized by the
physician presenting a balanced picture of both the positive and negative features. For example:

- "His young age would keep him in the standard risk because that’s under 10 years of age, but the white count kind of means that we would look at a high risk type of therapy." (LA-29)

*Family Prompts*

Only 17 (5.4%) of the 317 positive and negative illness severity comments described above were prompted by a family member. Of these 17 prompted comments, 12 were framed positively and 5 were framed negatively. *Positive Illness Severity* discussions were prompted by parent questions such as:

- "And the leukemia she has is the good leukemia, if there is such a thing?" (CIN-11)
- "Have you seen higher [WBC] numbers than that?" (LA-18)

Parent prompts for *Negative Illness Severity* discussions include:

- "For the AML, is it worse, then?" (CL-14)
- "So these masses, I mean, this mass on his head and under his arm is a rare case?" (LA-06)

*Prognosis:*

As with illness severity, the presentation and framing of the child’s prognosis might affect decision-making via the effect on how parents perceive the risks and benefits of treatment. The child’s prognosis was primarily measured by a detailed analysis of the ICC transcripts. First, all physician comments about the
child’s prognosis were pulled from the transcripts of the ICCs. Discussions of an increased chance of cure by participating in a clinical trial were excluded because they were coded under presentation of the benefits of trial participation (see Chapter 8).

Three (2.8%) ICCs had no discussion of the child’s prognosis. The discussions of the child’s prognosis found in the other 105 ICCs were then grouped according to whether they were framed positively, in terms of the chance of cure/survival, or negatively, in terms of the chance of death/recurrence. The death/recurrence group includes any mention of a chance that the child (or children with leukemia in general) could die, either from the leukemia itself or from chemotherapy-related toxicities.

These two groups were further coded into prognosis discussions that a) include numbers or not, and b) are framed generally or specifically for this child. Therefore, a total of 8 prognosis categories were formed. Every instance of each of the 8 categories was counted for each ICC. Frequencies for each of subcategories are shown in Table 6 below, and examples follow. As shown in Table 6, there were more than three times as many Prognosis – Cure/Survival discussions than Prognosis – Death/Recurrence discussions.
Table 6: Prognosis
(Number and Percent of Comments
Within Cure/Survival & Death/Recurrence Categories)

<table>
<thead>
<tr>
<th></th>
<th>No Numbers</th>
<th>Numbers</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>General</td>
<td>This Child</td>
<td>General</td>
</tr>
<tr>
<td></td>
<td>53</td>
<td>77</td>
<td>170</td>
</tr>
<tr>
<td></td>
<td>15.9%</td>
<td>23.0%</td>
<td>50.9%</td>
</tr>
</tbody>
</table>

Cure/Survival, No Numbers

Statements in this category mention prognosis in terms of cure/survival without using numbers. There were fifty-three statements in this category that were framed for children with leukemia in general and did not make reference to the particular child. For example:

- “We cure our kids with cancer. I run a long-term survival plan.” (CIN-02)
- “And we know that for most patients with ALL, we are going to be able to cure them.” (CL-20)
- “The cure rate is excellent.” (LA-29)

Seventy-seven statements in this category did refer to the particular child’s prognosis. For instance:

- “So first realize that this is a serious disease, and that I’m sorry that we have to tell you that. But really focus on the fact that this is a disease for which we have very effective therapy, and the odds are overwhelmingly in her favor that we’ll be able to cure her of this.” (DC-01)
Although they don’t include numbers, some discussions in this category are unequivocal statements about the child’s cure, as in:

- “You’re gonna live. And we’re gonna cure your leukemia.” (CIN-05)

Cure/Survival, Numbers

Statements coded in this category also frame the prognosis in terms of cure/survival, but attach numbers to the prognosis. Statements of this type that were framed generally, for all children with leukemia, were the most common type of prognosis discussion (N=170). For instance:

- “If we take all children with her kind of leukemia, at her age, the chances of cure are about 85%.” (CIN-11)
- “If you have 10 children in a room, approximately 6 to 7 out of those 10 will survive with, based on the medicine we have today and the way we use it.” (DC-06)
- “The cure rates are about 75%.” (LA-06)

There were 34 prognosis statements that discussed the particular child’s chance of cure using specific numbers, as in:

- “The goal of all this therapy is not only to put him into remission and make him better, but so that he’ll be one of the 80% that will be eventually cured of this disease.” (CL-03)
- “She has a 75 percent chance of being cured of this disease.” (HO-05)
"With chemotherapy, his chances of being cured, which means that we get the leukemia to go away and it never ever comes back, are about three out of four." (PH-01)

**Death/Recurrence, No Numbers**

This category includes prognosis statements framed in terms of the chance of death/recurrence without using numbers. There were 22 such statements that were framed generally, such as:

- "Um, you know, we do lose some kids who have leukemia." (CL-01)
- "Some kids will die of infection during this treatment as a complication of their therapy." (PH-27)

There were 24 statements in this category that made reference to the particular child's chance of death/recurrence without using numbers. For example:

- "If you look at it from the fairly statistical standpoint, the probability she is going to die from this is relatively small." (CL-18)
- "The likelihood that he will relapse is very small." (LA-34)

**Death/Recurrence, Numbers**

This category includes statements about the chance of death/recurrence that utilize numbers. Fifty such statements were framed generally, such as:

- "But then one out of four children will have the disease come back, and that's called relapse." (LA-06)
o "So there's a chance that even the treatment may be fatal, and about 1 in 10 children and young adults may die from the treatment during the first month of therapy." (PH-06)

o "But we do want to tell you that we know that this is serious, and that, you know, on the average 50% of kids don't make it." (PH-42)

The least common type of prognosis statement discussed the particular child's chance of death/recurrence using numbers (N=9). For instance:

o "There is a .5 to 1 percent chance that M. could die here in this part because of the complications of treatment and the infection." (LA-32)

o "There is one chance out of four that B. will die." (PH-01)

Many discussions included a prognosis framed in terms of both cure/survival and death/recurrence. For instance:

o "But to answer your question very directly, approximately 2 out of 100 children may die of the complications of treatment, but 75 out of 100 will be cured." (HO-05)

o "This certainly is a very serious problem, and there is a chance that she could die from this, but there is a much better chance that she'll survive and she'll grow up and she'll be okay." (LA-01)

o "Also, you need to know that most children with this do well. Most go on to live long happy lives. Some don't, but most do." (PH-08)

o "More children, many more children will survive their leukemia than will die from it, okay?" (PH-25)

In addition to the prognosis discussions in the 8 categories described above, there were 28 discussions in the 108 ICCs of the disease being fatal if left untreated, such as:
"Without treatment, all of the children will die." (HO-05)

"If we don't treat her leukemia, she will definitely die with the disease." (LA-21)

"She has acute lymphoblastic leukemia, which is a fatal disease left untreated." (PH-22)

There were also 24 conversations in the 108 ICCs about the meaning of numerical information relating to prognosis. In these conversations, physicians made statements about how they dislike attaching numbers to the prognosis and/or feel that the numbers should only be applied to populations and are meaningless for one child. For example:

"In other words, M. himself doesn't have an 80% chance. If there were 100 M.s in the room, we know that 80 M.s would survive. But M. is one little boy. He's either going to make it, which is what we hope, or he's not. There's no percentage on it. You don't 80% live and 20% not. You are 100 or 0." (CL-03)

"And we are optimistic about L.'s prognosis, but this is not the movies. And I cannot tell you that L. has a 70 percent chance or an 80 percent chance or a 60 percent chance. L. has a zero percent chance or a 100 percent chance. She is an individual, not a statistic." (PH-21)

Physicians' reticence to use numbers in giving a prognosis may also stem from their experience with people who misunderstand percentages. For example, one father mistakenly calculated that observation of something in 2 out of 2 people (100%) equalled 2%:
"But I noticed two things. And then I'll shut up. But my dad was a little hyper, but my brother, he was real hyper and he got leukemia. She's [the patient] hyper. And she has leukemia. That's 2 percent to me." (CIN-09)

Doctors may inadvertently confuse the issue further by trying to explain what prognostic figures mean. For example:

"I told you that we have at least a 70-75% chance of survival, you know, getting cured of this disease...[later in ICC]...numbers are very misleading. There is only one number for your child. It's 50/50. Either he makes it or he doesn't make it. There is no other number for your child....The other numbers help us have an idea of which 50 your son is gonna be in." (LA-18)

Fifty-five (12.5%) of the 439 total prognosis discussions were prompted by a family member. Of these 55 prognosis discussions, 31 were framed in terms of cure/survival, and 24 were framed in terms of death/recurrence.

Prognosis discussions framed in terms of cure/survival were prompted by parent questions such as:

"What is the success rate for someone his age?" (CL-14)

"What are the hopes that you can give us that she will get better?" (LA-17)

Prognosis discussions framed in terms of death/recurrence were prompted by parent questions such as:

"Can she die from this?" (CIN-09)

"What are the odds of it coming back?" (CL-03)
Some questions framed by family in terms of death/recurrence were answered by the clinician in terms of cure/survival. Since the purpose of the coding procedure is to describe how clinicians discuss prognosis, these discussions were coded according to which category the physician’s answer fit in. For instance, the following discussion was coded under cure/survival even though the mother’s question was framed in terms of death/recurrence:

- Mom: “With this kind of leukemia, what’s the death rate?”
  Doctor: “The success rate is very good with this kind of leukemia.” (DC-04)

**Numerical Prognosis Given**

Although there were 24 statements by physicians about their dislike of attaching numbers to a prognosis, in 97 (89.8%) of the 108 ICCs, the physician did actually use numbers in presenting the chance of cure/survival, including those prognosis discussions framed generally or for the particular child. The actual numbers used were examined, and the mean *Numerical Prognosis* for the 97 patients was 76.5 (SD = 9.4), with a range of 50-90.

The chance of cure presented during the ICC was compared to the physician’s reporting of the child’s chance of cure on the Case Specific Clinician Questionnaire using a paired-samples t-test. The mean *Numerical Prognosis* of 76.5 given by physicians to parents during the ICC was not significantly
different from the mean prognosis of 77.2 given by physicians on the Case Specific Clinician Questionnaire ($t=-1.3, p<.19$), and the two variables were highly correlated ($p<.01$). Thus, clinicians generally presented the same prognosis to parents during the ICC that they gave our research team in the questionnaire.

**Parent Factors**

The two major parent factors examined were sociodemographic variables and understanding variables. The sociodemographic variables collected include parent *gender, age, ethnicity, socioeconomic status, education*, and *religion*. The sample of 108 parents is demographically diverse, as shown in Table 7 below. The 108 parent interviews included 37.0% racial minority subjects. The interviews were conducted with 64 mothers and 44 fathers. Parent-subjects were an average of 35.5 years old (range 18-51). Sixteen parents had less than a high school education, 23 completed high school, and 68 had some college. One parent declined to give her education. We utilized data on occupation and education level to calculate the Hollingshead Index of Social Position (ISP), which assigns socioeconomic status, for each parent (Hollingshead 1957). On this scale of one to five, a lower ISP score represents a higher socioeconomic status. In our sample, 28.0% of parents fell into ISP category 1 or 2, 42.1% fell into category 3, and 30.0% fell into category 4 or 5. Fifty parents reported their religious preference as Protestant, 45 Catholic, 5 Non-Christian, and 8 None.
Table 7: Parent Demographics

<table>
<thead>
<tr>
<th>Category</th>
<th>Mean</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent Age</td>
<td>35.5</td>
<td>18-51</td>
</tr>
<tr>
<td>Parent Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>44 (40.7%)</td>
<td>64 (59.3%)</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parent Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Majority</td>
<td>68 (63.0%)</td>
<td>40 (37.0%)</td>
</tr>
<tr>
<td>Minority</td>
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<td></td>
</tr>
<tr>
<td>Parent ISP*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>30 (28.0%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>45 (42.1%)</td>
<td></td>
</tr>
<tr>
<td>4-5</td>
<td>32 (29.9%)</td>
<td></td>
</tr>
<tr>
<td>Parent Education*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than High School</td>
<td>16 (15.0%)</td>
<td></td>
</tr>
<tr>
<td>Completed High School</td>
<td>23 (21.5%)</td>
<td></td>
</tr>
<tr>
<td>Some College</td>
<td>68 (63.5%)</td>
<td></td>
</tr>
<tr>
<td>Parent Religion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protestant</td>
<td>50 (46.3%)</td>
<td></td>
</tr>
<tr>
<td>Catholic</td>
<td>45 (41.7%)</td>
<td></td>
</tr>
<tr>
<td>Non-Christian</td>
<td>5 (4.6%)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>8 (7.4%)</td>
<td></td>
</tr>
</tbody>
</table>

*1 Missing Value

For this dissertation, the 32 cases from the larger project (N=140) involving parents who had no understanding of choice between participation in a clinical trial or receiving treatment outside of the trial were excluded, leaving a sample of 108 for the dissertation. The 32 excluded cases included those parents who a) didn’t remember discussing a trial, and/or b) thought the trial was their only option. These parents were excluded because they didn’t know they had more than one option, therefore there was no decision to make from their perspective. The responses of these parents to our decision-making questions are generally limited to “to help my child get better” or “my child would die without treatment”, reflecting their misunderstanding that the trial is the
same as basic treatment for their child. Therefore, in the sample of 108 cases included in this dissertation, parent understanding of choice is held constant.

Randomization, or allocation by chance to one of multiple treatment arms in the trial, is the fundamental difference between participation in a Phase III cancer clinical trial and receiving treatment outside of the trial. Parent Understanding of Randomization was determined using the following protocol. Two interview questions that assessed understanding of randomization directly were evaluated first. These questions were: “In this clinical research study, how will it be decided which treatment your child will receive?” and “If your child enrolled in this clinical research study, will you be able to choose the treatment option you want?” If responses to these two items did not indicate parental understanding, I proceeded to a global search of the parent’s answers to all interview items for evidence of understanding. Parents were considered to understand randomization if at any point during the interview they were able to articulate that their child would be assigned by chance to one of multiple treatment arms if they chose to enroll on the clinical trial. Sixty-five (60.2%) of the 108 parents understood randomization.

Parents’ perception of the riskiness of the trial was measured using an analog item. Specifically, parents were asked, on a scale of 0-10, “How risky is therapy in the clinical research study compared to standard therapy?” with 0 being “much less risky” and 10 being “much more risky”. The average score for the 105 parents who answered this item (3 missing values) was 5.2 (SD = 1.9), with a minimum of 0 and a maximum of 10. Parent Perception of Risk was
compared to the physician's perception of risk from the Case Specific Clinician Questionnaire for each case using a paired-samples t-test. The mean score of 5.2 given by parents was significantly higher than the mean score of 4.8 given by clinicians (t=2.0, p<.05), and the two risk variables were not correlated (p<.98). Thus, parents tend to view the trial as riskier than their child's physician, which could influence their decision-making about the trial.

Examples From Focus Groups

There was much discussion during the focus groups about the impact of patient factors on parental decision-making. For example, in the first Cincinnati focus group, one mother explained how her son's illness severity and risk level influenced her decision-making:

- "Also our son was very, very ill. He had such a high blood cell count. He was so ill, and he went from no fever to being in intensive care. So at that point, what could be harder about this program? It couldn't hurt, and he was very high risk because he was sixteen, male, and his red blood cell count was so high. So again, that made us, or made me, lean toward it [the trial]."

In the second Philadelphia focus group, one parent described how his son's prognosis affected his decision-making about the trial:

- "Just one distinction, this study anyway said the chance of cure with any of the four treatments is expected to be 85%, so we were in a different percentile bracket. When you did the math, they were expecting a 2 to 3 percent, maybe, benefit from one of the other protocols so I was looking at a room with a hundred people, M. had to be one of the fifteen who wasn't going to be helped by the current treatment. And of those fifteen, maybe
two or three were going to be helped. Then I had to decide whether that was enough of an increment to expose him to the increased amount. As the percentages of recovery go higher with the protocol, the benefit of participating in a test goes down for your child. That's one of the things that the scientists pointed out to us. When cure rates are 50%, 30%, 20%, then you've got to participate.

Another parent who attended this focus group discussed her child's prognosis in a similar way, but from the opposite perspective. This parent's comment suggests that when the prognosis is low, parents will take any chance for an increase in cure rate:

- "The first thing they told us was that the standard treatment cures less than one out of two, and that's not the kind of number that you want to hear about your son. If you signed for the clinical trial and get randomized for it, then number one, it's not any worse. It could be better, and when you have numbers like that, you want that—I mean, you don't know what percent of the chances being better, but I mean you want to take anything you can get. That is the bottom line!"

A parent in the first Cleveland focus group discussed the effect of her child's risk level on her decision-making process:

- "My concern is that is this a right decision, or is one compared to the other could be worse chances of him recouping? Because he is at an older age and a higher risk. Not like some of the younger kids. They have a more better rate of recovery than older teenagers and younger adults. But we opted to go with it."

There was little discussion during the focus groups of the influence of parent factors on decision-making, but their influence is suggested by one mother's explanation of the role of faith in her decision-making:
"This is a horrible disease and I almost feel like only God knows if Tyler is going to get better, and we have to have faith. So I said I think that we should put him in the study because I didn't feel comfortable making the decision of what he got because I felt like I would second-guess myself. What if that wasn't the right one? The randomization – let them pick. And I kind of felt like I had an act of faith that God would know what would be best for T...And that's what made me comfortable because I, like I said, put it in God's hands. I put it in that little computer's hands to get whatever needs to be done." (3rd Philadelphia focus group)

Recoding of Variables

The 8 patient variables used to test the model in Chapter 10 include:

- **Patient Age**
- **Patient Gender**
- **Risk Level**
- **Total Positive Illness Severity**
- **Total Negative Illness Severity**
- **Total Prognosis—Cure/Survival**
- **Total Prognosis – Death/Recurrence**
- **Numerical Prognosis**

**Patient Gender** and **Risk Level** are dichotomous variables. For analyses conducted to test the model in Chapter 10, the other 6 patient variables were recoded into dichotomous variables. **Patient Age** was divided into <=5 years old (N=53, 49.1%) and over 5 years old (N=55, 50.9%). **Total Positive Illness Severity** comments and **Total Negative Illness Severity** comments were recoded into low and high groups to represent the number of comments in each. The new **Total Positive Illness Severity** variable includes 63 (58.3%) ICCs in the low group (<=1 comment), and 45 (41.7%) in the high
The new **Total Negative Illness Severity** variable includes 61 (56.5%) ICCs in the low group (no comments), and 47 (43.5%) in the high group (>=1 comment). **Total Prognosis – Cure/Survival** was divided into ICCs with <=2 statements (N=52, 48.1%) and >2 statements (N=56, 51.9%). **Total Prognosis – Death/Recurrence** was separated into ICCs with no prognosis discussions framed in terms of death/recurrence (N=45, 41.7%) versus at least one discussion (N=63, 58.3%). The **Numerical Prognosis** given was recoded into low prognosis defined as < 78.0 chance of cure (N=47, 48.5%), and high prognosis defined as >= 78.0 chance of cure (N=50, 51.5%). There are 11 missing values in this variable because physicians did not disclose a numerical chance of cure in 11 ICCs.

The 8 parent variables used to test the model in Chapter 10 include:

- **Parent Age**
- **Parent Gender**
- **Parent Ethnicity**
- **Parent Education**
- **Parent SES**
- **Parent Religion**
- **Parent Understanding of Randomization**
- **Parent Perception of Risk**

**Parent Gender, Ethnicity, and Understanding of Randomization** are dichotomous variables. For analyses conducted to test the model in Chapter 10, the other 5 parent variables were recoded into dichotomous variables. **Parent Age** was divided into <=35 years old (N=56, 51.9%) and over 35 years old (N=52, 48.1%). **Parent Education** was separated into lower education, defined as completing high school or less (N=39, 36.4%) and higher education, defined as anything beyond high school (N=68, 63.6%). There is one missing
value because one parent declined to answer this question. *Parent SES* is grouped into high SES using categories 1-3 of the Hollingshead Index of Social Position (N=75, 70.1%) and low SES using categories 4-5 (N=32, 29.9%).

Because *Parent Education* is part of *Parent SES*, the one missing value from *Parent Education* carries over to *Parent SES*. *Parent Religion* was recoded into Protestant (N=50, 46.3%) or Other Religion (Catholic, Non-Christian, None) (N=58, 53.7%). *Parent Perception of Risk* was divided into low risk, defined as a rating of <= 5.0 (N=43, 41.0%) and high risk, defined as >5.0 (N=62, 59.0%). There are three missing values because 3 parents declined to answer this question.
Chapter 5: Social Network Factors

Two types of social network factors were examined: 1) support given by social network members during the informed consent conference, and 2) support sought from and given by social network members during the parents' decision-making process. Both of these factors are important because the people parents bring with them to the ICC may be different from who they seek advice from due to proximity issues and the different roles network members play.

Support Given During ICC

Network Members Present:

The first type of support given by social network members during the ICC is the simple act of being present. All 108 ICCs were analyzed for the presence of social network members. For this analysis, the social network was considered anyone who was a) outside of the immediate nuclear family circle, (i.e., not the mother, father, or the patient's siblings), and b) not an employee of the hospital where the patient was admitted. The concept of a social (not biological) nuclear family circle was used, so step-parents and -siblings were deemed to be within the immediate family circle and were thus excluded from the analysis of network members present.

The patients' siblings were not included in this analysis because there were only 4 ICCs where a sibling was present, and in these cases the sibling was a very young child who was present because the parents needed to watch
over them. Therefore, in these few cases, the siblings were being cared for, not acting as part of the support system.

The types of network members present for these 108 ICCs included: grandmothers, grandfathers, aunts, uncles, cousins, doctors from outside the hospital, and other. The grandparent categories include great-grandparents. The other category includes 1 father’s girlfriend, 1 grandmother’s boyfriend, 1 patient’s girlfriend, and 2 unknown relatives. For cases with more than one ICC, all network members present at any ICC were included in the analyses, but each person was only counted once.

The average number of Network Members Present was 1.1 (SD = 1.9), with a range of 0 to 11. Sixty-nine (63.9%) of the 108 ICCs did not have any Network Members Present. For the 39 ICCs that did have at least one network member present, there were a total of 113 Network Members Present. The totals for the different categories of network members, in order of frequency, are shown in Table 8 below:

<table>
<thead>
<tr>
<th>Network Member</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grandmother</td>
<td>32</td>
</tr>
<tr>
<td>Aunt</td>
<td>29</td>
</tr>
<tr>
<td>Uncle</td>
<td>22</td>
</tr>
<tr>
<td>Grandfather</td>
<td>12</td>
</tr>
<tr>
<td>Cousin</td>
<td>9</td>
</tr>
<tr>
<td>Outside Doctor</td>
<td>4</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
</tr>
</tbody>
</table>

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Support Given During ICC: Network Questions and Comments

Support provided by network members during the ICC came in different types of questions and comments. All questions or comments from a social network member were extracted from the ICC transcripts. Next, the questions and comments were divided into 6 different categories, each representing a type of support given to the family by a social network member during the ICC: 1) questions about trial, 2) non-trial-related questions, 3) comments to doctor about the child or family, 4) offers of opinion or advice, 5) statements of solidarity, and 6) facilitation of communication.

Thirty-five (89.7%) of the 39 ICCs with a network member present involved questions or comments from a network member. Network members played many different roles in these 39 ICCs. For example, in case CIN-02, the patient’s grandmother and aunt ask almost all of the questions. In case CIN-05, the patient’s cousin sits by the patient’s bedside and repeatedly asks the patient if he has any questions or needs the doctor to explain anything differently. In case LA-20, the patient’s aunts and uncles tell the doctor that their role will be to explain the trial to the mother and be sure that she understands. In case PH-23, the aunt acts as an interpreter for the mother, who speaks Italian.

There were a total of 1,059 social network questions or comments (of any type) in the 108 ICCs. The average number of network questions or comments was 9.8 (SD = 22.1), with a range of 0 to 158. Table 9 below shows the number of ICCs with network support of each type, as well as the total number of questions or comments, for each of the 6 categories.
Network Questions About Trial

Twenty-six ICCs included network support in the **Network Questions About Trial** category, with a total of 214 questions asked. For all 108 ICCs, a mean of 2.0 (SD = 5.3) questions about the trial were asked, with a range of 0 to 32.

Network members asked very astute questions about the trial, including:

- **Cousin**: “Is there a set time when they have to give you a decision?” (CIN-05)
- **Grandmother**: “If it’s [the trial] okay, and the medicine’s okay, and it’s not harder to maintain than everybody else, then why is there papers to sign?” (CIN-10)
- **Aunt**: “What other choices are there besides that [trial]?” (LA-07)
- **Uncle**: “Where can I get the data that’s available for this study?” (PH-22)
- **Aunt**: “So it’s about the quantity of the medicine, not a difference in the medicine you are giving?” (PH-23)
- **Grandmother**: “Can I, just to summarize this, is there a benefit to M. to be in this random draw?” (PH-34)

There were many network questions about the randomization process in particular, such as:

<table>
<thead>
<tr>
<th>Questions about Trial</th>
<th># ICCs</th>
<th>Non-Trial Related Questions</th>
<th># ICCs</th>
<th>Comments About Child/Family</th>
<th># ICCs</th>
<th>Common Advice</th>
<th># ICCs</th>
<th>Statements of Solidarity</th>
<th># ICCs</th>
<th>Facilitation of Communication</th>
<th># ICCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICCs</td>
<td>26</td>
<td>14</td>
<td>33</td>
<td>24</td>
<td>98</td>
<td>18</td>
<td>47</td>
<td>11</td>
<td>30</td>
<td>22</td>
<td>71</td>
</tr>
</tbody>
</table>
o *Grandmother*: "What was you saying, excuse me, about somebody else picking it?" (CIN-02)

o *Grandmother*: "So you're flipping a coin?" (CIN-10)

o *Grandmother*: "And how did you say you would pick which one of these she would be on?" (CL-08)

**Network Non-Trial-Related Questions**

Thirty-three ICCs included network support in the *Network Non-Trial-Related Questions* category, with a total of 599 questions asked. For all 108 ICCs, a mean of 5.6 (SD = 13.8) questions were asked, with a range of 0 to 104.

Network members asked many questions about the disease and treatment in general, including:

o *Grandmother*: "Now leukemia, is it painful?" (CIN-15)

o *Grandmother*: "When will you find out if he has it in the brain?" (CL-03)

o *Grandmother's Boyfriend*: "Which medications will be given at home?" (CL-08)

o *Aunt*: "Does he get his chemotherapy like once a week or just once a month?" (CL-14)

o *Grandmother*: "What is the success rate for someone his age?" (CL-14)

o *Grandmother*: "And that thing y'all are puttin' in her chest, does that have to be flushed out each day?" (DC-01)

o *Aunt*: "He's going to be here for 28 days?" (LA-07)
"Grandfather: “I heard about bone marrow donors. Will she need a transplant?” (LA-26)

"Grandmother: “So how often does he have the bone marrow or a spinal?” (PH-26)

Network members also asked questions related to psychosocial issues or the effects of the disease and treatment on the child’s activities. For instance:

"Great Grandmother: “Will he be able to attend school and play?” (CIN-02)

"Grandmother: “Is there someone, like a psychologist, that could sit down and do games with her and tell her, you know, ‘your hair’s going to go’?” (CIN-10)

The purpose of some network questions was requesting explanation or definition of unknown terminology:

"Uncle: “So is that called a cure or a remission?” (CL-03)

"Grandmother: “What is acute leukemia?” (CL-16)

"Grandmother: “What do you call significant? I mean, what does that word mean?” (PH-34)

Some of the questions asked by network members might be seeking answers that the parents don’t want to hear, such as:

"Grandmother: “If she does live and come out good, and it goes into remission, is there always that chance that it could come back?” (CL-08)

"Aunt: “How do you die from leukemia?” (LA-26)
**Network Comments About Child/Family**

Twenty-four ICCs included network support in the *Network Comments About Child/Family* category, with a total of 98 comments. For all 108 ICCs, a mean of .9 (SD = 2.4) comments about the child/family were made, with a range of 0 to 12. Network members relayed important medical and psychosocial information about the child or family to the doctor, such as:

- *Grandmother:* “And he hates needles.” (CIN-02)
- *Grandmother:* “R. [patient’s mom] and C. [patient’s dad] are worried because they are in school, since it’s the last semester, and she’s wondering if she [mom] should drop out.” (CL-16)
- *Mom’s Cousin:* “It’s very important because she says that she wants to make the ninth grade at the same time as everybody else because she doesn’t want to miss going to high school.” (LA-02)
- *Aunt:* “She had a fever last night.” (PH-23)

**Network Offers of Opinion/Advice**

Eighteen ICCs included network support in the *Network Offers of Opinion/Advice* category, with a total of 47 offers of opinion or advice. For all 108 ICCs, a mean of .4 (SD = 1.2) offers of opinion or advice were made, with a range of 0 to 6. This variable was not included in any further quantitative analyses because only 17% of the 108 ICCs were coded for this variable. Network members offered their opinions or advice about practical issues, such as:
Grandmother. "I might just cut his hair off." (CIN-02)

Grandfather. "I know you wanna do this K., but you have to check with your insurance, 'cause there's a difference between us leaving here at 3 days or 4 days and staying here until 7 days and 8 days." (LA-26)

Network members also gave their opinion or advice about the trial during the ICC, including:

Grandfather. "I would say go and let them try anything they can try. I mean, she's a sick little girl." (DC-01)

Mom's Cousin: "Okay, I think you should go for it [the trial]." (LA-02)

Uncle: "I think that's a decision [about trial participation] that doesn't have to be made today. Let's get this going and get this started and then ask the family, and we can sit down and talk about that and see if that's the way if you choose that you want to go." (PH-22)

Network Statements of Solidarity

Eleven ICCs included network support in the Network Statements of Solidarity category, with a total of 30 statements of solidarity made. For all 108 ICCs, a mean of .3 (SD = 1.0) statements of solidarity were made, with a range of 0 to 7. This variable was not included in any further quantitative analyses because only 10% of the 108 ICCs were coded for this variable. Statements coded in this category include:

Cousin: "We got lots of family. I mean, even though we're facing those tough months. We'll all be around...He's got lots of support." (CIN-05)
Network Facilitation of Communication

Twenty-two ICCs included network support in the Network Facilitation of Communication category, with a total of 71 instances of assisting communication between the doctors and family. For all 108 ICCs, there was a mean of .7 (SD = 1.8) instances of network facilitation of communication, with a range of 0 to 10. Network members assisted in the communication process by relaying the questions and concerns of the family to the doctors, providing explanations of what the doctor said to the family, requesting information from the doctor, or encouraging the family to ask questions. For instance:

- **Cousin:** [to patient] "Do you have any questions or do you want him to explain anything a little more or differently?" (CIN-05)
- **Grandmother:** "Are we going to get a copy of this?" (CL-16)
- **Aunt:** "Will you give us a list of the drugs and side effects?" (CL-18)
- **Grandfather:** [to parents] "Either way, you could pull her off the program." (DC-01)
- **Mom's Cousin:** "She [the mom] just wants to know what the cons and the pros would be. You know, she doesn't want to put her child through any more than she should." (LA-02)
Negative Support

In addition to the positive support provided by network members described above, there were also instances of negative support from network members. The following examples illustrate some of the ways that the social network can worsen the situation from the parents' perspective:

- **Dad:** [to mom] "Your mom's here."
  **Mom:** (speaking tearfully) "She just makes it worse."
  **Doctor:** "Well, we'll just send her home. (Laughter) Why does your mother make it worse?"
  **Mom:** (sobbing) "She makes me sad."
  **Doctor:** "Your mother makes you sad?"
  **Mom:** (still weeping) "Because she's afraid." (CL-02)

- **Mom:** "Well, I think now that we have answers we have been very, very honest with C. I mean, to the point where it is really like irritating my father because he doesn't feel that we should be this honest with her."
  **Dad:** "He thinks we should hide stuff away from her."
  **Mom:** "And make her world real rosy, and that's not the way we believe." (PH-05)

- **Mom:** (interrupting physician) "Well, the brain is the most radio-tolerated organ in the body." [to grandfather, who is making a face] Will you stop?"
  **Grandfather:** "Well, you're giving a lecture." (LA-07)
Support Sought From and Given by Network During Decision-Making Process

Additional information about who parents sought and received advice from regarding the trial comes from follow up telephone interviews conducted 6 months after the child's diagnosis. Two variables were assessed using parent responses to two questions relating to the sources of information parents found helpful during decision-making and the people who helped them understand the clinical trial. Unfortunately, twenty of the 108 cases were lost to follow up, and we were unable to conduct 6 month interviews with these 20 parents. Because this social support information is missing for these cases, these two variables will not be included in any further quantitative analyses. A description of these variables for the 88 complete cases follows.

The first question was open-ended and asked: "What sources of information were most helpful to you in making your decision about whether or not to participate in this clinical research study?" Responses to this question fell into 7 categories, 4 of which refer to social networks. The 7 categories and the number of references to each in the 88 follow up interviews are shown in Table 10 below.
Table 10: Most Helpful Sources of Information During Decision-Making  
(n=88 cases)

<table>
<thead>
<tr>
<th>Source</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doctor/Discussions</td>
<td>45</td>
</tr>
<tr>
<td>Written Material</td>
<td>24</td>
</tr>
<tr>
<td>Family Member</td>
<td>8</td>
</tr>
<tr>
<td>Internet</td>
<td>7</td>
</tr>
<tr>
<td>Friend</td>
<td>5</td>
</tr>
<tr>
<td>Other Doctor</td>
<td>4</td>
</tr>
<tr>
<td>Other Parents</td>
<td>3</td>
</tr>
</tbody>
</table>

Although discussions with doctors and the written material received were the most frequently cited helpful sources of information, many parents did mention network members without any prompting. Five of the eight responses in the “family member” category mentioned a family member that is in the medical field, including a lab technician, a cancer specialist, a nursing student, a medical researcher, and a pharmaceutical representative. The other three included a lawyer and mention of “family” in general. One parent’s response was:

- “Fortunately, it was a group of us in my family, and one of my brother-in-laws works for a pharmaceutical company so he was well versed in some of the protocols. I work in a hospital so I knew a little something about the drugs and the protocols. One of my sister-in-laws is a lawyer so, you know, we had a lot of fairly good representation in there.” (PH-22)
Two of the answers in the “friends” category referred to friends who work in the medical field and one friend who had breast cancer. For example, one parent’s response to this question was:

- “I knew a friend of mine went through a similar experience several years ago with her son, who luckily did not have leukemia, but for some amount of time they thought he did. And she’s also a veterinarian so she has a lot of medical knowledge. So I discussed it with her and then I have another friend that has had breast cancer, and I discussed it with her.” (CIN-06)

Two of the “other doctors” mentioned were the child’s pediatrician, and the other two were unspecified. All four of the responses in the “other parents” category referred to other parents of children with leukemia in the hospital.

The second question about social networks asked “Since the time your child was diagnosed, have any of the following helped you better understand what a clinical research study is and how it works?” The social network options listed for parents to choose from were a) friends and family, b) other health care providers who do not work here, and c) other. Twenty-eight (31.8%) of the 88 parents chose friends and family, 18 (20.5%) chose other health care providers who do not work here, and 9 (10.2%) chose other. Two of the 9 parents that chose “other” listed two people, and the 11 responses include: 2 other children, 7 other parents in the hospital, 1 school teacher, and 1 day care worker.

Examples From Focus Groups

Several questions relating to parents’ use of their social network during decision-making were asked during the focus groups, including: Did you
discuss the research study with anyone outside this hospital? What sorts of things did you discuss with these people? What did these people feel or think about the research study? How did these discussions influence your decision about the research study?

There were many discussions during the focus groups of how parents sought or received support from their social network. Many parents expressed the value of having someone from their social network attend the ICC, including:

- "They called a family meeting: myself, my husband as well as my mother-in-law." (Moderator: "Did your mother-in-law have any special experience or training in leukemia?") "No, it was just the extra body there—a support system. Somebody to decipher the information that was presented." (2nd Philadelphia focus group)

- "We had a group of about twelve family members in the room. We decided, okay who is going to sit in on this panel? We asked the doctor, 'Can more than just the parents sit in?' And they said 'sure', so we had six people on our side, and it kind of empowered us, my wife and I, because we didn't feel threatened by being outnumbered. They had six people over there. We had six people over here. One of my brother-in-laws works for a pharmaceutical company, and he's pretty adept at knowing the research protocols, and he's asking a lot of good questions." (3rd Philadelphia focus group)

- "We asked, 'Can we have any family members?' They said the room is small, but we could have a few. I had to decide who was going to be there and who wasn't. My mother was here. She's a nurse so I thought that she should be there. My uncle, he has a doctorate in psychology and also dealt with sports medicine so I felt like he should
be there. I have a lot of confidence in my uncle, and I discussed it with him, and he told me his feelings." (3rd Philadelphia focus group)

- “My cousin is the one who had asked the questions.” (1st Los Angeles focus group)

- “All of my women friends got together at that meeting. And, we all said, ‘Yes, that's alright for the child to enter that study.’” (2nd Los Angeles focus group)

- “Somebody who is a very close friend or something, that you are very comfortable with -- it helps too. I mean, if you’ve got somebody sitting there, they might hear something that you really didn’t hear or understand something better. So if you have a relative or a friend, they can say, ‘Well this is what I got out of it.’ And, you know, you can sit there and kind of talk to each other about it. Or if they are allowed time to ask some questions, too, because that might be helpful.” (2nd Cincinnati focus group)

Other parents in the focus groups described seeking advice or information from their social network after the ICC. Some parents used their social network primarily for seeking advice about whether to participate in the trial. For example:

- “We have a personal friend who is a doctor here at University of Pennsylvania, who had really told us the value of being part of a protocol. So quite honestly, I believed him. My wife and I felt very comfortable because of the doctor friend that’s here who advocated the protocol position.” (1st Philadelphia focus group)

- “After we walked out of the room and we were on this time schedule, I called my family doctor back and I asked him, I said, ‘Okay here’s the deal.’ And I said – and you know, it’s like a relationship where he can tell me how he feels. He’s not going to persuade me, and he knows it – So I said,
"What would you do?" He said, "I wouldn't do it."
He said, "I wouldn't do it for my own kids so I can't
turn around and tell you to do it or not to do it. If I
were in your position, and I can only imagine it at
this point," he says, "I don't think I would." (1st
Philadelphia focus group)

- "I have a buddy of mine who is a pharmacist, and
  he was able to decipher a lot of it for me. About
  the drug use and all this other stuff. So I said,
  'I've read it. I didn't have a problem with it, but I
  wanted to make sure that somebody else had a
  chance that wasn't flipping out to read it.' I said,
  'Hey, doc, what do you think about this?'" (2nd
  Washington DC focus group)

Parents also described utilizing their social network for information gathering.

For instance:

- "We called my mother because she's a nurse -- a
  retired nurse. But anytime there's a sickness in
  the family they get a hold of Mom. If she doesn't
  know about it, she's got all the medical books.
  She looks up and tries to learn as much as she
  can so she can inform us as best she can." (1st
  Cleveland focus group)

- "The most impact was my father-in-law and my
  sister who lives out in California and has many
  friends in the medical field. And her husband is
  working with pharmaceutical companies and all
  kinds of things out there. She was busy doing all
  of my research for me. Like you said, you have
  such a small amount of time, so I was in no
  position to be calling lots of different people. So
  she was doing a lot of the calling and discussed it
  with her husband. And they said, 'You're in the
  best possible place you could be right now and go
  ahead with the research if you think...We feel
  comfortable with it, and you feel comfortable. Go
  for it.' And my husband's father said the same
  thing." (1st Cincinnati focus group)
Several parents discussed going to others for advice or information, while at the same time recognizing that the decision was ultimately theirs to make:

- "I talked to, again by coincidence, another friend of my wife's is married to a man who does oncology research – pediatric oncology research – in Massachusetts. I talked to him. I talked to another doctor who does research there because she's a good friend of close friends. So in other words, I couldn't make my mind up so I talked to all of these experts, and I got every possible option. I got support for every choice I could make. In other words, no one said it would be a mistake to participate in the study and give him more medicine, and no one said it would be a mistake not to participate. So it fell back to us to decide." (2nd Philadelphia focus group)

- "I went to other pediatricians. I went to other family members. I went to my aunt. She had had breast cancer, and I sent it [consent document] to her since she had a good relationship with her oncologist. I tried to get as much information as I could. Nobody was going to come out and say, 'Look, this is what you have to do.' I knew that we would have to make that decision." (2nd Cleveland focus group)

Recoding of Variables

The 6 social network variables used to test the model in Chapter 10 include:

- **Network Members Present**
- **Network Questions About Trial**
- **Network Non-Trial-Related Questions**
- **Network Comments About Child/Family**
- **Network Facilitation of Communication**
- **Total Network Questions/Comments**

For analyses conducted to test the model in Chapter 10, these 6 variables were recoded into dichotomous variables. *Network Members Present* was recoded
into no network members present (N=69, 63.9%) and one or more network members present (N=39, 36.1%). Network Questions About Trial was divided into no network questions about the trial (N=82, 75.9%) versus one or more questions about the trial (N = 26, 24.1%). Network Non-Trial-Related Questions was grouped into no non-trial-related questions (N=75, 69.4%) and one or more non-trial-related questions (N = 33, 30.6%). Network Comments About Child/Family was recoded into no comments about the child/family (N=84, 77.8%) versus one or more comments about the child/family (N = 24, 22.2%). Network Facilitation of Communication was separated into no instances of network facilitation of communication (N=86, 79.6%) and one or more instances (N = 22, 20.4%). Total Network Questions/Comments was recoded into no network questions/comments (N=73, 67.6%) versus at least one network questions/comments (N=35, 32.4%).
Chapter 6: Clinician Factors: Doctor/Parent Relationship

The significance of the doctor/parent relationship in decision-making about trial participation is exemplified by one parent’s comment during the PAGIC meeting:

- "Well, I just want to say that I heard you say earlier about the parent having some type of relationship with the doctor, and feeling a connection, and that was really important to me. Because I felt like I was making a huge decision for her [the patient]. She couldn’t make the decision."

This chapter describes two aspects of the doctor/parent relationship: level of shared decision-making and trust. Both of these variables are highly dependent on context. All 108 cases involved newly diagnosed children whose families were in a new hospital environment interacting with physicians and other health care professionals who they’d just met for the first time. In other words, these cases are typified by doctor/parent relationships that are just beginning to develop, as illustrated by the following parent comment during the PAGIC meeting:

- "It took me a few days to feel the connection between myself and the doctor. I needed to feel like they were truly being honest with me. I didn’t know these people. I’d never seen them before. I met them that day at that diagnosis. So...I think the connection has to do with it."

Shared Decision-Making

A standardized instrument, The Decision Making Preference Questionnaire (DMPQ), directly assessed parental preferences regarding decision-making
responsibility. The instrument was introduced to parents with the following script: "Some parents, after they have all the information they need about their child's illness and the possible treatments available to them, prefer to leave decisions about their treatment up to their doctor. Others prefer to participate in these decisions in a variety of ways. I am going to show you some cards. Please select the one card that best describes what you believe would be the ideal way for you to make a decision about treatment for your child with acute leukemia."

Figure 3: Decision-Making Preference Questionnaire
The 5 options parents were asked to choose between, and the frequency with which each was chosen, is shown in Figure 3 above. The variability in Decision-Making Preference among parents was articulated by one parent’s report during the PAGIC meeting of what parents in his focus group discussed:

- "And the reason I chose not to go to study personally was an issue of control. I chose not to give control to the doctors or anyone else. I figured if anyone is going to be in charge of my daughter’s treatment, it should be me. Other people within the [focus] group, they weren’t as confident. They said, ‘I don’t know anything about medicine. I don’t want to make this choice. It’s up to you. We’re going to go to the protocol.’ They just surrendered the choice to the doctor, and said, ‘We’re going to go with whatever you’ve recommended, and that’s it.’"

In addition to the DMPQ, we asked both parents and clinicians the question: "Who was most important in directing this decision [about the trial]?") Respondents were asked to choose between the physician, a nurse or other health care provider, the parents, the patient, or other. Since this chapter focuses on the doctor-parent relationship, only the number of responses in the “doctor” and “parent” categories was examined, and the results are shown in Table 11 below. Seven parents and seven doctors chose both doctor and parents. Table 11 shows that both parents and doctors tended to rate themselves as most important in directing the decision about trial participation. Four variables resulted from this analysis: Parent-Directed Decision by Parent Report, Doctor-Directed Decision by Parent Report, Parent-Directed Decision by Doctor Report, and Doctor-Directed Decision by Doctor Report.
Table 11: Doctor and Parent Views of Who Directed the Trial Decision

<table>
<thead>
<tr>
<th>Respondent</th>
<th>Doctor</th>
<th>Parents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doctor</td>
<td>60</td>
<td>39</td>
</tr>
<tr>
<td>Parents</td>
<td>38</td>
<td>63</td>
</tr>
</tbody>
</table>

In order to characterize the doctor/parent relationship further, the ICCs were analyzed for evidence of shared decision-making relating to trial participation, including a) parents sharing their opinions about the trial or decision-making process, b) parents requesting the physician's recommendation about the trial, c) physician eliciting the opinions or decision of parents regarding the trial, d) discussion of parent and physician decision-making roles, and e) discussion of how the decision about participation in the trial should be made. Every instance in each of the 5 categories was counted for all 108 ICCs. There was a total of 255 instances of shared decision-making in all ICCs, with a mean of 2.4 (SD = 4.1) and range of 0 to 37. Thirty-two (29.6%) ICCs had no evidence of shared decision-making. Table 12 below shows the number of ICCs with shared-decision making of each type, as well as the total number of instances, for each of the 5 categories. These five categories of shared decision-making were combined for each case to form the variable *Total Shared Decision-Making*, which was used in the analyses described in Chapter 10.
Table 12: Shared Decision-Making During ICC

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>ICCs</td>
<td>#</td>
<td>ICCs</td>
<td>#</td>
<td>ICCs</td>
</tr>
<tr>
<td>55</td>
<td>159</td>
<td>29</td>
<td>36</td>
<td>23</td>
</tr>
</tbody>
</table>

Parental Sharing of Opinions/Decision-Making Process

In 55 ICCs, parents shared their opinions about the trial or discussed their decision-making process with the doctor. Often, these occurred together, with parents offering their feelings about participating in the trial followed by their reasons for feeling that way. Examples include:

- "I'm kind of leaning towards not going onto the study because with her not being as, I guess, as serious or hard to treat." (CIN-14)

- "My concern is how far apart are they [delayed intensifications phases] going to be? And I know that if it's not good for him, I wouldn't want it to be too far apart, but there's only so much a person can take. It will wear him down, and that can't be good. That's my big concern." (CL-09)

- Dad: "So again, the aggressive side of me is saying let's go after this. If it's gonna help us increase those chances, let's do it. But then talking out the other side of my mouth, I'm saying, well, you're telling us all these good signs so far, you know, and everything you told us today, so..." Mom: "It sounds like the standard might work." (CL-10)
“If you want my opinion, I would rather go with the random decision by the computer because there’s an option that he could get a better treatment. I would rather give him that option.” (LA-07)

“I do understand all of that. And I understand helping others and all that other fun stuff, but at the same time it’s very difficult to say to yourself, ‘Could I possibly be giving my son something that’s not the best by participating in this study?’ Yet, on the other side you tell me that kids do better on the studies.” (PH-01)

“I find this a horrible choice to make. I just want you to know what we’re feeling inside. If we go for standard and he has a recurrence, I’ll hate myself to the very end.” (PH-34)

**Parent Request for Recommendation**

Twenty-nine of the ICCs included a parental request for the physician’s recommendation regarding the trial. These requests suggest a preference for decision-making that ranged from shared to completely physician-directed. For instance:

“So you as his doctor would recommend being on a protocol? I mean, for his best interest as opposed to, you know, everybody? I’m just concerned about my child.” (CIN-16)

“Is this what you two would decide? ‘Cause you’ve seen this so much. I would really feel comfortable with what you decide for him.” (CIN-07)

A common way for parents to request a recommendation was to ask the doctor what (s)he would do in the same situation, such as:

“But if D. were your child, this is what you would put him on?” (CIN-12)
So then if it was your daughter, would you pick the study?” (DC-06)

“Would you consider this for your child?” (PH-22)

**Physician Elicits Parental Opinion/Decision**

Twenty-three ICCs contained at least one occurrence of the physician eliciting the opinions or decision of the parents about the trial. This category relates to the parental sharing of opinions category above in that some physician elicitations did result in parental sharing of opinions. As the table shows, however, there are many more instances of parental sharing of opinions so the majority are not in response to a physician’s request. Physician questions relating to what parents think about the trial include:

- “So, with what you read, was there anything about the study or determining whether he gets one pill versus the other, or three medicines in the spinal taps, that you had questions with or problems with or anything that bothered you?” (CL-03)

- “What do you guys think of the study?” (CL-17)

Other physician questions in this category were more focused on the parents’ decision about participation in the trial, such as:

- “Okay, do you want to be on the study or off the study? That’s the hard part.” (LA-13)

- “You guys want to talk about this a little bit before we have you sign this or do you feel comfortable about what’s going on here?” (PH-26)
Discussion of Decision-Making Roles

Eighteen ICCs had some discussion of the parents' and physician's decision-making roles. These discussions included the physician giving the decision-making responsibility to the parents, discussion of shared decision-making, and the parents abdicating all decision-making responsibility. Sometimes the doctor brought up decision-making roles in response to a parents' request for a recommendation. In these situations, the physician declined giving a recommendation and put the decision back in the parents' hands, as in:

- "My job is to explain this well enough so that you can make a good decision." (CIN-12)
- "So again, it's a decision which is not an easy one, and it is not...I don't think it is fair for us to be asking you to make this decision, but that is how things work." (CIN-16)
- "I don't want to bias you with my opinion because I want you to make this decision independent of me." (LA-20)

There were few physician statements that mentioned joint parent-physician decision-making. For instance:

- "It's not about me talking and telling you this and dictating it to you. It's about discussing it and trying to come up with the best plan, whether it's just us three right now, or whether it involves other people as well." (CIN-12)
- "Because you're right. That's part of our job to try to figure out what we think is good for C. too. And part of your job is to ask us questions and figure out, do you think this is good for C. too. And then we both, everybody, gets together and makes the decision about that." (CL-09)
"If we decide to do the study... If at any time, if we do agree to go on study... and then we can make a decision." (LA-29)

Many parents articulated their feeling that they were unqualified to make the decision and asked the doctor to decide for them. For example:

- "That's your job. You're telling us, but that's your job. I wouldn't know from Adam. I can fix your car or build you a fence or remodel your house, but I couldn't do it [make the decision]... But I'm ready to let you work on my son. Whatever you think is best." (CIN-01)

- "And the fact that my child is getting all of these medications, it's not my area. So I think you're the best person to decide on these things. Whatever is best for our kid." (LA-06)

- "'Cause I want you to tell me where to sign because I want him, I mean, I'm a signer. Well, the fact is that you know what you're doing. If you don't, I'll come get you, don't worry. No, I'm just kidding about that." (PH-35)

Discussion of How Decision Should Be Made

There were only 5 instances of the physician giving guidance to the parents about how they should make their decision regarding trial participation, including:

- "What you need to do is weigh the risks and benefits." (CL-13)

- "But no one here has that answer. It's something only in your heart you can answer for yourself and your daughter. But when you make the decision [about the trial], be comfortable with it. I would never look back." (DC-06)
Trust

A standardized instrument called The Individualized Trust Scale was used to measure parents’ level of Trust in their child’s physician. The Trust Scale asks parents how they feel about their child’s doctor. It lists 15 pairs of antonymous adjectives with 7 positions between them. Parents are asked to place an X in one of the 7 positions that represents their immediate “feelings” about the doctor, in the direction of the adjective that seems to be most characteristic of the doctor. For example,

Trustworthy ___:___:___:___:___:___:___ Untrustworthy

The mean score on the trust scale was 93.3 (SD = 7.8), with a range of 51 to 98. This variable is highly skewed (-2.8) towards higher trust levels.

Discussion of trust during the ICC was also explored, and examples are included below for description of the variable. Both doctors and parents initiated discussions about trust. Physician-initiated discussions of trust include:

- “My goal, when I wake up in the morning, my first goal is to take care of the kids. And that, you’ve gotta trust me that that’s what I will always have as my first interest.” (LA-18)

- “And what I can tell you is that the reality is that we are gonna tell you what it is we are recommending that we do. For the most part, we’re gonna give you all the information, but the reality is there is gonna be a level of trust and a level of just going with what we recommend.” (PH-35)
More often, parents initiated discussions of trust during the ICC, as in:

- "I believe every word you tell me. I do. I believe every word you tell me." (CIN-01)

- "You know what, because I believe in you, and you believe that it's good, I'll just go ahead and sign it." (LA-02)

- Dad: "You have to have some inherent trust in your caregiver, I mean, 'cause we don't know medicine."
  Doctor: "And that's the truth. It's the same thing, you know, when you fly -- if you don't have trust in the pilot, you should never get on." (LA-32)

- "But it's just how I feel, you know. I mean, I guess any parent would feel that way. Just do whatever you have to do. I can sell you furniture, 'cause that's what I do for a living, and you might not know much about furniture. And I don't know nothing about what you do, but I would trust you just as much as I'd hope you'd trust me." (PH-35)

- Doctor: "I believe in this [trial] or I wouldn't offer it."
  Dad: "And I'm glad to hear you say that because obviously, you know, I've said it before, but I have a lot of confidence in you." (CL-10)

Examples From Focus Groups

Parents were very vocal during the focus groups about their high levels of trust in their child's doctor. As shown in many of the examples below, parents' statements of trust in the doctor were often given as a reason for letting the doctor make the decision about trial participation. For example:

- "I trust doctors completely. I will do whatever they tell me to do." (3rd Philadelphia focus group)
• “I just at that point figured that they knew what they were talking about. They were the doctors. They knew what was best.” (1st Philadelphia focus group)

• “All I could do was put my trust in the doctors and their word, and that's it. I have a lot of confidence in the doctors here. I'm not going to apologize for it. I do. I really, really do.” (3rd Philadelphia focus group)

• “I think the overriding thing, for me anyways, was that ultimately you kind of have to place your trust in the doctor that's treating you son. Relative to that, they've been through this with bunches of patients, and I just kind of passed the responsibility on them.” (1st Los Angeles focus group)

• “And I realized at that minute that I had to let it all go and give it to her. And at that minute, I just-- You know they say give it to God? I gave it to Dr. C. I said, ‘You're going to get my son well, I know. Whatever you think I should do, I am just going to follow your…’ I just had such trust in her, and I just decided that I would follow whatever things she thought...I just had to give it to her. I had to trust in somebody. I had to make somebody in charge here. I couldn't be in charge of getting him well. I had to have someone other than God to take control of his illness and get him well...I knew that within myself, that it wasn't even worth trying to understand, that I had to trust somebody. I'm smart, I'm in the medical field, and I'm not just like someone off the street. I understand somewhat, but this was beyond me.” (1st Los Angeles focus group)

• “We had such confidence in our doctor. We had established an immediate rapport, and I just felt I can give my daughter's life to you and whatever happens, she'd do all she could. I just felt comfortable with her.” (1st Cincinnati focus group)
There was also discussion during the focus groups of the parents’ decision-making preferences. Some parents clearly articulated their desire to maintain control over decision-making. For example:

- “Just you coming to me and respecting me as his mother first, and I have the last word in all of this, was very, very important...Dealing with these children, we know that sometimes other people might feel like they know what’s best, and sometimes you want to make sure they remember, ‘No, it’s my baby.’ I don’t want them to take that control from me.” (Moderator: “Did you ever ask the doctor what he or she would do if that was their child?” “No. I wouldn’t care. I really, it didn’t cross my mind.” (1st Cleveland focus group)

- “But I felt better about the entire experience because I was in total control.” (3rd Philadelphia focus group)

- “I think it should be up to the parents. I think the impression she gave me was that it was totally our decision.” (1st Cincinnati focus group)

Other parents’ statements represent a preference for shared or doctor-directed decision-making, with many parents describing how they requested a recommendation from the doctor. For instance:

- “Later I came out and asked him, ‘If this was your kid, what would you do?’ And of course he can’t answer, but, you know, I just felt like I had to ask him that.” (1st Philadelphia focus group)

- “I asked for her recommendation knowing that I would fully abide by it one way or the other.” (2nd Philadelphia focus group)

- “And I just came out and I asked Dr. N. ‘Would you do this if this were your child? That’s how torn I am, I really don’t know what to decide.’ He said, ‘I would decide for the study because I know my
child is going to live, and I will be benefiting children in the future, and that would be my decision.’ And that is why we decided to go on the program. That’s what it came down to...I asked him because I trusted him. I felt a very closeness with him from the beginning, and I trusted what he would say.” (1st Cleveland focus group)

- “I remember asking them, ‘What would they do?’ They were very supportive, and they told me to do what I felt and guaranteed me that it wasn’t going to affect what benefits she would have. It’s a very scary decision to make, and you don’t want to be the only one to make it.” (1st Cincinnati focus group)

**Recoding of Variables**

The 7 doctor-parent relationship variables used to test the model in Chapter 10 include:

- **Trust Scale**
- **Decision-Making Preference**
- **Total Shared Decision-Making**
- **Parent Directed Decision by Parent Report**
- **Doctor Directed Decision by Parent Report**
- **Parent Directed Decision by Doctor Report**
- **Doctor Directed Decision by Doctor Report**

The last 4 variables are dichotomous, and the first three were recoded into dichotomous variables for analyses conducted to test the model in Chapter 10. **Trust** was recoded into lower trust (<=97, N=57, 52.8%) and higher trust (>97, N=51, 47.2%). **Decision-Making Preference** was recoded to doctor decides (N = 33, 30.6%) and shared/parent decides (N = 75, 69.4%). **Total Shared Decision-Making** was divided into <=1 (N=53, 49.1%) or >1 (N=55, 50.9%) instance of shared decision-making.

127
Chapter 7: Clinician Factors: Physician Recommendation

The physician's recommendation of the trial, and the particular language used in doing so, can have a powerful influence on parental decision-making, as is evidenced by the following discussion during an ICC:

Doctor: "I think it's a wise decision. I really believe in these studies."

Mom: "If you recommend it, then I've got to go with that. Why don't we just start it? I want to just start it, so where do I sign?" (LA-07)

Most Strongly Recommended Treatment Option

The physician's recommendation of the trial was evaluated in a number of ways. First, parents were asked the question “Which treatment option did the doctor most strongly recommend for your child?” The parallel question that was asked of physicians in the Case Specific Clinician Questionnaire was “What treatment options did you recommend most strongly for this patient?” The three response categories analyzed for this dissertation and the frequency with which each was cited by parents and clinicians are shown in Table 13 below.

Table 13: Parent and Physician Views of the Most Strongly Recommended Treatment Option

<table>
<thead>
<tr>
<th>Respondent</th>
<th>Most Strongly Recommended Treatment Option</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trial</td>
</tr>
<tr>
<td>Parents</td>
<td>33 (31%)</td>
</tr>
<tr>
<td>Doctor</td>
<td>78 (72%)</td>
</tr>
</tbody>
</table>
The table shows that doctors listed the trial as the most strongly recommended option more often than parents, while parents more frequently said that no recommendation was made. A chi-square test was performed to examine the relationship between doctors' and parents' reports that the trial was the most strongly recommended treatment, and the relationship between these two variables approaches significance ($X^2=3.8$, $p<.06$). In cases where the doctor says that (s)he most strongly recommended the trial, the parent is more likely to also say that the trial was the most strongly recommended treatment. These two variables, Trial Most Recommended by Parent Report and Trial Most Recommended by Doctor Report, were used in the analyses in Chapter 10.

Strength of Recommendation

The strength of the physician's recommendation of the trial was measured using a scale of 0 (very strongly) to 10 (not very strongly), and was rated by parents, clinicians, and the research associate (RA) who observed the ICC. Descriptive statistics for the three raters are shown in Table 14 below:

<table>
<thead>
<tr>
<th>Rater</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doctor</td>
<td>3.2</td>
<td>1.6</td>
<td>0 – 7.7</td>
</tr>
<tr>
<td>Parent</td>
<td>4.8</td>
<td>2.9</td>
<td>0 – 10.0</td>
</tr>
<tr>
<td>Research Associate</td>
<td>5.1</td>
<td>2.7</td>
<td>0 – 10.0</td>
</tr>
</tbody>
</table>
Parent, physician, and RA perceptions of the strength of recommendation were compared for each case using paired-samples t-tests. The mean score of 3.2 given by doctors was significantly lower (stronger) than the mean score of 4.8 given by parents ($t=6.2$, $p<.01$) and the mean score of 5.1 given by RAs ($t=8.2$, $p<.01$). The average score given by parents did not differ significantly from the mean score given by RAs ($t=.7$, $p<.50$). The three variables were all highly correlated with each other ($p<.01$). Thus, physicians tend to rate their recommendation of the trial as stronger than both parents and RAs. Only **Strength of Recommendation (Parent)** was used in the analyses described in Chapter 10.

**Physician Introduction and Recommendation of Trial**

The different ways that physicians introduce or recommend the clinical trial to families were categorized by analyzing the ICC transcripts. Every introduction and recommendation of the trial was extracted from the ICCs for all 108 cases. An exploration of the extracted text revealed three major categories into which the introductions and recommendations were divided: neutral presentation, implicit recommendation, and explicit recommendation. Each of these three categories was further coded for descriptive purposes based upon the actual language used by physicians in introducing or recommending the trial.
Neutral Presentation:

The first category contains neutral presentations or introductions of the trial. Text coded in this category generally represents discussions of the trial as one of multiple treatment options to choose among. There is no suggestion, implicit or explicit, in these discussions that the trial is a better option than any other or is preferred by the physician. Fifty-five (50.9%) ICCs had at least one neutral presentation of the trial. The total number of neutral presentations for all 108 ICCs was 94, with a mean of .9 (SD = 1.1) and range of 0 to 6. There were six different ways that physicians presented the trial neutrally in the ICCs, and each is defined by the actual words used by the physician. The subgroups are: 1) consideration, 2) discussion, 3) presentation, 4) eligibility, 5) choice, and 6) availability. Frequencies for each of these subgroups are shown in Table 15 below, and examples follow.

Table 15: Neutral Presentations of Trial

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Consideration</td>
<td>19</td>
</tr>
<tr>
<td>Discussion</td>
<td>18</td>
</tr>
<tr>
<td>Presentation</td>
<td>15</td>
</tr>
<tr>
<td>Eligibility</td>
<td>15</td>
</tr>
<tr>
<td>Choice</td>
<td>15</td>
</tr>
<tr>
<td>Availability</td>
<td>12</td>
</tr>
<tr>
<td>Total Neutral Presentations</td>
<td>94</td>
</tr>
</tbody>
</table>

Consideration

Statements coded in this category include presentations of the trial as something for the family to think about or consider. For instance:
Now what I did want to at least start to talk to you about, um, just before we stop for today, is the study, um, that I want you to think about." (CL-01)

"The treatment that we would...that I would present to you for your consideration is to have your daughter participate in a research study that we are doing." (HO-05)

Discussion

This category includes introductions of the trial as a topic for discussion. For example:

- "I want to talk to you today about a study that we're doing, comparing slightly different ways of giving the same medicines." (LA-02)

- "And I do have a study I would like to discuss with you." (LA-07)

Presentation

Physician statements of this type contain the words "present" or "offer", as in:

- "And as a part of this chemotherapy, I also like to present a study that is done nationally for children to you as well." (LA-36)

- "And since that time it's been common practice for every child newly diagnosed with leukemia to be offered enrollment in a similar clinical research study, and I'll talk to you about that in a minute." (PH-09)
Eligibility

These introductions of the trial involve an explanation of the patient's eligibility.

For instance:

- "I'm also going to give you the option of being enrolled on one of these Children's Oncology Group studies which you're actually eligible for." (CL-13)
- "And this particular study that C. is eligible for asks a couple of different questions." (PH-05)

Choice

Statements coded in this category are presented like a question for the family to answer, using words such as "whether" and "if". For example:

- "One thing you guys will need to consider in the next day is whether you'd like to have A. enrolled in a study like this." (CIN-04)
- "We're actually going to ask you if you want to be part of one of the national studies that's going on." (CL-01)

Availability

This type of statement focuses on the trial as one of the available treatment options. For instance:

- "Right now there is an open study for standard risk acute leukemia." (PH-13)
- "Currently we have a study going on around the country, at many different hospitals that treat kids." (LA-06)
Implicit Recommendation:

In contrast to the neutral presentations of the trial described above, discussions coded as an implicit recommendation of the trial contain language that suggests the trial is the best or physician-preferred option. These discussions are typified by presentation of the trial as the primary treatment option that parents need to consent to or actively refuse. Fifty-eight (53.7%) ICCs contained at least one implicit recommendation of the trial. The Total Implicit Recommendations for all 108 ICCs was 91, with a mean of .8 (SD = 1.0) and range of 0 to 5. This category has four subgroups which separate different implicit recommendations by the specific language used: 1) acceptance, 2) the norm, 3) endorsement, and 4) opportunity. Frequencies for each of these subgroups are shown in Table 16 below, and examples follow.

<table>
<thead>
<tr>
<th>Table 16: Implicit Recommendations of Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptance</td>
</tr>
<tr>
<td>The Norm</td>
</tr>
<tr>
<td>Endorsement</td>
</tr>
<tr>
<td>Opportunity</td>
</tr>
<tr>
<td>Total Implicit Recommendations</td>
</tr>
</tbody>
</table>

Acceptance

Physician statements about the trial that fit in this subgroup imply that the trial is what the physician prefers and the parents are being asked to accept it. For example:

- "I'll be asking you if you will allow her to participate in this national group, this national treatment study." (CL-20)
"And the purpose of this meeting is to see if, uh, if you would be willing to have S. entered on that study." (DC-01)

"So on this study, if you were to agree to enroll M. on it, he would have a 50% chance of either, from this period of time on, getting one medication into the spinal fluid or three." (LA-06)

**The Norm**

This type of implicit recommendation contains a hint of urging parents to go along with the norm. For instance:

- "And I will explain to you, when we treat children with leukemia, what we generally do is treat them under what's called a protocol. And what that means is a study." (DC-16)

- "...but I just want to let you know that most kids here do go onto studies." (PH-08)

- "It's standard medical practice to treat children with leukemia on national studies like this." (PH-13)

**Endorsement**

Recommendations in this category contain a suggestion of physician partiality to the trial through statements of support or backing of the trial. For example:

- "And from my standpoint, I would not offer you this if I did not believe in it." (CL-11)

- "I believe this is a good study. I believe it is an important study." (LA-02)
Opportunity

These implicit recommendations suggest that the trial is the best/superior option because they are framed using positive language. For instance:

- "You have an opportunity...B. has an opportunity to be on this new type of treatment, meaning that she would be part of a research study." (LA-30)
- "We're inviting you to participate in a national research study that seeks to increase our success rate further." (LA-34)
- "Every child with standard risk like her ALL will be offered the chance to participate." (PH-25)

Explicit Recommendation:

Explicit statements of recommendation were subdivided into 7 categories. Five of the categories of explicit recommendation were further separated into whether the physician made a recommendation for this particular child/family, or for children/families in general. One of the categories, Statement of Fact, is by definition framed for a particular child/family, and another category, I Would Participate, is best described as a general recommendation. Seventy-six (70.4%) ICCs had at least one explicit recommendation of the trial. The Total Explicit Recommendations for all 108 ICCs was 185, with a mean of 1.7 (SD = 2.1) and range of 0 to 13. The Total Explicit Recommendations for This Child was 124, with a mean of 1.2 (SD = 1.4) and range of 0 to 7. The Total Explicit Recommendations for All Children was 61, with a mean of .6 (SD = 1.0) and range of 0 to 6. The categories of explicit recommendation are: 1) best
treatment, 2) preference, 3) request, 4) recommend, 5) encourage, 6) statement of fact, and 7) I would participate. Frequencies for each of these subgroups are shown in Table 17 below, and examples follow.

<table>
<thead>
<tr>
<th></th>
<th>This Child</th>
<th>General</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Best Treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preference</td>
<td>23</td>
<td>14</td>
</tr>
<tr>
<td>This Child</td>
<td>35</td>
<td>12</td>
</tr>
<tr>
<td>General</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>Request</td>
<td>23</td>
<td>4</td>
</tr>
<tr>
<td>This Child</td>
<td>30</td>
<td>4</td>
</tr>
<tr>
<td>General</td>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td>Recommend</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>This Child</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>General</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Encourage</td>
<td>124</td>
<td>61</td>
</tr>
</tbody>
</table>

**Best Treatment**

This category includes unequivocal statements that the trial is the best option for this child or children with leukemia in general. For example:

- "I believe that your child has the best chance for cure by participating in this study." (HO-05)
- "It is our hope with this study to give your daughter the best possible treatment." (LA-17)
"I will tell you that I firmly believe that the therapy that's being offered on this protocol is the best possible therapy for standard risk leukemia."
(CIN-12)

"I think it's always optimal to get on the protocol. You know, that always has the best results."
(DC-06)

Preference

This type of explicit recommendation contains language indicating that the doctor would prefer it if the child (or children in general) is enrolled on the trial.

For instance:

"But we would love it if you would participate in the study." (CIN-12)

"One of the things that we would like to do is enroll M. on our most recent study of kids with leukemia." (CL-03)

"And it's not the end of the world, really. I mean, he doesn't have to be on study. It would be nice if he was on study." (LA-14)

"Now I feel, and we feel, very strongly that we would like all of our families to participate in these trials." (LA-01)

"And so the way that we like to treat kids with leukemia is to enroll them in studies, in research studies." (PH-23)

Request

This category includes explicit requests that the child participate in the trial, such as:
o "We will ask you to join Children’s Cancer Group and to participate in one of the studies." (CIN-05)

o "So one thing we would want to ask is that you participate in a study we’re doing right now on leukemia." (PH-08)

o "Children who are diagnosed with cancer, whether it’s leukemia or another kind of cancer, when we’re about to start therapy, the oncologist will sit down with the parents and ask them to participate.” (CIN-12)

o "We ask every family to participate in the research that we do here.” (PH-24)

**Recommend**

This category contains the most straightforward recommendations that utilize the word “recommend” or one of its synonyms, “propose”, “suggest” or “advise”, or state that the trial is what “should” be chosen. For example:

- “I think you should go on the study.” (LA-34)

- “About the study, my recommendation as one of E.’s physicians is to participate in the study.” (PH-10)

- “So what I’m gonna tell you about is how I would propose to treat him. It’s part of a clinical trial.” (PH-38)

- “We recommend that people go on these studies.” (CIN-04)

- “I think kids should go on studies because everything we’ve learned to date we’ve learned from these studies.” (LA-06)
Encourage

Unlike the 4 categories above, this group of recommendations is rarely made for a particular child, and is typically presented as urging all families to participate. For example:

- "I encourage the study more because I think your child's benefiting from children previously who were on study." (DC-13)
- "We really encourage people to join if they wish." (CIN-05)
- "We very much encourage all of our families to participate." (LA-01)

Statement of Fact

Eleven ICCs involved an unambiguous declaration by the physician that the child will be treated on a clinical trial. Although these ICCs all include a statement that the trial is voluntary at a later point, this first introduction of the trial gives the impression that it is the only option. For instance:

- "So the treatment we have is a study. It's a clinical study." (LA-13)
- "This protocol that we're putting you on, you'll learn all the numbers and all the jargon and everything, is Children's Cancer Group 1991." (PH-26)
I Would Participate

Fourteen instances of this type of recommendation were found in the 108 ICCs, and all but one of these were in response to a family question regarding what the physician would do in the same situation. For example:

- **Mom:** “If it was your baby, would you do it?”
  **Doctor:** “I can honestly say that I would participate in the study if it were my child.” (CIN-10)

- **Dad:** “If I were to ask you if you had your children, what would you say, knowing that you know exactly what kind of medication, this is what chances you would be. And of course I’m not going to base mine on yours, but you having the knowledge of this type of medication and stuff, where would you stand on that?”
  **Doctor:** “Well, it’s the most common question I get sitting across the table like this. And it’s a difficult question to answer because I would be in a very different frame of mind I think, but I would participate in the study.” (PH-09)

Family Requests for Recommendation:

As described in Chapter 6, 29 ICCs contained a family request for the doctor's recommendation, and there were a total of 36 such requests in these 29 ICCs. Fifteen (41.7%) of the 36 requests were in the “If it was your child, what would you do?” format. These 36 requests for a recommendation resulted in no recommendation from the physician in 14 (38.9%) instances. Interestingly, 8 of the 14 instances where the physician declined to give a recommendation when asked were preceded by unsolicited explicit recommendations during the ICC. Therefore, these physicians were reticent to provide a recommendation when
directly asked for one, but used language that explicitly recommended the trial elsewhere in the ICC. Six of the 14 instances where the physician declined to give a recommendation when asked were embedded in ICCs involving only neutral presentations of the trial, reflecting either the physician's lack of bias toward the trial or a disinclination to acknowledge their bias.

Physicians who did provide a recommendation when requested by the family sometimes made more than one statement of recommendation, giving an implicit recommendation in 2 instances, an explicit recommendation for children/families in general in 20 instances, and an explicit recommendation for this child/family in 10 instances. Of the 276 implicit and explicit statements of recommendation made by physicians, only 32 (11.6%) were in response to a family's request. Therefore, the vast majority (88.4%) of the recommendations were unsolicited.

Recommendation Score

A new variable, Recommendation Score, was created to measure the strength of recommendation based on the actual language used during the ICC. This score comes directly from the coding of the physicians' statements, as opposed to the more subjective assessment of the strength of recommendation provided by the analog ratings described above. Each of the 108 ICCs was given a recommendation score by assigning one point to each implicit recommendation, 2 points for each explicit recommendation made for children/families in general, and 3 points for each explicit recommendation made for the particular child.
Neutral presentations were not scored. The average \textit{Recommendation Score} for all ICCs was 5.4 (SD = 5.6), with a range of 0 to 34. Sixteen ICCs (14.8\%) had a \textit{Recommendation Score} of 0, representing a completely neutral presentation of the trial.

\textbf{Pressure}
An additional variable that relates to the physician’s recommendation is the amount of \textit{Pressure} parents felt to participate in the trial. Parents were asked the question \textit{“Did you feel that you were under any pressure to permit your child to enroll in the clinical research study?”} Eighty-five (78.7\%) parents reported feeling no pressure to participate in the trial, 19 (17.6\%) felt some pressure, and 4 (3.7\%) felt much pressure.

\textbf{Clinician Perspectives}
At the beginning of the larger project from which these data come, a General Clinician Questionnaire was mailed to all physicians, advanced practice nurses, and case managers in pediatric oncology at the institutions participating in the project (Simon, et al. 2001). Two items on the questionnaire provide evidence of physicians’ views on recommending the trial. First, clinicians were asked to choose one of 4 statements that best describes the way they approach informed consent discussions with parents. Table 18 below shows the percentage of clinicians who chose each of the 4 options. The first option relates to clinicians who reportedly provide a neutral presentation of the trial,
while the last option is associated with clinicians who say they provide an explicit recommendation of the trial.

Table 18: Clinician Self-Report of Approach to Informed Consent (N = 89)

<table>
<thead>
<tr>
<th>Approach to Informed Consent</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>I describe the CCG study without any attempt to influence their decision</td>
<td>21 (23.6%)</td>
</tr>
<tr>
<td>I tell families about the CCG study and suggest that their child will benefit from our knowledge based on previous studies</td>
<td>30 (33.7%)</td>
</tr>
<tr>
<td>I tell families about the CCG study and suggest that other children will benefit from what we learn in the current study</td>
<td>25 (28.1%)</td>
</tr>
<tr>
<td>I explain the disease and its treatment and recommend that the child go on the CCG study</td>
<td>13 (14.6%)</td>
</tr>
</tbody>
</table>

Clinicians were also asked to rank how directive they are in recommending a clinical trial using a five-point scale ranging from non-directive to very directive. Twenty-seven (30.3%) of clinicians rated themselves as non-directive or minimally directive, 37 (41.6%) reported being moderately directive, and 25 (28.1%) said they were more than moderately directive or very directive.

Examples From Focus Groups

During the focus groups, parents were asked the questions: Did your child's doctor recommend that your child participate in the research study? How strong was this recommendation? How much did the doctor's recommendation influence your decision about the research study? Our data show that some doctors strongly recommend to parents that they enroll their child in a research
study. What do you think about this? Do you think it is helpful to parents for
doctors to strongly recommend the research study?

Some parents discussed the influence that the doctor’s recommendation
could have on parental decision-making. For example:

- “If I think about it, if he had said go A, I would
  have gone straight to A. If he said go to B, I
  would have gone straight to B. Because at that
time he is the most knowledgeable person in front
of me…I don’t know if it’s because it is such a
shock. I know that’s what we would have done.
Because if he had said, ‘This is what we are going
do’, we’d have said, ‘Go for it.’” (1st Cincinnati
focus group)

- “I just kind of signed because, on the other hand,
  we were getting such good treatment and the
whole system was working so well that you don’t
want to disappoint these folks. And I didn’t feel at
all pushed. There was no pressure on me
whateversever except that, you know, these guys –
you’re going to be in a relationship from now on,
and you know this is going to go on for about a
year or a year and a half, and you got to be
friends with these people. And they’re not telling
you anything—it’s not like the cop calling on your
door ‘Do you want to donate to the policeman
retirement?’ No, but it went through my mind…”
(1st Washington DC focus group)

Some parents reported that their child’s physician had presented the trial in a
neutral manner. For example:

- “I think he was pretty neutral about it. He didn’t
  say you do it or not do it. And, again, I assumed it
was all the lawsuits in this country. No one wants
to say you should do it, and it doesn’t work, and
then you sue them. So we just assumed they are
going to be non-committal, and it’s up to us to
make the decision. And they just gave you the
information that you need in order to make the
decision.” (1st Los Angeles focus group)
"I felt like the doctors went out of their way not to push it down our throats. I really felt like it was like our decision... They said, 'You can do this, but you don’t have to do this. He'll still get the best of care no matter...' He never said, 'This is the best thing.' It was clearly our decision." (1st Cincinnati focus group)

Other statements by parents during the focus groups referred to the physician’s implicit recommendation of the trial. Some parents felt that the presentation of the trial is in itself an implicit recommendation, while others pointed out the implied recommendation resulting from the time spent on discussion of the trial or the positive framing of the trial. For instance:

- "If they didn’t think she was a good candidate for it, then they wouldn’t have told us about it." (1st Philadelphia focus group)

- "First of all, we went in for a family meeting, before we started talking, they handed out that clinical trial, and they said, 'Here, we are going to go for this.' And that is what they used. That is what they based everything on. Then when they were done, they said you could choose not to do this, but it was after an hour of them talking about this clinical trial." (2nd Philadelphia focus group)

- "Well, when we sat with the doctors, they weren’t pushing the study at all. They talked more about the study than not so it seemed ...so in that sense, they were pushing for me to enroll my child in the study." (3rd Philadelphia focus group)

- "I think it was more the way they presented it in a positive way. It wasn’t like selling anything. You can do it positively or negatively, and I think it was all presented in a positive way." (2nd Washington DC focus group)

Several parents shared their view that the trial had been explicitly recommended by the physician, as in the following statements:
"They told me that they wanted her to be part of a study." (1st Philadelphia focus group)

"The doctor recommended her to go...That is the reason I took it. Because I said, 'I don't know anything about this.' Because to me it was like something that didn't exist, or if it happened it only happened in soap operas or in the movies. And the female doctor, she told me that she recommended that one. That it was going to be the best one. And I told her that well, she was the one who knew more. And then I left it at that. And for that reason my daughter is here. Because she recommended it." (2nd Los Angeles focus group)

"The doctor recommended it—he said this is really a very good thing to participate." (1st Washington DC focus group)

One parent commented on his child’s doctor not giving a recommendation after he had requested one. While this father thinks that the doctor should share their opinion of the trial, he understands that it might be difficult for physicians to do so:

"And if they have a gut feeling, they need to share it...I would ask these doctors that I happen to know, ‘What would you do for your own child?’ And it was amazing to see them not know. They couldn’t answer because they are scientists, but once you turn them into parents, they’re just as stuck as we were. And rightfully so. The reason we can’t deal with these things that are hard is because they are hard." (2nd Philadelphia focus group)

Parent Perspectives: PAGIC

Several discussions during the PAGIC meeting provide insight into parent perspectives of the physician’s recommendation. During the PAGIC meeting,
parents listened to examples of the audiotaped ICCs in 3 small groups. After
discussing the different examples in the smaller groups, a spokesperson from
each group presented the group’s views and suggestions to the rest of the
meeting participants. These parents’ thoughts about the physician’s
recommendation are illustrated in the excerpts from the PAGIC meeting below.

There was general agreement among the 9 parents at the meeting that
the physician’s offer or presentation of the trial is in itself an implicit
recommendation of the trial:

- “And this whole question of a passive or implicit
recommendation of the study – why would they
even bring this up unless they thought it was best
for their health? So maybe in our interpretation of
the data here, we coded 38% of these actual
explicit recommendations, but someone could
look at this and say, ‘Well any kind of doctor that
brings up a study, they’re implying that this is
good.’”

- “But let me go back to you and try to say, by virtue
of the fact that the study is being described and
being discussed, when the clinicians bring it up at
all, the thing speaks for itself. That is the degree
of recommendation that is appropriate, and if you
go any more than that, you’re on the risk of it
being perceived as being too pushy. So my
answer to that is that if the doctor doesn’t want to
recommend the study in that gentle way, he
shouldn’t be talking about it at all.”

The parents strongly advocated against the physician giving an explicit
recommendation unless they are specifically asked for one by the parents.

Importantly, the PAGIC members also stated that physicians who are directly
asked for a recommendation should always give one:
o "And we also felt that the recommendation was coercive [in the taped example]. And P., you brought it up that the fact that it's okay for the doctor to make a recommendation, but only if the parent asks for it. And she said what they did was they actually said, 'If this was your child what would you do?' And I asked the group, 'What if the doctor declined to answer that question and said I can't answer that?' And everyone said that they would expect an answer because they're relying on this expert to give them advice and say, 'My recommendation is that you get it.' But if the clinician says they aren't comfortable answering it, they need to say why they aren't comfortable answering the question."

o "I think the more interesting thing is something that we said in our group too is it's a really subtle but really important difference here - this idea that the doctor should present the study and should not, should refrain...I think everyone is saying doctors should not be making a recommendation, but they should be good listeners, and if the parent asks for a recommendation, then they darn well better be prepared to make a recommendation."

o "As far as recommendations, as you all mentioned, some of our group didn't want the recommendations. They thought that was pushy in itself, unless it was asked for, like you said."

Recoding of Variables

The 9 recommendation variables used to test the model in Chapter 10 include:

- Trial Most Recommended by Parent Report
- Trial Most Recommended by Doctor Report
- Pressure
- Strength of Recommendation (Parent)
- Recommendation Score
- Total Implicit Recommendations
- Total Explicit Recommendations for This Child
- Total Explicit Recommendations for All Children
- Total Explicit Recommendations
The continuous variables were recoded into dichotomous variables for analyses conducted to test the model in Chapter 10. *Pressure* was recoded into no pressure (N=85, 78.7%) versus some or much pressure (N=23, 21.3%). *Strength of Recommendation (Parent)* was recoded into a dichotomous variable, with a more strong recommendation defined as \( \leq 5.0 \) (N=61, 56.5%), and a less strong recommendation defined as \( >5.0 \) (N=47, 43.5%). The *Recommendation Score* was recoded into low (\( \leq 4 \), N=62, 57.4%) and high (\( >4 \), N=46, 42.6%) scores. *Total Implicit Recommendations* was divided into none (N=50, 46.3%) or \( \geq 1 \) (N=58, 53.7%). *Total Explicit Recommendations for This Child* was separated into none (N=43, 39.8%) or \( \geq 1 \) (N=65, 60.2%). *Total Explicit Recommendations for All Children* was grouped into none (N=73, 67.6%) and \( \geq 1 \) (N=35, 32.4%). Finally, *Total Explicit Recommendations* was recoded into \( \leq 1 \) (N=68, 63.0%) versus \( >1 \) (N=40, 37.0%).
Chapter 8: Clinician Factors: Presentation of Benefits

The physician's explanation of the clinical trial, including the risks and benefits of participation, is the primary way in which parents learn about the trial. Given the limited time frame for decision-making, it may be the only avenue for information gathering for some parents, as expressed by one father during the ICC:

- "We can't get on the internet and do research, so we have to listen to what you're saying." (CIN-08)

The purpose of this chapter is to describe how doctors presented the benefits of the trial. The physician's presentation of risk will follow in Chapter 9. The physician's presentation of two major types of benefit during the ICC was analyzed: direct benefit and altruism.

Direct Benefit

In the General Clinician Questionnaire sent to all pediatric oncology clinicians at the research sites, 75 (84.3%) of the clinicians who returned the questionnaire responded affirmatively to the question, "Do you believe that current patients receive direct benefit from participation in CCG studies?" (Simon, et al. 2001). In order to examine whether and how this prominent belief is expressed when presenting a trial to parents, a content analysis of the ICCs was conducted, focusing on direct benefit discussion. First, all discussions of direct benefit were extracted from the ICC transcripts. For this analysis, discussions of improving the cure rate as the rationale for conducting trials were excluded. A total of 325 discussions of direct benefit (Total Direct Benefit) were found in
the 108 ICCs, with a mean of 3.0 (SD = 2.6) and range of 0 to 16. Fifteen (13.9%) ICCs contained no mention of direct benefit from trial participation.

These discussions were then grouped according to whether the physician's statement made reference to benefit for this particular child or presented benefit more generally. Both of these groups were further coded for descriptive purposes based upon the actual language used by physicians in presenting the benefits of the trial.

**Direct Benefit – This Child**

This category contains discussion of the benefits of trial participation, with specific reference made to the particular child. The total number of direct benefit discussions referring to the particular child (Total Direct Benefit – This Child) for all 108 ICCs was 91, with a mean of .8 (SD = 1.3) and range of 0 to 7. Sixty-two (57.4%) ICCs had no discussion of direct benefit to the particular child. There were three different ways that physicians presented direct benefit for the particular child in the ICCs. The 3 subgroups are: 1) chance of benefit from trial overall, 2) chance of benefit from one arm of trial, and 3) best chance of cure. Frequencies for each of these subgroups are shown in Table 19 below, and examples follow.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chance of Benefit Overall</td>
<td>43</td>
</tr>
<tr>
<td>Chance of Benefit One Arm of Trial</td>
<td>40</td>
</tr>
<tr>
<td>Best Chance of Cure</td>
<td>8</td>
</tr>
<tr>
<td>Total Direct Benefit – This Child</td>
<td>91</td>
</tr>
</tbody>
</table>

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**Chance of Benefit from Trial Overall:**

The most common way that physicians discussed benefit to the particular child was in reference to the chance of benefit from participating in the trial as a whole, with no mention of a particular arm of the trial. For example:

- "This way you have the chance of getting a therapy that might be more beneficial." (CIN-10)
- "The study may help her." (LA-21)
- "I think it gives potential benefit to your daughter." (PH-21)

**Chance of Benefit from One Arm of Trial:**

Statements in this category mention potential benefit to the child from treatment on a particular arm of the trial. For instance:

- "She may by luck get assigned to one of these that proves a better cure rate over the standard." (CIN-09)
- "The additional changes in chemotherapy do offer some potential benefits. It could be the addition of a couple extra drugs may be what N. needs." (CL-16)
- "The potential benefit to C. for participating in this study would be if she was randomized or assigned to the triple intrathecal arm and it proved to be better and it prevented a relapse." (PH-09)
**Best Chance of Cure:**

This category was infrequently coded (N = 8 discussions) and includes unconditional statements that the trial provides this child with the best possible chance of being cured. For instance:

- "We do think that this offers her the absolute best chance of survival, now in the immediate and the next few months and long term." (PH-27)

In addition to the three categories described above, there were 32 explicit statements by physicians that the particular child will **not** benefit from participation in the trial. For example:

- "Will my child benefit from this study? The answer is ‘no’. We won’t tabulate the data until later.” (CIN-12)

- "There is no advantage to L. to going on the study. I mean, there’s no advantage. He’s only one kid. Um, one kid is either gonna survive or not survive. It’s either 100% or 0%. And as one family liked to think of it, you know, basically these treatments are the same, and they’re either gonna work or not work. And for my child there’s very little chance that even if he gets the experimental arm, that there’d be a survival advantage for that ‘cause he was probably gonna make it anyway. So there is no advantage." (CL-02)

**Direct Benefit – General**

Physicians more commonly discussed direct benefit by framing their statements generally. Although benefit to the child is implied in the statements coded in this category, specific reference to the particular child is not made. The total number of general direct benefit discussions (**Total Direct Benefit – General**)
for all 108 ICCs was 234, with a mean of 2.2 (SD = 2.1) and range of 0 to 14.

Twenty-five (23.1%) ICCs had no discussion of direct benefit framed generally. There were five different ways that physicians presented direct benefit generally in the ICCs. The 5 subgroups are: 1) chance of benefit from trial overall, 2) chance of benefit from one arm of trial, 3) best available therapy, 4) inclusion benefit, and 5) better monitoring. The first 3 categories are parallel to the three categories in the Direct Benefit – This Child group, but differ in their lack of reference to the particular child. Frequencies for each of these subgroups are shown in Table 20 below, and examples follow.

<table>
<thead>
<tr>
<th>Table 20: Direct Benefit – General</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chance of Benefit from Trial Overall</td>
</tr>
<tr>
<td>Chance of Benefit from One Arm of Trial</td>
</tr>
<tr>
<td>Best Available Therapy</td>
</tr>
<tr>
<td>Inclusion Benefit</td>
</tr>
<tr>
<td>Better Monitoring</td>
</tr>
<tr>
<td>Total Direct Benefit – General</td>
</tr>
</tbody>
</table>

*Chance of Benefit from Trial Overall:*

This category is the most common and is analogous to the first category with the same title in the Direct Benefit – This Child group. It includes statements that the trial or any of its arms could be better than standard treatment, such as:

- "These new therapies may give patients a better chance." (CIN-02)
- "I think it has the chance to be more efficacious." (CL-17)
"With the newer treatment we're really hoping that we'll have a better outcome than what we had just with the standard." (DC-19)

"This new treatment may have benefits. The new plan may turn out to be better in treating AML in the long run than the treatments that we've used in the past." (PH-06)

**Chance of Benefit from One Arm of Trial:**

As with the corresponding category of the same name in the Direct Benefit – This Child group, this category contains discussions about a particular arm of the trial being better than standard therapy:

- "There's some evidence that the 6TG might work slightly better." (CIN-04)

- "So it's [arm D of trial] longer and it's tougher and, you know, potentially has a better chance of cure. I think that, you know, it makes sense that if you give more intense treatment and you give longer treatment, the chance of the leukemia coming back is going to be lower." (CL-13)

- "But we think maybe this one, the idarubicin, may be a little bit more effective than the doxorubicin." (LA-16)

**Best Therapy Available:**

Like the Best Chance of Cure category in the Direct Benefit – This Child group, this category includes unqualified statements that the trial offers the best treatment. For example:

- "The benefits of the protocol is, you know, that it certainly is the very best treatment we have to offer." (CIN-05)
o “And it’s considered to be the best possible therapy for standard risk leukemia.” (CIN-12)

*Inclusion Benefit:*

The inclusion benefit category contains statements that children who are on a clinical trial do better than children who are not on a clinical trial, regardless of the particular trial or treatment received within the trial. Only eleven such statements were made in the 108 ICCs, including:

o “It’s known that children do better on protocols than not on protocols. For whatever reason. It’s probably because everything is followed right to the letter on a protocol. The success rate is better for children on protocols than not on protocols – on studies, protocols.” (DC-06)

o “Historically, when we compare the survival results for children who are on research studies versus a similar group of children who are treated not on research studies, there is sometimes a slight advantage for children who are on research studies. I have never been able to understand why that happens, but it is a statistical fact. So, for whatever reason, being on a research study may afford a slightly better chance of doing well.” (PH-04)

*Better Monitoring:*

This category was infrequently coded (N=7 discussions) and includes statements concerning the benefit of being watched more closely when participating in the trial. For instance:
"I think, and we think, there are advantages to being on the study 'cause we think that a kid on a study is followed more closely than kids off of the study, and we think that's true no matter what hospital you're in in the country." (PH-42)

Altruism

All discussions during the ICC regarding altruism as a reason for participating in the clinical trial were extracted from the transcripts for coding. For this analysis, discussion of altruism was considered to be "any mention of benefit to others through this patient's participation in the trial." Discussions of altruism that were not related to participation in the trial were excluded from the analyses. Therefore, discussions of altruism related to consenting to banking tissue samples or participating in non-clinical research were not included. Eighty-four (77.8%) of the 108 ICCs had some discussion of altruism. In these 84 ICCs, there were a total of 157 discrete discussions of altruism (Total Altruism Discussions). Thirty-two (20.3%) of the 157 discrete discussions of altruism were initiated by a family member. The mean number of altruism discussions in the 108 ICCs was 1.5 (SD = 1.3), with a range of 0 to 6.

The altruism discussions were then examined for any defining categories. The altruism discussions contained mention of a variety of recipients of benefit from the patient's participation in the trial. Many discussions of altruism included reference to multiple recipients of benefit from the family's altruistic behavior, and every recipient was categorized for each discrete discussion. Multiple references to the same recipient in one discrete
discussion were only counted once. The total number of recipients mentioned in the 108 ICCs was 377 (Total Altruism Recipients), with a mean of 3.5 (SD = 3.4), and range of 0 to 13.

Seven categories of recipients developed from the data: 1) doctors/researchers, 2) science/progress, 3) treatment/cure, 4) future patients/children, 5) other patients/children, 6) like your child, and 7) unspecified others. The “unspecified others” category included reference to vague recipients like “others” and the “future”. The 20 recipients coded in this category were excluded from further analyses because of their ambiguity. The remaining six categories of recipients were divided into two major domains: other patients/children and clinicians/science. Frequencies for each of categories are shown in Table 21 below, and examples follow.

Table 21: Recipient Categories

<table>
<thead>
<tr>
<th>Recipient Domain</th>
<th>Recipient Category</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinicians/Science</td>
<td>Doctors/Researchers</td>
<td>105</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>Science/Progress</td>
<td>91</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>Treatment/Cure</td>
<td>68</td>
<td>19</td>
</tr>
<tr>
<td>Other Patients/Children</td>
<td>Future Patients/Children</td>
<td>66</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Other Patients/Children</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Like Your Child</td>
<td>7</td>
<td>2</td>
</tr>
</tbody>
</table>

Clinicians/Science Recipients

Two hundred sixty four (73.9%) of the 357 recipients mentioned during the ICCs fell into the clinicians/science domain. Many discussions included several
recipients from this domain, therefore the examples below show the recipients for each particular category in bold.

**Doctors/Researchers**

This category is the most commonly coded and includes any reference by the physician to him/herself as a recipient of benefit from the patient’s participation in the trial. This self-reference is in some cases explicit (“I”), and in other cases expanded to include the group to which the physician belongs (“us”, “we”, “doctors”, “researchers”):

- “It gives us increased knowledge.” (CIN-02)
- “What I get from the study is that I get to help advance our knowledge.” (CL-15)
- “But the information that D. can give to us, to the group of scientists studying childhood leukemia, is information that for children that come after D., that we’ll be able to say, ‘Well, your cure rate is 90%.'” (CIN-13)

**Science/Progress**

The “Science/Knowledge” category includes any reference to the advancement of science, contribution to knowledge, provision of information, or improvement of understanding as a result of the patient’s participation in the trial. For instance:

- “It’s his contribution to science.” (CIN-13)
- “But we’re confident, we’re convinced that it will help us advance in the science.” (PH-09)
"It would be nice if he was on study because we would gain a lot of information." (LA-14)

**Treatment/Cure**

This category includes any mention of an increased cure rate or improved treatment as a result of the patient's participation in the trial. Some illustrative examples include:

- "And the major benefit is to learn more about better ways to treat leukemia." (CIN-05)
- "...to improve our results, so that we get better, you know, so that we, uh, next time we can say 'over 90%, over 95%'." (DC-13)
- "So this isn’t a study that’s gonna tell us with A. whether or not she’s gonna do better getting one thing or another thing, but it’s gonna tell us down the road what is the best treatment in the year 2004." (PH-42)

**Other Patients/Children Recipients**

Only 26.1% (N = 93) of the 357 recipients mentioned during the ICCs fell into the other patients/children domain.

**Future Patients/Children**

The "Future Patients/Children" category includes any reference to future patients, children, or families as the recipient of benefit from the patient's participation in the trial. For instance:
"So the only reason for participating in the study is to help other kids who will be diagnosed 6, 7, 8, 9, 10 years from now with their leukemia so they'll be able to get better therapy at that time." (CL-03)

"Allowing her to be part of the study will help us to understand and help children in the future." (LA-16)

Other Patients/Children

The "Other Patients/Children" category includes any reference to other patients or children as the recipient of benefit from the patient's trial participation. For example:

"And when she completes the whole course of therapy, the information on how she responded will then help all of the other children." (LA-01)

"This has a potentially major impact. It's what we do for other kids." (LA-18)

Like Your Child

The "Like Your Child" category includes any reference to the recipient of benefit from the patient's trial participation being "like" the patient or having the same type of cancer/leukemia. For instance:

"But I believe these are very important questions to help the next generation of children with the same type of leukemia that your daughter has." (LA-02)
“Well, the only reason that we encourage people to go on our studies is so that we can get enough information from 1000 children across the world so that when a patient like A. comes along 5 or 10 years from now...that that child 5 or 10 years from now will be able to benefit from the information that A. participated in.” (CL-08)

Other Content of Altruism Discussion

In the 108 ICCs, there were 15 discussions that referred to the patient benefiting from the past altruistic behavior of others. For example, one physician said:

- “I encourage the study more because I think your child’s benefitting from children previously who were on study.” (DC-13)

Eight of the altruism discussions included a value judgment that related to altruistic behavior, 5 of which were introduced by a family member. Positive judgments of participating in research used the terms “good” and “compassionate”, while negative judgments of not participating in research used the term “selfish”. For instance:

- “I’m saying in trying to be compassionate for others, we would like to have our son involved in something that would help others.” (CIN-16)

- “Yes [we will participate in the study]. I think it will be too selfish if not. It’s a good thing I’m not selfish.” (LA-01)
Examples From Focus Groups

During the focus groups, parents were prompted to talk about their perceptions of the benefits of trial participation and how these benefits may have influenced their decision-making. Many parents discussed the chance of direct benefit to their child from participation in the trial. For example:

- "If it will make him better, a little bit better, his odds a little bit better, we felt we had a little bit better chance to make him better, we had to grab it. That was it!" (2nd Philadelphia focus group)

- "It seems to me, or my perception of it, is that it's cut and dried. Either you want a little bit better for your kid or you want the same. And that was the way I perceived it as being presented at that point...That in and of itself, you want the best for your kid, and there's only two choices here: the best or the same. You know, a little bit better and the same." (2nd Philadelphia focus group)

- "And there was one thing about the study that really did push my husband over the edge. It was when a child is in the study, they are watched more closely." (3rd Philadelphia focus group)

- "I think everybody in here said the same thing. You want to be sure your child, first and foremost, is going to get the treatment. Everybody likes to know that they are part of some sort of ability to help other people, but first things come first, and that's your child's health and that's your child's cure." (1st Cleveland focus group)

- "But the reason why we made the decision of going with the treatment was because the probability to have a better outcome was higher." (1st Washington DC focus group)

Altruism was another common topic of conversation during the focus groups, with parents making statements such as:
"I thought if being on this study will help other kids...if, God forbid, I should lose my daughter to this dreaded disease, being on this study will help children in the future. And that's something that our family has always been real big on as far as helping others." (1st Philadelphia focus group)

"In twenty years, I want a child with the same thing as my daughter to be cured and not have to go through all that my daughter is going through. Twenty years ago if a child had not done a study, they would not know what they know today. So I felt that it benefited other children. Twenty years, fifty years from now, but eventually it will benefit another child." (3rd Philadelphia focus group)

"I thought about the future. I kept saying, 'You know what? If some parent wasn't unselfish twenty years ago then they wouldn't even know these three different arms that they have now to help, so I want to help somebody else.' I just kept thinking that's my grandchildren I may be helping one day. I was thinking about I would never want T. to feel the way me and my husband felt at that time if his child was going through that." (3rd Philadelphia focus group)

"So we just really felt like it was almost our duty to repay all the people who did that for us to give N. such a chance to live. We just felt it was the right thing to do." (2nd Cleveland focus group)

"I remember thinking if we choose the different treatment options under this protocol, then something good is going to come out of this illness, and it can help other kids. And that was very, very important to me. The idea of bringing good out of evil is so important." (1st Cincinnati focus group)

In response to other parents' reports of altruistic reasons for participating in the trial, some parents very honestly stated that benefit to other children was not something that factored into their decision-making. For these parents, the
effect of trial participation on their child was the only or primary consideration.

For instance:

- “And I guess I feel guilty or ashamed, but I guess the bottom line is I was going to do what was best for my son. And I gave that consideration in absolutely no way. And I admire and take my hat off to people who gave credit to that, but to tell you the truth, at that moment, I could have cared less about the rest of the world.” (2nd Philadelphia focus group)

- “I hear you guys, and I’m amazed that you’re thinking ahead ten years and how it will affect other people. To be quite honest, I wasn’t thinking about anyone else but my child. I was just thinking about my child. How is this going to affect my child?” (3rd Philadelphia focus group)

- “I didn’t even think about other children. I may have been selfish, but I was really...We were just devastated because nothing like this ever happens to you. It happens to other people. And I just didn’t think about other children. I was thinking about my child.” (1st Cincinnati focus group)

Recoding of Variables

The 7 presentation of benefit variables used to test the model in Chapter 10 include:

- Total Direct Benefit – This Child
- Total Direct Benefit – General
- Total Direct Benefit
- Total Altruism Discussions
- Total Clinicians/Science Recipients
- Total Other Patients/Children Recipients
- Total Altruism Recipients
For analyses conducted to test the model in Chapter 10, these 7 variables were recoded into dichotomous variables. *Total Direct Benefit – This Child* was separated into no mention of direct benefit for this child (N=62, 57.4%) versus at least one mention of direct benefit for this child (N = 46, 42.6%). *Total Direct Benefit – General* was divided into <=1 mention of direct benefit framed generally (N=47, 43.5%) and >1 mention of direct benefit framed generally (N=61, 56.5%). *Total Direct Benefit* was grouped into <=2 statements about direct benefit (N=53, 49.1%) and >2 statements about direct benefit (N=55, 50.9%). *Total Altruism Discussions* was separated into <=1 altruism discussion (N=67, 62.0%) versus >1 altruism discussion (N=41, 38.0%). *Total Clinicians/Science Recipients* was divided into <=1 reference to a clinicians/science recipient (N=48, 44.4%) and >1 reference to a clinicians/science recipient (N=60, 55.6%). *Total Other Patients/Children Recipients* was grouped into no references to other patients/children recipients (N=53, 49.1%) and at least 1 reference to other patients/children recipients (N=55, 50.9%). Finally, *Total Altruism Recipients* was separated into <=2 recipients mentioned (N=52, 48.1%) versus >2 recipients mentioned (N=56, 51.9%).
Chapter 9: Clinician Factors: Presentation of Risks

The purpose of this chapter is to describe how doctors present the risks of participation in the trial. It is important to point out that the physician's presentation of the risks of the trial includes discussion of the lack of risk, or safety, of the trial. Therefore, this analysis encompasses discussions during the ICC about increased risk from participation in the trial, as well as statements about minimization of risk in the trial.

Many aspects of the risks of the trial were covered by physicians during the ICC, including increased toxicity, decreased cure rate, uncertainty, similarity to standard, experimental nature, and mechanisms of oversight and control. Discussions of all these facets of risk involve either an implicit or explicit comparison to standard treatment or the standard arm of the trial. There are many risks associated with chemotherapy of any kind, therefore physicians' presentation of the risks of the trial necessarily compare the risks of the trial to the risks of standard treatment rather than using a baseline of no risk for comparison.

Increased Toxicity

All physician statements about an increased risk of side effects were extracted from the ICC transcripts for coding, including discussion of increased side effects from participation in the trial in general, from receiving treatment on a particular arm of the trial, or from administration of a particular chemotherapeutic agent that is specific to the experimental arms of the trial.
Increased toxicity was further divided into two categories: possible and unlikely. The *Increased Toxicity – Possible* category includes statements indicating that there is a chance of more side effects on the trial or on a specific arm of the trial. The *Increased Toxicity – Unlikely* category contains statements that there are not more side effects on the trial, on a specific arm of the trial, or with a particular chemotherapeutic agent. Every mention of increased toxicity was counted for each ICC. Frequencies for these two toxicity categories are shown in Table 22 below, and examples of each follow.

### Table 22: Increased Toxicity Discussions

<table>
<thead>
<tr>
<th>Increased Toxicity – Possible</th>
<th>467</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased Toxicity – Unlikely</td>
<td>63</td>
</tr>
<tr>
<td>Total Increased Toxicity Disc.</td>
<td>530</td>
</tr>
</tbody>
</table>

*Increased Toxicity – Possible*

The majority of the discussions about increased toxicity were coded in this category (N=467, 88.1%). The average number of *Increased Toxicity – Possible* statements for the 108 ICCs was 4.3 (SD = 5.3), with a range of 0 to 26. Thirty (27.8%) of the 108 ICCs had no discussions about the possibility of increased toxicity from participation in the trial. Some physician statements from this category indicate a chance for more side effects on the trial. For example:

- "The risk is that the more chemotherapy you give, you get more toxicity. So you get more side effects. And so that would be a very legitimate reason for you to say that you're not comfortable with your child going on the study because that is the risk." (CIN-13)
"Almost for sure giving three drugs instead of one in the spinal fluid has the potential for creating additional side effects." (CL-06)

"These treatments may have more side effects because they are longer and more intense." (LA-20)

"The risk of participating in this research study in terms of this question is that there would be a side effect with the Ara-C or the hydrocortisone that C. could have that she would not be exposed to if she goes on the standard treatment arm." (PH-09)

"And with every small change in chemotherapy, there's also a risk of a new side effect or additional side effects." (PH-32)

Other physician statements in this category mention a higher chance of experiencing a particular side effect in the trial. For instance:

"They [stronger arms of trial] have more risks because there are more side effects to these stronger medicines. The kids, quote, go through more. I mean, they'll have periods of mouth sores, low counts, fevers." (CIN-09)

"Now what's the drawback of going on one of those more intensive arms? The drawback is that it's more therapy. So there's more chance for side effects from the therapy. More chances for being hospitalized with fever, low blood counts on those arms." (DC-16)

"When the methotrexate is given IV, it tends to have more side effects in terms of causing nausea and affecting the liver. It can also cause more problems with ulcers." (LA-30)
“The theoretic risk – again, the theoretic risk to E. is that he would have a bad reaction to the 6TG that he would never have seen with the 6MP. So the side effects are the things that we’ve already talked about: low blood counts, depression of the immune system, very very rarely it can irritate the liver and cause inflammation of the liver. So there’s a chance that 6TG for whatever reason would be more powerful in inducing that in E. if he was randomized to that arm.” (PH-10)

**Increased Toxicity – Unlikely**

Only 11.9% (N=63) of the discussions about increased toxicity were coded in this category. Physician statements coded in this category provide assurance of the safety of the trial by indicating that there are not increased side effects associated with the trial, a particular arm of the trial, or a specific chemotherapeutic agent. The average number of *Increased Toxicity – Unlikely* statements for the 108 ICCs was .6 (SD = 1.1), with a range of 0 to 7. Seventy-five (69.4%) of the 108 ICCs had no discussions about the lack of increased toxicity from participation in the trial. Statements from this category that refer to the safety of the trial in general include:

- “There’s no harm.” (CIN-03)
- “Overall, the level of toxicity between all the protocol arms should be, is, you know, pretty standard.” (CL-07)
- “It’s not gonna hurt her.” (DC-01)
- “I think that it’s safe.” (PH-10)

Physicians also made statements about the lack of increased risk of a particular side effect, such as:
"We don’t have any information that these patients are more at risk than these patients are for a long-term heart problem." (LA-29)

**Decreased Cure Rate**

Two categories relating to the risk of a lower cure rate on the trial developed from the data. As with the toxicity categories above, the *Decreased Cure Rate — Possible* category includes any mention that there is the potential for a decreased cure rate. The *Decreased Cure Rate — Unlikely* category includes unequivocal statements that the trial will be at least as good as standard therapy, as well as statements declaring it very improbable that the trial would be worse than standard. Every mention of a lower cure rate on the trial was counted for each ICC. In contrast to discussions of increased toxicity, statements of the possible chance for a lower cure rate on the trial were much less common than statements that a lower cure rate is unlikely. Frequencies for the two decreased cure rate categories are shown in Table 23 below, and examples of each follow.

<table>
<thead>
<tr>
<th>Table 23: Decreased Cure Rate Discussions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decreased Cure Rate — Possible</strong></td>
</tr>
<tr>
<td><strong>Decreased Cure Rate — Unlikely</strong></td>
</tr>
<tr>
<td><strong>Total Decreased Cure Rate Discussions</strong></td>
</tr>
</tbody>
</table>

**Decreased Cure Rate — Possible**

Only 13.5% (N=15) of the discussions about a decreased cure rate were coded in this category. The average number of *Decreased Cure Rate — Possible* statements for the 108 ICCs was .1 (SD = .4), with a range of 0 to 2. Ninety-
four (87.0%) of the 108 ICCs had no discussions about a potential decrease in
cure rate from participation in the trial. Statements from this category include:

- "There's a chance that it may be worse." (CL-19)
- "It's possible that by doing this, let's say that
  there'll be some kids who will get infections that
  won't get well, and so instead of being 80%, we'll
  be down to 75%." (LA-31)

**Decreased Cure Rate – Unlikely**

The majority of the discussions about decreased cure rate were coded in this
category (N=96, 86.5%). The average number of **Decreased Cure Rate –
Unlikely** statements for the 108 ICCs was .9 (SD = 1.4), with a range of 0 to 7.

Fifty-nine (54.6%) of the 108 ICCs had no discussions about the improbability of
a decrease in cure rate from participation in the trial. Most statements from this
category refer specifically to the outcome of treatment on the trial being at least
as good as standard therapy. For instance:

- "But we don't expect it to be any less than the
  85%." (CIN-11)
- "I can tell you, though, that obviously he won't get
  anything inferior. The least he can get is what he
  would get if you don't participate in the study."
  (CIN-15)
- "If I thought it was going to be less efficacious
  than standard therapy, I would not offer it." (CL-
  17)
- "And some people say I don't want to do
  something that's going to hurt my child's chances
  potentially of being cured. And in my assessment
  anyway, in my opinion, this study isn't asking that
  kind of question." (PH-07)
Physicians sometimes explained that the cure rate would not be inferior on the trial because the treatment received would be at least what is given as standard therapy. For example:

- "Do we expect that any would be less effective as far as leukemia treatment? I don't think so because the treatments, the various modifications, are really more intense, are actually more intense, not less intense. So I don't think that we're going to see that any of these are going to be less effective than our 85% cure rate." (CIN-11)

- "I can tell you that if she goes on study, she will at least get the standard treatment." (LA-20)

Uncertainty

Another way that risk is presented is through the physician's acknowledgment and discussion of doubt associated with the outcomes, both positive and negative, of the trial. All statements relating to the uncertainty of trial outcomes were extracted from the ICC transcripts. The lack of certainty surrounding the child's prognosis and which arm the child would be randomized to were excluded from this analysis. In addition, the analysis was limited to explicit statements of uncertainty, using language such as "don't/won't know", "can't say", or "can't guarantee/promise". A listing of the research questions in the trial (i.e., "Will three drugs work better than one?") was not included in the analysis unless it was coupled with an explicit statement that the answer is unknown. Every mention of uncertainty was counted for each ICC. There was a total of 554 statements of uncertainty (Total Uncertainty Discussions) in the
108 ICCs, with a mean of 5.1 (SD = 4.1) and range of 0 to 19. Only 13 (12.0%) of the 108 ICCs had no discussion of uncertainty. The statements of uncertainty include references to many different people as the possessor of doubt (i.e., “I don’t know”, “we can’t say”, “nobody knows”).

Uncertainty statements were then separated into two categories, according to whether they related to the risks or benefits of the trial. Discussions of uncertainty relating to benefit were much more common than discussions of uncertainty relating to risk. Frequencies for the two uncertainty categories are shown in Table 24 below, and examples of each follow.

Table 24: Uncertainty Discussions

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncertainty About Benefit</td>
<td>472</td>
</tr>
<tr>
<td>Uncertainty About Risk</td>
<td>82</td>
</tr>
<tr>
<td>Total Uncertainty Discussions</td>
<td>554</td>
</tr>
</tbody>
</table>

**Uncertainty About Benefit**

The majority of the uncertainty discussions were coded in this category (N=472, 85.2%). The average number of statements of Uncertainty About Benefit for the 108 ICCs was 4.4 (SD = 3.7), with a range of 0 to 18. Only 13 (12.0%) of the 108 ICCs had no discussions of uncertainty relating to the benefits of the trial. Statements coded in this category include:

- “The possibility exists, and we hope that one of these mechanisms will increase his chances from there. And we’re not certain of that.” (CIN-08)

- “I have no way of telling you it will be better than him getting arm A, which is the standard treatment. There is no way I can guarantee that.” (LA-14)
"There is no human being in the world, and I'm 100 percent certain about this, that can tell you that one of these is better than the other. We just don't know." (PH-22)

Some statements of uncertainty incorporate a discussion of equipoise as the ethical foundation for conducting the research or offering the trial. For instance:

- "If I knew, or even if I had a bet that one of them was really better, I wouldn't be offering you the choice of going on this. I'd say I think it's probably better to do one versus the other. I mean, it wouldn't be ethical for me to do it. I wouldn't feel comfortable doing it." (CL-06)

- "Now, if I knew what was right, if I knew which is the best thing, obviously that's what I would give your daughter. But I don't know. No one knows what is the best." (LA-02)

- "If we knew which one was better, it would be unethical for me to give you a less effective therapy. So we really do not know at the outset of the study which of these treatments is better for AML." (PH-06)

Other statements in this category use uncertainty as the rationale for conducting the trial, such as:

- "Right now we think they're probably all an improvement, but we don't know, obviously, and that's the purpose of the study." (CIN-05)

- "There may not be any big benefit at all. It might be a big benefit. We don't know. That's why we're asking that question." (CIN-14)

- "If we knew the answer to the question, we wouldn't be doing the study." (CL-18)
There is preliminary data suggesting that three drugs may be better, but we don’t know that for a fact. The only way to find out if one treatment is better than another is to compare them directly by giving some children one treatment and some children the other one.” (PH-04)

Some physicians describe uncertainty as the reason behind the randomization process:

- “We don’t know yet. We don’t know. That’s why we need the computer to tell us.” (LA-13)
- “And the reason why it’s chosen by a computer is because I don’t know, no one knows, what is the best treatment.” (LA-17)
- “Since we don’t know which is best, we let the study, by essentially a flip of a coin, tell us what will be given for your child.” (PH-32)

**Uncertainty About Risk**

Only 14.8% (N=82) of the discussions about uncertainty were coded in this category. The average number of statements of Uncertainty About Risk for the 108 ICCs was .8 (SD = 1.1), with a range of 0 to 4. Sixty-three (58.3%) of the 108 ICCs had no discussions of uncertainty relating to the risks of the trial. Examples from this category include:

- “There’s no way of knowing whether one of these is going to cause more of a particular side effect than another.” (CL-09)
- “We don’t expect the toxicity will be remarkably higher than what we get on standard. So I’m telling you we don’t expect it. Can I promise? No. And that’s why I have to ask your permission and willingness to participate.” (DC-06)
o "Maybe he would have more side effects. I can't tell you that ahead of time." (LA-14)

o "It's also happened that we've said, 'Gee, you know, we put all that extra work into arm D and all we got for it was more side effects and the same results, so we're not going to do that anymore.' That's happened too. But in the absence of good crystal balls, we don't know that until a few years after the study is over." (PH-01)

**Similarity to Standard**

Some physicians present the lack of risk, or safety, of the trial by discussing its treatment or the small differences between the arms of the trial. This type of discussion is common in the phase III leukemia RCT context because the cure rates for leukemia have improved to the point where drastic changes are no longer being made in the therapy. The language used in the statements coded here (i.e., "tweaking", "minor variations on a theme") reflect the cautious nature of the questions asked in these trials. In the 108 ICCs, there was a total of 123 statements relating to the similarity between the trial and standard treatment or between the arms of the trial, with a mean of 1.1 (SD = 1.5) and range of 0 to 6. Forty-six (42.6%) of the 108 ICCs included no statements in this category. Some statements in this category referred specifically to the similarity between the trial and standard treatment. For example:

o "So we've taken what we believe is the best at 85% and made that one group, and then we sort of tweaked it a little bit to make 3 other groups." (CIN-12)
"So of the, I want to say 14 or so, drugs that are used to treat leukemia, there's a 1 drug difference in the study that he'd get or not get." (CL-03)

"Even though we're talking about slightly increased doses for some arms and slightly increased duration, we are not talking about the therapeutics being really very different. It is what you would call subtly different. Not very different. So no matter what arm of the study you go on, you still see the same drugs." (CL-08)

"Except for a couple of exceptions, which I'll tell you about, it's pretty much the same whether you go on the study or not. Just the combinations and the doses will be a little bit different." (CL-13)

"And a Phase III study is a fine-tuning study. So we're starting with a baseline and we're tweaking things to try to fine tune things." (DC-09)

"All of the core treatment is the same, but we're gonna make a small variation in one part or two parts of the treatment." (PH-32)

Several statements focused on the similarity between specific drugs given in the trial versus standard treatment:

"The drugs are nearly the same. They're in the same class." (CL-03)

"They're all in the same family. It's just that they have slightly different properties." (LA-18)

Other statements related to the similarity between arms of the trial, such as:

"And you can see that the chemotherapy that each of these groups is getting is really pretty much the same. The issues we're talking about are very minor." (CIN-12)

"And on this one I honestly think that the differences between the arms are really small." (CL-06)
But essentially, they’re very similar. We use the same medicines at slightly different doses and slightly different schedules. (CL-21)

Physicians often explained that the similarity between the trial and standard therapy is due to fear of jeopardizing the already high cure rate by making drastic changes in the treatment. For instance:

- "Now, so there are differences between these four. They’re not the same, but on the other hand they’re not wildly different either because we’re doing too well with this disease to stray too far from what is the standard." (CL-10)

- "But it’s a relatively subtle change. And we only make small changes with studies like this where we have a very good cure rate because the general rule is ‘if it ain’t broke, don’t fix it.’ You don’t want to try to mess with something that’s working well." (PH-07)

Mechanisms of Oversight and Control

One way that physicians talk about the safety of the trial is through discussion of four types of oversight or control that are part of clinical research: Family Right to Withdraw, Data Safety and Monitoring, Allowance for Modification Within Trial, and Physician Right to Withdraw. These four mechanisms of oversight and control are presented by doctors during the ICC as factors that mitigate the risks of the trial. They are also often discussed as offsetting the lack of control associated with randomization. While parents and physicians have no control over choosing the arm of the trial the child is treated on, they do have the power to stop participation in the trial and adjust treatment according to the patient’s needs.
Every ICC transcript was evaluated for the presence or absence of each of these four mechanisms, and each ICC was given a total score of 0 to 4 based on how many of the 4 mechanisms were present. The average Total Oversight/Control Mechanisms score was 2.1 (SD = 1.2), with a range of 0 to 4. Figure 4 below shows the frequency with which each of the total scores (0-4) was found in the 108 ICCs.

### Figure 4: Total Oversight/Control Mechanisms

The number and percentage of ICCs that included a discussion of each of the four types of oversight/control is shown in Table 25 below, and examples of each follow.
Table 25: Types of Oversight and Control Mechanisms

<table>
<thead>
<tr>
<th>Type of Mechanism</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Right to Withdraw</td>
<td>86 (79.6%)</td>
</tr>
<tr>
<td>Data Safety &amp; Monitoring</td>
<td>62 (57.4%)</td>
</tr>
<tr>
<td>Allowance for Modification Within Trial</td>
<td>40 (37.0%)</td>
</tr>
<tr>
<td>Physician Right to Withdraw</td>
<td>34 (31.5%)</td>
</tr>
</tbody>
</table>

**Family Right to Withdraw**

This control mechanism relates to the family’s ability to stop the child’s participation in the trial at any time. Statements coded in this category include:

- “But you have to remember, if you’re on the study, if at any time you wanna come off the study, you can. You can always.” (DC-19)

- [reading consent document] “I am aware that I may withdraw from this study at any time. That’s an important thing because that means if you sign this today, and then next week you think, ‘you know, I really don’t want to do this’ then you say, ‘I don’t want to do this anymore.’ And that’s the end of the discussion.” (CL-09)

- “If any time you want, you say you don’t want to be on study, she comes back to get the standard treatment.” (LA-20)

**Data Safety & Monitoring**

This category refers to the oversight of the trial by a data safety and monitoring committee. Statements in this category often include discussion of what would happen if one arm of the trial was found to be significantly better or worse than the others while the trial is being conducted. For example:
"And certainly with these studies, I can tell you they are monitored very closely by Children's Oncology Group. And if toxicity levels are too great, the study is either stopped or modified." (CIN-10)

"And that data is analyzed constantly. It actually is analyzed thoroughly every six months. And if at any point in time it became apparent that one treatment was better than the other, or one was worse than the other, we would immediately be told about that. Immediately, as in that day. And then all patients, regardless of what treatment they had been getting, would get what we see is best." (CL-04)

"If at any time during the course of the treatment we find out that one treatment is better than the other, all of the children are converted or changed over to the better treatment." (LA-01)

**Allowance for Modification Within Trial**

These statements relate to the physician's ability to make needed changes to the child's treatment within the trial, and often make reference to the primacy of the patient's best interests. For instance:

"The therapy is not chiseled into stone. If for whatever reason M. were to have complications that would require us to alter the therapy, we would do that, whether you're on the study or not. The number one priority is treating M." (CIN-10)

"We don't have any control over picking which one of these he would be assigned to get, but once he is assigned to get one or the other, we still have to make judgments." (CL-09)
“We wouldn’t say, ‘You’re on study. We’ll just see how you do on study.’ We’ll say, ‘You’re on study. Well, you’re not doing so well with that. Maybe we should make this adjustment.’ We’re able to do that, okay?” (CL-15)

“As we talk about the clinical study, I think the most important thing to keep in mind is that our number one priority is doing our best for B. The clinical study is just guidelines. And if we give him some drug and his nose turns green, that’s data, and we won’t give him that drug anymore.” (PH-01)

“And if there’s any kind of toxicity that is limiting, a really big toxicity, we make modifications. We wouldn’t just plunge ahead with this.” (PH-26)

**Physician Right to Withdraw**

This category of oversight/control includes explicit statements that the doctor can take the patient off the trial. For example:

- “If it doesn’t work or the side effects are way out of proportion to what we expect, we’ll take him off the protocol.” (CIN-07)

- “If at any time Dr. K. or I, or one of our colleagues, feels that the medicines that A.’s getting are not in her best interest, then we would take her off the study.” (CL-08)

- “Not only you have the option of taking him off, but we have the option of taking him off as well. Our reason for taking him off would be if he has an increased amount of toxicity, which means he’s having certain side effects to the medication that we’re giving. We will take him off the protocol as well. So there’s two levels of control – one is you and one is us.” (CL-14)
Experimental Nature

Another facet of risk is the degree to which the trial is experimental. The physician's discussion of the experimental nature of the trial was explored by first extracting all statements that contained some variant of the word "experiment" from the ICC transcripts. These statements were then divided according to the positive or negative framing of the statement. The Experimental – Yes category includes those statements containing a positive assertion that some aspect of the trial is experimental, and the Experimental – No category includes those statements negating the experimental nature of the trial. Every statement within these two categories was counted for each of the 108 ICCs. There were 16 instances of a parent using the word “experiment” first. There were a total of 86 statements in the Experiment – Yes category, with a mean of .8 (SD = 1.3) and range of 0 to 7. Sixty-three (58.3%) of the 108 ICCs included no statements in this category. A total of 105 statements in the Experiment – No category were found in the ICCs, with a mean of 1.0 (SD = 1.1) and range of 0 to 4. Forty-eight (44.4%) of the 108 ICCs included no statements in this category.

In addition to these two types of statements using the word “experiment”, there were 13 statements using the word “guinea pig”. For instance:

- “So participation in a study does not mean, again, that we’re using this child as a guinea pig.” (LA-23)

These guinea pig statements were not included in the totals for the two experiment categories, but were included in the grand total number of
experiment/guinea pig discussions. The total number of statements that included some form of the word "experiment" or the word "guinea pig" (Experiment Total) in the 108 ICCs was 204, with a mean of 1.9 (SD = 1.8) and range of 0 to 8. Thirty-two (29.6%) of the 108 ICCs contained no statements using the word "experiment" or "guinea pig".

Experiment Categories

Both of the experiment categories were further coded into four different subgroups according to the particular aspect of the trial that the term "experiment" was applied to. Frequencies for the four subgroups in both experiment categories are shown in Table 26 below, and examples of each follow.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Arms</th>
<th>Drugs</th>
<th>Protocol/Study</th>
<th>Treatment</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>17</td>
<td>5</td>
<td>35</td>
<td>29</td>
<td>86</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>65</td>
<td>27</td>
<td>13</td>
<td>105</td>
</tr>
</tbody>
</table>

Arms

Statements that the arms of the trial are experimental include:

- “When we talk further about the experimental arms of this study, we will talk about how they deviate from standard therapy.” (CL-16)
"Or there's a chance that she could get the completely experimental arm, both the thioguanine and the triple intrathecal." (PH-09)

There were no statements that the arms of the trial are not experimental.

Drugs

Physicians rarely (N=5) said that the medicines in the trial were experimental. One example is:

- "The use of this drug in people with AML is still experimental." (PH-06)

In contrast to the infrequency of statements highlighting the experimental nature of the drugs, statements indicating that the drugs are not experimental were the most common type of experiment statement found in the ICCs. For instance:

- "None of the medications that she would receive are experimental." (CL-04)

- "You need to understand that this study does not use any experimental drugs." (HO-05)

- "But again, the medicines are standard. There's no experimental medicines so I think it makes it even easier to think about this decision. Versus sometimes a family may have a child with a cancer that's very hard to treat or resistant, we know very little about it, and so we may be talking about using experimental medicines in that setting, but we're not talking about that for this type of cancer." (LA-33)

- "So being on a study, the one thing that I think we should just clarify up front is that experimental doesn't mean experimental drugs." (PH-05)
Protocol/Study

There were a similar number of positive and negative statements about the experimental nature of the protocol or trial as a whole. Positive statements include:

- "Now during the course of any research project that we did, any experiment that we did, we monitor outcome and the toxicity." (CL-16)

- "And you have every right to be told this is an experimental study, a research study, meaning we don’t know of the four which one is the best." (LA-13)

- "While it is an experiment, I wouldn’t use that word." (PH-08)

In their assertions that the protocol or trial is not experimental, physicians often offered an alternative term for experiment, like “clinical trial” or “opportunity”, as shown in some of the examples below:

- "These are not what we would consider experimental protocols." (CIN-02)

- "It’s not experimentation on children...So in other words, the study is an oppor—I look at it not as experimentation, which I think is a negative, but as an opportunity for you to participate." (DC-18)

- "The way we’re achieving these benefits is through large cooperative studies. And that’s not experiments in the way that you might think of a scientist experimenting. It’s really a statistical term." (PH-12)

- "They’re not like the kind of experiments you’ve heard about. It’s not really an experiment. It’s a clinical trial where patients are treated differently and then we come up with the best answer." (PH-24)
Treatment

Physicians made more comments about the treatments on the trial being experimental than comments indicating that the treatments are not experimental. **Experiment – Yes** comments about treatment include:

- "There’s the standard treatment and three what we call experimental treatments." (CIN-11)

- "The experimental treatment regimen, and that would be the thioguanine or the three spinal medicines, may or may not improve the chance of cure." (PH-04)

- "I would say of all the potential complications that happen for any kind of treatment, whether we do standard treatment or experimental treatment, infection is the most likely to be life threatening." (PH-34)

Less commonly, physicians framed statements about the treatment being experimental negatively, as in the following examples:

- "There is no experimental treatment going on here." (CL-04)

- "None of them is experimental in that they are all well established, successful treatments for ALL." (PH-01)

Prior Use

A third category of the experimental nature of the trial also developed from the data. This category includes statements regarding the **Prior Use** of the drugs or treatments in the trial. The 108 ICCs included a total of 165 statements in this category, with a mean of 1.5 (SD = 1.9) and range of 0 to 9. Forty-one (38.0%) of the 108 ICCs contained no discussion of the **Prior Use** of the
medicines in the trial. Two different types of comments about the Prior Use of the therapies in the trial were found in the transcripts. Frequencies for each are found in Table 27 below, with examples following.

<table>
<thead>
<tr>
<th>Prior Use Statements</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not New/Used Before</td>
<td>114</td>
</tr>
<tr>
<td>Known Efficacy/Toxicity</td>
<td>51</td>
</tr>
<tr>
<td>Totals</td>
<td>165</td>
</tr>
</tbody>
</table>

**Not New/Used Before**

One hundred fourteen (69.1%) of the prior use statements related to the drug or treatments being used previously and/or not being new. For example:

- "They've all been used in his type of leukemia before." (CIN-01)
- "None of the medications that she would receive are experimental, okay? None. They've been around for years and years and have been used extensively." (CL-04)
- "We have used this, and this is explained in the protocol, we've used this two delayed intensifications. We use it for lots of patients, ones that are higher risk. So it's not as if we've never done this before." (CL-11)
- "There's nothing that's a brand new medicine that hasn't been tested." (DC-19)
- "These are all drugs that my colleagues and I have used to treat leukemia for many years." (HO-05)
Known Efficacy/Toxicity

Fifty-one (30.9%) of the prior use statements referred to the fact that the effectiveness of the drugs or treatments has been proven and their associated side effects are known. For instance:

- "I think the main thing is that all the drugs you’re going to get are drugs that we know work for leukemia." (CIN-07)

- "We’re using all drugs that we know are effective for the type of leukemia that you have.” (CL-07)

- "All of them are drugs that have been approved for a very long period of time so we know a lot about their side effects. We know a lot about how well they work. We know a lot about how your body gets rid of them and what the toxicities are.” (CL-18)

As many of the examples above show, the three categories relating to the experimental nature of the trial (Experiment - Yes, Experiment - No, and Prior Use) are linked in many ways. First, it is common for physicians to couple discussion of the ways that the trial is experimental with an explanation of the ways that the trial is not experimental. Also, many statements indicating that the medicines are not experimental are followed by an account of the drug’s prior use. In fact, there were some discussions that included all three of these categories. For instance:
“When we say it’s a study, I don’t want you to think there’s anything experimental about it. It’s scientific in its experimental design, but all the medicines and the chemo drugs on there are not experimental. They’ve been used for years, and we have a lot of experience with all of the medicines on there. What’s new is the different combinations of them, and the frequency of them. And the other thing to remember is that we’re not, we don’t think of D. as a guinea pig.” (CIN-13)

Examples From Focus Groups

As with benefits, parents in the focus groups were asked to discuss their perceptions of the risks of the trial and how they influenced their decision-making about trial participation. Many parents related how the likelihood or improbability of increased toxicity on the trial impacted their decision-making. For instance:

- “We chose not to take it...I figured, again, knowing how drugs have adverse affects on people, I just didn’t feel comfortable putting my daughter through something more difficult than what it had to be.” (3rd Philadelphia focus group)

- “As long as I knew they weren’t going to cause her any more pain, I was completely for it. And once I understood that, I was fine.” (2nd Cleveland focus group)

- “Our doctors were our conduit to the world, and, you know, I made damn sure I understood the risks when I read. We didn’t perceive any risks of the clinical trials and being that we were going to benefit from 20 years of clinical trials, we almost felt the duty to do it. Had I perceived a risk though – I’m not that altruistic – had I perceived a risk, I wouldn’t have done it. It’s just that simple.” (1st Washington DC focus group)
Some parents reported being told there was a chance of a decreased cure rate on the trial, which swayed their decision-making, while others reported being assured by the doctor that the chance of cure would be at least as good as treatment received off the trial. For example:

- "Then, you know, there was the option of, well, she could do less. Her chances could be less if she’s on the research than if she just does the general. So we said unless you have a guarantee that she was going to do as good or better, we weren’t going to do it. So that’s how we came up with a decision... That her chances could have been worse. I heard that clearly said. The chances could be worse if you were on it, and as much as I wanted to help everyone else...And that was the argument between my husband and me was well, you know, we could help other people. It really could, but he said, “Yeah, but it may not help your daughter.” (1st Cleveland focus group)

- "We clearly know that the other medicine doesn’t make it any worse.” (2nd Philadelphia focus group)

- “So it was explained to the group that each arm, it would never be less medication for our child. It would always be more. She wouldn’t be compromised.” (1st Cincinnati focus group)

Parents also reported that the uncertainty related to the trial had some bearing on their decision-making:

- "We just decided to go with what they already knew. They really couldn’t tell you what to expect from the three other legs of treatment, you know. They had an idea—that’s why they were doing it, because they didn’t know. So you might not know answers for a few years. We just decided to go with what they knew.” (2nd Philadelphia focus group)
The basic understanding of the research study was there are going to be different drugs that they give you. They don’t know if they are any better or worse. And that’s basically how our decision was made for us. You can’t tell us it’s any better, and you definitely can’t tell us it’s going to be worse.” (1st Cleveland focus group)

The trial’s similarity to standard treatment was also brought up during focus groups:

“But when you look at them and all the rates are about the same successes, and they’re just trying to tweak the system. And in fact, that’s what one of them said, ‘We’re trying to tweak it and make it just a little bit better.’ I’m thinking that’s fine. If you’re going to just tweak it, that’s fine. If you are going to go off into left field, then we got a whole other problem.” (1st Cincinnati focus group)

The right of the physician and the parents to withdraw from the trial at any time was a frequent topic of conversation during the focus groups. Parents sometimes discussed the right to withdraw as empowering or decreasing the feeling of pressure that accompanied the decision-making, as shown in the examples below:

“Like you said, L., we had the option at anytime of getting out of it if we wanted to. And so that empowered us. That gave us that feeling that if anything didn’t go right, we still had the option of not participating in the study.” (1st Los Angeles focus group)

“We were asking him every particular thing about the study we could. If we decide, you know, at the last minute we don’t want to go through this extra delayed intensification – I know we signed this that we would – but could we back out? We knew we could back out if it came down to it, so I didn’t feel pressured.” (2nd Cleveland focus group)
"Yeah, there was one thing that was in my mind that we were told that we could drop this at any time. That we didn’t have to follow this if we changed our mind a year later." (1st Philadelphia focus group)

"He told us right away that if you sign up for it...if you don’t like it, you can cancel it at that time. So that’s the reason we said yes. We went over the three treatments. We had already decided that if he got picked for the third treatment, which was the worst one with all the side effects, that we would say ‘no’. So we let him go through it. We let him through their lottery thing, but he told us right away. ‘If you get picked for the third one and you’re not comfortable with that, you can say no right away.’ So we said, ‘Alright, sign us up.’" (1st Cleveland focus group)

Parents also mentioned the importance of the power of the physician to stop the child’s participation in the trial:

"It also helped that they said you could drop out of it anytime if your child wasn’t responding appropriately, if you will, or whatever, that they would change it—that it wasn’t cast in stone that you would be on this come hell or high water." (2nd Washington DC focus group)

"There was always an out. I mean, and it was an out if you wanted to choose the out, you could choose it, or if something is not working that the doctor would come and say, ‘This ain’t working.’" (2nd Washington DC focus group)

The primacy of the patient’s best interests and the ability of making adjustments to treatment within the trial were also discussed by parents. For instance:

"They would always do what was best for the child." (1st Cleveland focus group)
Parents commented on negative associations with the experimental nature of the trial and the significance of previous experience with the treatment. For example:

- "Everybody out there, you're wonderful for doing it, but they are not experimenting on that little kid." (1st Philadelphia focus group)

- "My husband, knowing that, he went, ‘Okay, as long as she’s not going to be a guinea pig.’ And they assured us that everything on the study had been tried and proven. It wasn’t just some experimental drug they were deciding to use. It was tried and proven to work. If it had not been that, we would never have put him on the study." (3rd Philadelphia focus group)

- "I kept thinking, 'If I get in this, does this make my son the guinea pig?' That’s one thing I thought of." (Moderator: “And did you talk to the doctor about that?”)
  "Yeah, and they assured me. These are proven things that do work. You know, because that was something I said. ‘Do you...is he a guinea pig?’ But after talking to the doctors and, you know, they explained it a little better, all these are approved treatments of leukemia. ‘We are not trying something brand new or throwing you out there to the wolves.’” (2nd Cincinnati focus group)
Recoding of Variables

The 17 presentation of risk variables used to test the model in Chapter 10 include:

- Increased Toxicity – Possible
- Increased Toxicity – Unlikely
- Decreased Cure Rate – Possible
- Decreased Cure Rate – Unlikely
- Uncertainty About Benefit
- Uncertainty About Risk
- Total Uncertainty Discussions
- Similarity to Standard
- Family Right to Withdraw
- Data Safety & Monitoring
- Allowance for Modification Within Trial
- Physician Right to Withdraw
- Total Oversight/Control Mechanisms
- Experiment – Yes
- Experiment – No
- Experiment Total
- Prior Use

The four separate Oversight/Control variables (Parent Right to Withdraw, Data Safety & Monitoring, Allowance for Modification Within Trial, and Physician Right to Withdraw) were originally set up as dichotomous variables, with ICCs coded for the presence or absence of each of these. For analyses conducted to test the model in Chapter 10, the remaining 13 presentation of risk variables were recoded into dichotomous variables.

Increased Toxicity – Possible was separated into <=2 statements (N=55, 50.9%) or >2 statements (N=53, 49.1%). Increased Toxicity – Unlikely was divided into no statements (N=75, 69.4%) versus at least one statement (N=33, 30.6%). Decreased Cure Rate – Possible was separated into no statements (N=94, 87.0%) or at least one statement (N=14, 13.0%).
*Decreased Cure Rate – Unlikely* was grouped into no statements (N=59, 54.6%) and at least one statement (N=49, 45.4%).

*Uncertainty About Risk* was divided into no statements (N=63, 58.3%) versus at least one statement (N=45, 41.7%). *Uncertainty About Benefit* was grouped into <=3 statements (N=53, 49.1%) versus >3 statements (N=55, 50.9%), and *Uncertainty Total* was divided into <=4 statements (N=55, 50.9%) versus >4 statements (N=53, 49.1%).

*Similarity to Standard* was separated into no statements (N=46, 42.6%) or at least one statement (N=62, 57.4%). *Total Oversight/Control Mechanisms* was separated into <=2 statements (N=66, 61.1%) or >2 statements (N=42, 38.9%). *Experiment – Yes* was grouped into no statements (N=63, 58.3%) and at least one statement (N=45, 41.7%). *Experiment – No* was divided into no statements (N=48, 44.4%) versus at least one statement (N=60, 55.6%). *Prior Use* was separated into no statements (N=41, 38.0%) or at least one statement (N=67, 62.0%). Finally, *Experiment Total* was divided into <=1 statement (N=49, 45.4%) and >1 statement (N=59, 54.6%).

198

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Chapter 10: Testing the Model

The preceding chapters provided an in-depth description of each of the variables included in the model shown in Figure 1. The preliminary data analyses resulted in 8 dependent variables: the on/off trial decision, and the following 7 reasons for participating in the trial: direct benefit, altruism, the right to withdraw, comparison to standard, safety, doctor, and better monitoring. A total of 62 independent variables resulted from the preliminary analyses, including 8 patient variables, 8 parent variables, 40 clinician variables, and 6 social network variables. The 40 clinician variables include 7 doctor-parent relationship variables, 9 recommendation variables, 7 presentation of benefit variables, and 17 presentation of risk variables.

This chapter reports the results of analyses focused on identifying the variables that are associated with the groups of the dependent variable. First, chi-square analyses were performed to examine the relationship between each of the 62 independent variables and the 8 dependent variables. The results of these analyses are presented separately for each of the 8 dependent variables in Figures 5-12 below. The independent variables are divided into the four factors of the model: patient, parent, clinician, and social network factors. Both relationships significant at the p<.05 level (in bold) and relationships that approach significance (p<.10) are shown below. Relationships are listed in descending order, starting with the strongest relationships at the top. Following each figure is a table showing the direction of the significant relationships and the frequencies for the 2 categories of each variable.
On/Off Trial Decision

Figure 5: Relationships Between Independent Variables and the On/Off Trial Decision

Patient Factors
None

Social Network Factors
- Network Members Present: $X^2 = 10.43, p < .01$
- Network Facilitation of Communication: $X^2 = 10.36, p < .01$
- Network Total Questions/Comments: $X^2 = 6.84, p < .01$
- Network Non-Trial Questions: $X^2 = 5.30, p < .03$

Parent Factors
- Religion: $X^2 = 3.70, p < .06$

Clinician Factors
- Parent-Directed Decision (Doctor): $X^2 = 14.11, p < .01$
- Doctor-Directed Decision (Doctor): $X^2 = 11.12, p < .01$
- Recommendation Score: $X^2 = 6.77, p < .01$
- Total Explicit Recs for This Child: $X^2 = 5.24, p < .03$
- Total Explicit Recommendations: $X^2 = 4.46, p < .04$
- Total Direct Benefit – This Child: $X^2 = 4.38, p < .04$
- Similarity to Standard: $X^2 = 3.99, p < .05$
- Doctor-Directed Decision (Parent): $X^2 = 3.80, p < .06$
- Total Oversight/Control: $X^2 = 3.50, p < .07$

On/Off Trial Decision

There were 11 variables that were significantly related to the on/off trial decision: 0 patient variables, 0 parent variables, 7 clinician variables, and 4 social network variables. Three additional variables approached significance, including 1 parent variable and 2 clinician variables.
Table 28: Factors Related to the On/Off Trial Decision

<table>
<thead>
<tr>
<th>Independent Variables (% Within Variable)</th>
<th>On/Off Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% On Trial</td>
</tr>
<tr>
<td>Religion</td>
<td>Protestant (46.3%)</td>
</tr>
<tr>
<td></td>
<td>Other (53.7%)</td>
</tr>
<tr>
<td>Network Members Present</td>
<td>None (63.9%)</td>
</tr>
<tr>
<td></td>
<td>&gt;=1 (36.1%)</td>
</tr>
<tr>
<td>Network Facilitation of Communication</td>
<td>None (79.6%)</td>
</tr>
<tr>
<td></td>
<td>&gt;=1 (20.4%)</td>
</tr>
<tr>
<td>Network Total Questions/Comments</td>
<td>None (67.6%)</td>
</tr>
<tr>
<td></td>
<td>&gt;=1 (32.4%)</td>
</tr>
<tr>
<td>Network Non-Trial Questions</td>
<td>None (69.4%)</td>
</tr>
<tr>
<td></td>
<td>&gt;=1 (30.6%)</td>
</tr>
<tr>
<td>Parent-Directed Decision (Doctor)</td>
<td>No (63.9%)</td>
</tr>
<tr>
<td></td>
<td>Yes (36.1%)</td>
</tr>
<tr>
<td>Doctor-Directed Decision (Doctor)</td>
<td>No (44.4%)</td>
</tr>
<tr>
<td></td>
<td>Yes (55.6%)</td>
</tr>
<tr>
<td>Recommendation Score</td>
<td>Low, &lt;=4 (57.4%)</td>
</tr>
<tr>
<td></td>
<td>High, &gt;4 (42.6%)</td>
</tr>
<tr>
<td>Total Explicit Recs for This Child</td>
<td>None (39.8%)</td>
</tr>
<tr>
<td></td>
<td>&gt;=1 (60.2%)</td>
</tr>
<tr>
<td>Total Explicit Recommendations</td>
<td>&lt;=1 (63.0%)</td>
</tr>
<tr>
<td></td>
<td>&gt;1 (37.0%)</td>
</tr>
<tr>
<td>Total Direct Benefit – This Child</td>
<td>None (57.4%)</td>
</tr>
<tr>
<td></td>
<td>&gt;=1 (42.6%)</td>
</tr>
<tr>
<td>Similarity to Standard</td>
<td>None (42.6%)</td>
</tr>
<tr>
<td></td>
<td>&gt;=1 (57.4%)</td>
</tr>
<tr>
<td>Doctor-Directed Decision (Parent)</td>
<td>No (64.8%)</td>
</tr>
<tr>
<td></td>
<td>Yes (35.2%)</td>
</tr>
<tr>
<td>Total Oversight/Control</td>
<td>&lt;=2 (61.1%)</td>
</tr>
<tr>
<td></td>
<td>&gt;2 (38.9%)</td>
</tr>
</tbody>
</table>

Patient and Parent Factors:

Parents were more likely to participate in the clinical trial if they reported their

*Religion* as Protestant.
Social Network Factors:

Parents were less likely to participate in the clinical trial if they had at least one Network Member Present for the ICC. Parents were also less likely to participate in the trial if their ICC included at least one Network Non-Trial Related Question, at least one Network Facilitation of Communication, or at least one Total Network Questions/Comments.

Clinician Factors – Doctor/Parent Relationship:

Parents were more likely to participate in the trial in cases where the physician rated him or herself as the most important in making the decision about trial participation (Doctor-Directed Decision (Doctor)). Similarly, parents were more likely to participate in the trial in cases where the parent rated the physician as the most important in making the decision (Doctor-Directed Decision (Parent)). In contrast, parents were less likely to participate in the trial in cases where the physician rated the parents as the most important in making the decision (Parent-Directed Decision (Doctor)).

Clinician Factors – Physician Recommendation:

Parents were more likely to participate in the trial if their ICC contained at least one Explicit Recommendation for Their Child. Similarly, parents were more likely to participate in the trial if their ICC included more than one explicit recommendation of any kind (Total Explicit Recommendations). In addition,
parents were more likely to participate in the trial if they were involved in an ICC with a Recommendation Score greater than 4.

Clinician Factors – Presentation of Risks and Benefits:
Parents were more likely to participate in the trial if the doctor made at least one statement about the chance for direct benefit for their particular child during the ICC (Total Direct Benefit – This Child). Likewise, parents were more likely to participate in the trial if the doctor discussed the trial’s Similarity to Standard treatment at least once during the ICC. On the contrary, parents were less likely to participate in the trial if more than two Total Oversight/Control Mechanisms were discussed during the ICC.
There were 5 variables that were significantly related to citing direct benefit as a reason for participation in the trial: 0 patient variables, 1 parent variable, 4 clinician variables, and 0 social network variables. Nine additional variables
approached significance, including 1 patient variable, 2 parent variables, and 6 clinician variables.

Table 29: Factors Related to Citing Direct Benefit as a Reason for Participation in the Trial

<table>
<thead>
<tr>
<th>Independent Variables (% within variable)</th>
<th>Total Benefit</th>
<th>( \geq 1 \text{ (57.3%)} )</th>
<th>86.3</th>
<th>13.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Positive Illness Severity</td>
<td>( \leq 1 \text{ (57.3%)} )</td>
<td>71.1</td>
<td>28.9</td>
<td></td>
</tr>
<tr>
<td>Total Positive Illness Severity</td>
<td>( &gt;1 \text{ (42.7%)} )</td>
<td>71.1</td>
<td>28.9</td>
<td></td>
</tr>
<tr>
<td>Understanding of Randomization</td>
<td>No (41.6%)</td>
<td>91.9</td>
<td>8.1</td>
<td></td>
</tr>
<tr>
<td>Understanding of Randomization</td>
<td>Yes (58.4%)</td>
<td>71.2</td>
<td>28.8</td>
<td></td>
</tr>
<tr>
<td>Parent Ethnicity</td>
<td>Majority (64.0%)</td>
<td>73.7</td>
<td>26.3</td>
<td></td>
</tr>
<tr>
<td>Parent Ethnicity</td>
<td>Minority (36.0%)</td>
<td>90.6</td>
<td>9.4</td>
<td></td>
</tr>
<tr>
<td>Parent Age</td>
<td>( \leq 35 \text{ (53.9%)} )</td>
<td>72.9</td>
<td>27.1</td>
<td></td>
</tr>
<tr>
<td>Parent Age</td>
<td>( &gt;35 \text{ (46.1%)} )</td>
<td>87.8</td>
<td>12.2</td>
<td></td>
</tr>
<tr>
<td>Total Implicit Recommendations</td>
<td>None (46.3%)</td>
<td>74.0</td>
<td>26.0</td>
<td></td>
</tr>
<tr>
<td>Total Implicit Recommendations</td>
<td>( \geq 1 \text{ (53.7%)} )</td>
<td>58.6</td>
<td>41.4</td>
<td></td>
</tr>
<tr>
<td>Trust</td>
<td>( \leq 97 \text{ (49.4%)} )</td>
<td>68.2</td>
<td>31.8</td>
<td></td>
</tr>
<tr>
<td>Trust</td>
<td>( &gt;97 \text{ (50.6%)} )</td>
<td>91.1</td>
<td>8.9</td>
<td></td>
</tr>
<tr>
<td>Experiment – No</td>
<td>None (42.7%)</td>
<td>92.1</td>
<td>7.9</td>
<td></td>
</tr>
<tr>
<td>Experiment – No</td>
<td>( \geq 1 \text{ (57.3%)} )</td>
<td>70.6</td>
<td>29.4</td>
<td></td>
</tr>
<tr>
<td>Total Direct Benefit – This Child</td>
<td>None (52.8%)</td>
<td>70.2</td>
<td>29.8</td>
<td></td>
</tr>
<tr>
<td>Total Direct Benefit – This Child</td>
<td>( \geq 1 \text{ (47.2%)} )</td>
<td>90.5</td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td>Total Shared Decision-Making</td>
<td>( \leq 1 \text{ (48.3%)} )</td>
<td>72.1</td>
<td>27.9</td>
<td></td>
</tr>
<tr>
<td>Total Shared Decision-Making</td>
<td>( &gt;1 \text{ (51.7%)} )</td>
<td>87.0</td>
<td>13.0</td>
<td></td>
</tr>
<tr>
<td>Total Direct Benefit</td>
<td>( \leq 2 \text{ (48.3%)} )</td>
<td>72.1</td>
<td>27.9</td>
<td></td>
</tr>
<tr>
<td>Total Direct Benefit</td>
<td>( &gt;2 \text{ (51.7%)} )</td>
<td>87.0</td>
<td>13.0</td>
<td></td>
</tr>
<tr>
<td>Total Uncertainty</td>
<td>( \leq 4 \text{ (51.7%)} )</td>
<td>87.0</td>
<td>13.0</td>
<td></td>
</tr>
<tr>
<td>Total Uncertainty</td>
<td>( &gt;4 \text{ (48.3%)} )</td>
<td>72.1</td>
<td>27.9</td>
<td></td>
</tr>
<tr>
<td>Experiment Total</td>
<td>( \leq 1 \text{ (46.1%)} )</td>
<td>87.8</td>
<td>12.2</td>
<td></td>
</tr>
<tr>
<td>Experiment Total</td>
<td>( &gt;1 \text{ (53.9%)} )</td>
<td>72.9</td>
<td>27.1</td>
<td></td>
</tr>
<tr>
<td>Doctor-Directed Decision (Parent)</td>
<td>No (60.7%)</td>
<td>74.1</td>
<td>25.9</td>
<td></td>
</tr>
<tr>
<td>Doctor-Directed Decision (Parent)</td>
<td>Yes (39.3%)</td>
<td>88.6</td>
<td>11.4</td>
<td></td>
</tr>
<tr>
<td>Total Direct Benefit – General</td>
<td>( \leq 1 \text{ (43.8%)} )</td>
<td>71.8</td>
<td>28.2</td>
<td></td>
</tr>
<tr>
<td>Total Direct Benefit – General</td>
<td>( &gt;1 \text{ (56.2%)} )</td>
<td>86.0</td>
<td>14.0</td>
<td></td>
</tr>
</tbody>
</table>

Patient and Parent Factors:

Parents were more likely to say direct benefit was a reason for participation in the trial if they were of minority Ethnicity or were over the Age of 35. On the
other hand, parents were less likely to cite direct benefit as a reason for participation in the trial if they understood randomization or if the physician made more than one positive illness severity statement during the ICC.

Clinician Factors – Doctor/Parent Relationship:
Parents were more likely to cite direct benefit as a reason for participation in the trial if they had higher levels of trust in their child’s physician or if their ICC involved more than one instance of shared decision-making. Parents were also more likely to mention direct benefit as a reason for their decision if they rated the doctor as the most important in directing the decision (Doctor-Directed Decision (Parent)).

Clinician Factors – Physician Recommendation:
Parents were less likely to mention direct benefit as a reason if they were given at least one implicit recommendation of the trial by the physician during the ICC.

Clinician Factors – Presentation of Risks and Benefits:
Parents were more likely to cite direct benefit as a reason for participation in the trial if their ICC contained at least one mention of direct benefit for their child (Total Direct Benefit – This Child), more than one mention of direct benefit in general (Total Direct Benefit – General), or more than two mentions of direct benefit of any kind (Total Direct Benefit).
On the contrary, parents were less likely to list direct benefit as a reason for participation in the trial if their ICC involved at least one statement in the **Experiment – No** category or more than one Experiment statement of any kind (**Total Experiment**). Parents were also less likely to mention direct benefit as a reason if their ICC contained more than 4 statements of uncertainty of any kind about the trial (**Total Uncertainty**).
Altruism

Figure 7: Relationships Between Independent Variables and Altruism as a Reason for Participation in the Trial

Patient Factors
- Total Positive Illness Severity: $X^2=4.01$, $p<.05$

Social Network Factors
- None

Parent Factors
- Understanding of Randomization: $X^2=3.28$, $p<.07$

Clinician Factors
- Similarity to Standard: $X^2=3.33$, $p<.07$
- Experiment – Yes: $X^2=3.28$, $p<.07$
- Physician Right to Withdraw: $X^2=2.98$, $p<.09$

There was only 1 variable that was significantly related to citing altruism as a reason for participation in the trial: 1 patient variable, 0 parent variables, 0 clinician variables, and 0 social network variables. Four additional variables approached significance, including 1 parent variable and 3 clinician variables.
Table 30: Factors Related to Citing Altruism as a Reason for Participation in the Trial

<table>
<thead>
<tr>
<th>Independent Variables (% Within Variable)</th>
<th>Altruism</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Yes</td>
</tr>
<tr>
<td>Total Positive Illness Severity</td>
<td></td>
</tr>
<tr>
<td>&lt;=1 (57.3%)</td>
<td>58.8</td>
</tr>
<tr>
<td>&gt;1 (42.7%)</td>
<td>78.9</td>
</tr>
<tr>
<td>Understanding of Randomization</td>
<td></td>
</tr>
<tr>
<td>No (41.6%)</td>
<td>56.8</td>
</tr>
<tr>
<td>Yes (58.4%)</td>
<td>75.0</td>
</tr>
<tr>
<td>Similarity to Standard</td>
<td></td>
</tr>
<tr>
<td>None (38.2%)</td>
<td>55.9</td>
</tr>
<tr>
<td>&gt;=1 (61.8%)</td>
<td>74.5</td>
</tr>
<tr>
<td>Experiment – Yes</td>
<td></td>
</tr>
<tr>
<td>None (58.4%)</td>
<td>75.0</td>
</tr>
<tr>
<td>&gt;=1 (41.6%)</td>
<td>56.8</td>
</tr>
<tr>
<td>Physician Right to Withdraw</td>
<td></td>
</tr>
<tr>
<td>No (70.8%)</td>
<td>61.9</td>
</tr>
<tr>
<td>Yes (29.2%)</td>
<td>80.8</td>
</tr>
</tbody>
</table>

Patient and Parent Factors:

Parents were more likely to cite altruism as a reason for participation in the trial if the physician made more than one Positive Illness Severity statement during the ICC. Parents were also more likely to list altruism as a reason if they Understood Randomization.

Clinician Factors – Presentation of Risks and Benefits:

Parents were more likely to mention altruism as a reason for their participation in the trial if their ICC included at least one discussion of the trial’s Similarity to Standard treatment or if the Physician’s Right to Withdraw the child from the trial was discussed during the ICC. On the other hand, parents were less likely to list altruism as a reason for their decision if their ICC contained at least one statement in the Experiment – Yes category.
Right to Withdraw

Figure 8: Relationships Between Independent Variables and Right to Withdraw as a Reason for Participation in the Trial

Patient Factors
- Age: $X^2 = 9.81, p < .01$

Parent Factors
- Understanding of Randomization: $X^2 = 9.36, p < .01$
- Ethnicity: $X^2 = 6.01, p < .02$
- SES: $X^2 = 3.54, p < .06$
- Education: $X^2 = 3.16, p < .08$
- Religion: $X^2 = 2.95, p < .09$

Social Network Factors
- None

Clinician Factors
- Total Explicit Recs for This Child: $X^2 = 4.51, p < .04$
- Decreased Cure Rate – Unlikely: $X^2 = 2.72, p < .10$

Right to Withdraw is Reason for Participation (Yes/No)

There were 4 variables that were significantly related to citing the right to withdraw as a reason for participation in the trial: 1 patient variable, 2 parent variables, 1 clinician variable, and 0 social network variables. Four additional variables approached significance, including 3 parent variables and 1 clinician variable.
### Table 31: Factors Related to Citing the Right to Withdraw as a Reason for Participation in the Trial

<table>
<thead>
<tr>
<th>Independent Variables (% Within Variable)</th>
<th>Right to Withdraw (% Yes)</th>
<th>% No</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;=5 (49.4%)</td>
<td>43.2</td>
<td>56.8</td>
</tr>
<tr>
<td>&gt;5 (50.6%)</td>
<td>13.3</td>
<td>86.7</td>
</tr>
<tr>
<td><strong>Understanding of Randomization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (41.6%)</td>
<td>10.8</td>
<td>89.2</td>
</tr>
<tr>
<td>Yes (58.4%)</td>
<td>40.4</td>
<td>59.6</td>
</tr>
<tr>
<td><strong>Parent Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Majority (64.0%)</td>
<td>36.8</td>
<td>63.2</td>
</tr>
<tr>
<td>Minority (36.0%)</td>
<td>12.5</td>
<td>87.5</td>
</tr>
<tr>
<td><strong>Parent SES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High, 1-3 (69.3%)</td>
<td>34.4</td>
<td>65.6</td>
</tr>
<tr>
<td>Low, 4-5 (30.7%)</td>
<td>14.8</td>
<td>85.2</td>
</tr>
<tr>
<td><strong>Parent Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;=High School (38.6%)</td>
<td>17.6</td>
<td>82.4</td>
</tr>
<tr>
<td>&gt;High School (61.4%)</td>
<td>35.2</td>
<td>64.8</td>
</tr>
<tr>
<td><strong>Religion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protestant (50.6%)</td>
<td>20.0</td>
<td>80.0</td>
</tr>
<tr>
<td>Other (49.4%)</td>
<td>36.4</td>
<td>63.6</td>
</tr>
<tr>
<td><strong>Total Explicit Recs for This Child</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None (34.8%)</td>
<td>41.9</td>
<td>58.1</td>
</tr>
<tr>
<td>&gt;=1 (65.2%)</td>
<td>20.7</td>
<td>79.3</td>
</tr>
<tr>
<td><strong>Decreased Cure Rate – Unlikely</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None (53.9%)</td>
<td>20.8</td>
<td>79.2</td>
</tr>
<tr>
<td>&gt;=1 (46.1%)</td>
<td>36.6</td>
<td>63.4</td>
</tr>
</tbody>
</table>

Patient and Parent Factors:

Parents were more likely to list the right to withdraw as a reason if they understood Randomization or had higher Education. On the contrary, parents were less likely to cite the right to withdraw as a reason for their decision to participate in the trial if their child was over the Age of 5. Parents were also less likely to mention the right to withdraw as a reason if they were of minority Ethnicity, low Socioeconomic Status, or Protestant Religion.
Clinician Factors – Physician’s Recommendation:

Parents were less likely to cite the right to withdraw as a reason if their ICC contained at least one *Explicit Recommendation for Their Child* to participate in the trial.

Clinician Factors – Presentation of Risks and Benefits:

Parents were more likely to cite the right to withdraw as a reason for participation in the trial if the physician made at least one *Decreased Cure Rate – Unlikely* statement during the ICC.
Comparison to Standard

Figure 9: Relationships Between Independent Variables and Comparison to Standard as a Reason for Participation in the Trial

Patient Factors
Risk Level:
\[ X^2 = 3.90, \ p < .05 \]
Numerical Prognosis:
\[ X^2 = 3.23, \ p < .08 \]

Social Network Factors
Network Non-Trial Questions:
\[ X^2 = 4.29, \ p < .04 \]
Network Facilitation of Communication:
\[ X^2 = 4.10, \ p < .05 \]
Network Total Questions/Comments:
\[ X^2 = 3.61, \ p < .06 \]
Network Comments About Child/Fam:
\[ X^2 = 3.50, \ p < .07 \]
Network Trial Questions:
\[ X^2 = 2.81, \ p < .10 \]

Parent Factors
Understanding of Randomization:
\[ X^2 = 3.72, \ p < .06 \]
Parent Perception of Risk:
\[ X^2 = 3.46, \ p < .07 \]

Clinician Factors
Strength of Rec (Parent):
\[ X^2 = 5.82, \ p < .02 \]
Total Implicit Recommendations:
\[ X^2 = 3.31, \ p < .07 \]
Doctor-Directed Decision (Parent):
\[ X^2 = 3.03, \ p < .09 \]

Comparison to Standard is Reason for Participation (Yes/No)

There were 4 variables that were significantly related to citing comparison to standard as a reason for participation in the trial: 1 patient variable, 0 parent variables, 1 clinician variable, and 2 social network variables. Eight additional
variables approached significance, including 1 patient variable, 2 parent variables, 2 clinician variables, and 3 social network variables.

Table 32: Factors Related to Citing Comparison to Standard as a Reason for Participation in the Trial

<table>
<thead>
<tr>
<th>Independent Variables (%) Within Variables</th>
<th>None (74.2%)</th>
<th>&gt;=1 (25.8%)</th>
<th>None (73.0%)</th>
<th>&gt;=1 (27.0%)</th>
<th>None (77.8%)</th>
<th>&gt;=1 (22.2%)</th>
<th>None (78.7%)</th>
<th>&gt;=1 (21.3%)</th>
<th>More Strongly, &lt;=5 (58.4%)</th>
<th>Less Strongly, &gt;5 (41.6%)</th>
<th>None (46.3%)</th>
<th>&gt;=1 (53.7%)</th>
<th>No (60.7%)</th>
<th>Yes (39.3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Level</td>
<td>Low (49.4%)</td>
<td>36.4</td>
<td>High (50.6%)</td>
<td>17.8</td>
<td>Low, &lt;=78 (48.1%)</td>
<td>17.9</td>
<td>High, &gt;=78 (51.9%)</td>
<td>35.7</td>
<td>17.8</td>
<td></td>
<td>17.9</td>
<td>82.1</td>
<td>35.7</td>
<td>63.6</td>
</tr>
<tr>
<td>Numerical Prognosis</td>
<td>No (41.6%)</td>
<td>16.2</td>
<td>Yes (58.4%)</td>
<td>34.6</td>
<td>Low, &lt;=78 (48.1%)</td>
<td>17.9</td>
<td>High, &gt;=78 (51.9%)</td>
<td>35.7</td>
<td>83.8</td>
<td></td>
<td>83.8</td>
<td>16.2</td>
<td>65.4</td>
<td>34.6</td>
</tr>
<tr>
<td>Understanding of Randomization</td>
<td>Low, &lt;=5 (44.3%)</td>
<td>35.9</td>
<td>High, &gt;5 (55.7%)</td>
<td>18.4</td>
<td>64.1</td>
<td>18.4</td>
<td>81.6</td>
<td>64.1</td>
<td>18.4</td>
<td></td>
<td>81.6</td>
<td>18.4</td>
<td>64.1</td>
<td>18.4</td>
</tr>
<tr>
<td>Parent Perception of Risk</td>
<td>No (41.6%)</td>
<td>16.2</td>
<td>Yes (58.4%)</td>
<td>34.6</td>
<td>Low, &lt;=5 (44.3%)</td>
<td>35.9</td>
<td>High, &gt;5 (55.7%)</td>
<td>18.4</td>
<td>64.1</td>
<td></td>
<td>64.1</td>
<td>18.4</td>
<td>64.1</td>
<td>18.4</td>
</tr>
<tr>
<td>Network Non-Trial Questions</td>
<td>Low (49.4%)</td>
<td>36.4</td>
<td>High (50.6%)</td>
<td>17.8</td>
<td>Low, &lt;=78 (48.1%)</td>
<td>17.9</td>
<td>High, &gt;=78 (51.9%)</td>
<td>35.7</td>
<td>82.1</td>
<td></td>
<td>82.1</td>
<td>17.9</td>
<td>63.6</td>
<td>17.8</td>
</tr>
<tr>
<td>Network Facilitation of Communication</td>
<td>No (41.6%)</td>
<td>16.2</td>
<td>Yes (58.4%)</td>
<td>34.6</td>
<td>Low, &lt;=5 (44.3%)</td>
<td>35.9</td>
<td>High, &gt;5 (55.7%)</td>
<td>18.4</td>
<td>64.1</td>
<td></td>
<td>64.1</td>
<td>18.4</td>
<td>64.1</td>
<td>18.4</td>
</tr>
<tr>
<td>Network Total Questions/Comments</td>
<td>Low (49.4%)</td>
<td>36.4</td>
<td>High (50.6%)</td>
<td>17.8</td>
<td>Low, &lt;=78 (48.1%)</td>
<td>17.9</td>
<td>High, &gt;=78 (51.9%)</td>
<td>35.7</td>
<td>82.1</td>
<td></td>
<td>82.1</td>
<td>17.9</td>
<td>63.6</td>
<td>17.8</td>
</tr>
<tr>
<td>Network Comments About Child/Family</td>
<td>No (41.6%)</td>
<td>16.2</td>
<td>Yes (58.4%)</td>
<td>34.6</td>
<td>Low, &lt;=5 (44.3%)</td>
<td>35.9</td>
<td>High, &gt;5 (55.7%)</td>
<td>18.4</td>
<td>64.1</td>
<td></td>
<td>64.1</td>
<td>18.4</td>
<td>64.1</td>
<td>18.4</td>
</tr>
<tr>
<td>Network Trial Questions</td>
<td>Low (49.4%)</td>
<td>36.4</td>
<td>High (50.6%)</td>
<td>17.8</td>
<td>Low, &lt;=78 (48.1%)</td>
<td>17.9</td>
<td>High, &gt;=78 (51.9%)</td>
<td>35.7</td>
<td>82.1</td>
<td></td>
<td>82.1</td>
<td>17.9</td>
<td>63.6</td>
<td>17.8</td>
</tr>
<tr>
<td>Strength of Recommendation (Parent)</td>
<td>More Strongly, &lt;=5 (58.4%)</td>
<td>36.5</td>
<td>Less Strongly, &gt;5 (41.6%)</td>
<td>13.5</td>
<td>36.5</td>
<td>63.5</td>
<td>13.5</td>
<td>86.5</td>
<td>36.5</td>
<td></td>
<td>63.5</td>
<td>13.5</td>
<td>86.5</td>
<td>36.5</td>
</tr>
<tr>
<td>Total Implicit Recommendations</td>
<td>Low (49.4%)</td>
<td>36.4</td>
<td>High (50.6%)</td>
<td>17.8</td>
<td>Low, &lt;=78 (48.1%)</td>
<td>17.9</td>
<td>High, &gt;=78 (51.9%)</td>
<td>35.7</td>
<td>82.1</td>
<td></td>
<td>82.1</td>
<td>17.9</td>
<td>63.6</td>
<td>17.8</td>
</tr>
<tr>
<td>Doctor-Directed Decision (Parent)</td>
<td>No (60.7%)</td>
<td>20.4</td>
<td>Yes (39.3%)</td>
<td>37.1</td>
<td></td>
<td>20.4</td>
<td>79.6</td>
<td>37.1</td>
<td>62.9</td>
<td></td>
<td>62.9</td>
<td>37.1</td>
<td>62.9</td>
<td>37.1</td>
</tr>
</tbody>
</table>

Patient and Parent Factors:

Parents were more likely to mention comparison to standard as a reason for their decision if they Understood Randomization or rated the trial as lower risk (Riskiness of Trial (Parent)). On the other hand, parents were less likely to
cite comparison to standard as a reason if their child had a high Risk Level or was given a low Numerical Prognosis during the ICC.

Social Network Factors:
Parents were more likely to cite comparison to standard as a reason if during the ICC there was at least one Network Trial Question, Network Non-Trial-Related Question, Network Facilitation of Communication, Network Comment About the Child or Family, or Total Network Questions/Comments.

Clinician Factors – Doctor/Parent Relationship:
Parents were more likely to say comparison to standard was a reason for their decision if they rated the doctor as the most important in directing the decision (Doctor-Directed Decision (Parent)).

Clinician Factors – Physician’s Recommendation:
Parents were more likely to list comparison to standard as a reason for participation in the trial if they rated the doctor’s recommendation of the trial more strongly (Strength of Recommendation (Parent)) or were given at least one Implicit Recommendation of the trial during the ICC.
Safety

Figure 10: Relationships Between Independent Variables and Safety as a Reason for Participation in the Trial

There were 8 variables that were significantly related to citing safety as a reason for participation in the trial: 3 patient variables, 3 parent variables, 2 clinician variables, and 0 social network variables. Two additional variables approached significance, including 1 patient variable and 1 clinician variable.
Table 33: Factors Related to Citing Safety as a Reason for Participation in the Trial

<table>
<thead>
<tr>
<th>Independent Variables (% Within Variable)</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Yes</td>
</tr>
<tr>
<td>Numerical Prognosis</td>
<td></td>
</tr>
<tr>
<td>Low, &lt;78 (48.1%)</td>
<td>12.8</td>
</tr>
<tr>
<td>High, &gt;=78 (51.9%)</td>
<td>35.7</td>
</tr>
<tr>
<td>Risk Level</td>
<td></td>
</tr>
<tr>
<td>Low (49.4%)</td>
<td>34.1</td>
</tr>
<tr>
<td>High (50.6%)</td>
<td>13.3</td>
</tr>
<tr>
<td>Total Negative Illness Severity</td>
<td></td>
</tr>
<tr>
<td>None (57.3%)</td>
<td>31.4</td>
</tr>
<tr>
<td>&gt;=1 (42.7%)</td>
<td>13.2</td>
</tr>
<tr>
<td>Total Prognosis – Cure Survival</td>
<td></td>
</tr>
<tr>
<td>&lt;=2 (48.3%)</td>
<td>32.6</td>
</tr>
<tr>
<td>&gt;2 (51.7%)</td>
<td>15.2</td>
</tr>
<tr>
<td>Understanding of Randomization</td>
<td></td>
</tr>
<tr>
<td>No (41.6%)</td>
<td>8.1</td>
</tr>
<tr>
<td>Yes (58.4%)</td>
<td>34.6</td>
</tr>
<tr>
<td>Parent Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Majority (64.0%)</td>
<td>31.6</td>
</tr>
<tr>
<td>Minority (36.0%)</td>
<td>9.4</td>
</tr>
<tr>
<td>Parent Education</td>
<td></td>
</tr>
<tr>
<td>&lt;=High School (38.6%)</td>
<td>11.8</td>
</tr>
<tr>
<td>&gt;High School (61.4%)</td>
<td>31.5</td>
</tr>
<tr>
<td>Allowance for Modification in Trial</td>
<td></td>
</tr>
<tr>
<td>No (65.2%)</td>
<td>31.0</td>
</tr>
<tr>
<td>Yes (34.8%)</td>
<td>9.7</td>
</tr>
<tr>
<td>Decreased Cure Rate – Unlikely</td>
<td></td>
</tr>
<tr>
<td>None (53.9%)</td>
<td>14.6</td>
</tr>
<tr>
<td>&gt;=1 (46.1%)</td>
<td>34.1</td>
</tr>
<tr>
<td>Total Oversight/Control</td>
<td></td>
</tr>
<tr>
<td>&lt;=2 (61.1%)</td>
<td>25.8</td>
</tr>
<tr>
<td>&gt;2 (38.9%)</td>
<td>9.5</td>
</tr>
</tbody>
</table>

Patient and Parent Factors:

Parents were more likely to cite safety as a reason for participation in the trial if their child was in the lower Risk Level group or was given a higher Numerical Prognosis during the ICC. Parents were also more likely to list safety as a reason if they Understood Randomization. On the contrary, parents were less likely to cite safety as a reason if they were of minority Ethnicity or had lower Education. Parents were also less likely to say safety was a reason for their decision if the physician made at least one Negative Illness Severity statement or more than two Prognosis – Cure/Survival statements during the ICC.
Clinician Factors – Presentation of Risks and Benefits:

Parents were less likely to say safety was a reason for their decision if their ICC included at least one Decreased Cure Rate – Unlikely statement. Parents were also less likely to list safety as a reason for participation in the trial if their ICC contained a statement about the ability to Modify Treatment Within the Trial or more than two Total Oversight/Control statements.
Figure 11: Relationships Between Independent Variables and the Doctor as a Reason for Participation in the Trial

Patient Factors

None

Social Network Factors

Network Non-Trial Questions:
\[ X^2 = 3.67, p < .06 \]
Network Total Questions/Comments:
\[ X^2 = 3.20, p < .08 \]

Parent Factors

Age:
\[ X^2 = 4.30, p < .04 \]

Clinician Factors

Strength of Rec (Parent):
\[ X^2 = 11.82, p < .01 \]
Trust:
\[ X^2 = 8.21, p < .01 \]
Total Oversight/Control:
\[ X^2 = 5.61, p < .02 \]
Total Other Patients Recipients:
\[ X^2 = 5.21, p < .03 \]
Doctor-Directed Decision (Parent):
\[ X^2 = 4.34, p < .04 \]
Parent-Directed Decision (Parent):
\[ X^2 = 2.83, p < .10 \]
Uncertainty About Risk:
\[ X^2 = 2.78, p < .10 \]
Physician Right to Withdraw:
\[ X^2 = 2.75, p < .10 \]

Doctor is Reason for Participation (Yes/No)

There were 6 variables that were significantly related to citing the doctor as a reason for participation in the trial: 0 patient variables, 1 parent variable, 5 clinician variables, and 0 social network variables. Five additional variables

219
approached significance, including 3 clinician variables and 2 social network variables.

**Table 34: Factors Related to Citing the Doctor as a Reason for Participation in the Trial**

<table>
<thead>
<tr>
<th>Independent Variables (% Within Variable)</th>
<th>Doctor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes %</td>
</tr>
<tr>
<td><strong>Parent Age</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;=35 (53.9%)</td>
<td>8.3</td>
</tr>
<tr>
<td>&gt;35 (46.1%)</td>
<td>24.4</td>
</tr>
<tr>
<td><strong>Network Non-Trial Questions</strong></td>
<td></td>
</tr>
<tr>
<td>None (74.2%)</td>
<td>10.6</td>
</tr>
<tr>
<td>&gt;=1 (25.8%)</td>
<td>30.4</td>
</tr>
<tr>
<td><strong>Network Total Questions/Comments</strong></td>
<td></td>
</tr>
<tr>
<td>None (73.0%)</td>
<td>10.8</td>
</tr>
<tr>
<td>&gt;=1 (27.0%)</td>
<td>29.2</td>
</tr>
<tr>
<td><strong>Strength of Recommendation (Parent)</strong></td>
<td></td>
</tr>
<tr>
<td>More Strongly, &lt;=5 (58.4%)</td>
<td>26.9</td>
</tr>
<tr>
<td>Less Strongly, &gt;5 (41.6%)</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Trust</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;=97 (49.4%)</td>
<td>4.5</td>
</tr>
<tr>
<td>&gt;97 (50.6%)</td>
<td>26.7</td>
</tr>
<tr>
<td><strong>Total Oversight/Control</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;=2 (61.1%)</td>
<td>19.7</td>
</tr>
<tr>
<td>&gt;2 (38.9%)</td>
<td>2.4</td>
</tr>
<tr>
<td><strong>Total Other Patients Recipients</strong></td>
<td></td>
</tr>
<tr>
<td>None (50.6%)</td>
<td>24.4</td>
</tr>
<tr>
<td>&gt;=1 (49.4%)</td>
<td>6.8</td>
</tr>
<tr>
<td><strong>Doctor-Directed Decision (Parent)</strong></td>
<td></td>
</tr>
<tr>
<td>No (60.7%)</td>
<td>9.3</td>
</tr>
<tr>
<td>Yes (39.3%)</td>
<td>25.7</td>
</tr>
<tr>
<td><strong>Parent-Directed Decision (Parent)</strong></td>
<td></td>
</tr>
<tr>
<td>No (43.8%)</td>
<td>23.1</td>
</tr>
<tr>
<td>Yes (56.2%)</td>
<td>10.0</td>
</tr>
<tr>
<td><strong>Uncertainty About Risk</strong></td>
<td></td>
</tr>
<tr>
<td>None (58.4%)</td>
<td>21.2</td>
</tr>
<tr>
<td>&gt;=1 (41.6%)</td>
<td>8.1</td>
</tr>
<tr>
<td><strong>Physician Right to Withdraw</strong></td>
<td></td>
</tr>
<tr>
<td>No (70.8%)</td>
<td>20.6</td>
</tr>
<tr>
<td>Yes (29.2%)</td>
<td>3.8</td>
</tr>
</tbody>
</table>

**Patient and Parent Factors:**

Parents were more likely to cite the doctor as a reason for their decision to participate in the trial if they were over the Age of 35.
Social Network Factors:
Parents were more likely to list the doctor as a reason if their ICC contained at least one *Network Non-Trial-Related Question* or *Total Network Questions/Comments*.

Clinician Factors – Doctor/Parent Relationship:
Parents were more likely to list the doctor as a reason for participation in the trial if they had higher *Trust* in their child’s physician. Parents were also more likely to say the doctor was a reason for their decision if they rated the doctor as most important in directing the decision (*Doctor-Directed Decision (Parent)*). In contrast, parents were less likely to cite the doctor as a reason if they rated themselves as most important in directing the decision (*Parent-Directed Decision (Parent)*).

Clinician Factors – Physician’s Recommendation:
Parents were more likely to cite the doctor as a reason if they rated the physician’s recommendation of the trial stronger (*Strength of Recommendation (Parent)*).

Clinician Factors – Presentation of Risks and Benefits:
Parents were less likely to say the doctor was a reason for their decision if their ICC included a discussion of the *Physician’s Right to Withdraw* the child from the trial or more than two *Total Oversight/Control Mechanisms*. Parents

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were also less likely to cite the doctor as a reason if their ICC contained at least one statement of *Uncertainty About Risk* or at least one mention of *Other Patients/Children as Recipients* of benefit from their child’s participation in the trial.
Better Monitoring

Figure 12: Relationships Between Independent Variables and Better Monitoring as a Reason for Participation in the Trial

Patient Factors
Total Prognosis – Death/Recurrence:
$X^2 = 3.99, p < .05$

Social Network Factors
None

Parent Factors
Religion:
$X^2 = 4.23, p < .04$

Clinician Factors
Increased Toxicity – Unlikely:
$X^2 = 4.86, p < .03$
Decision-Making Preference:
$X^2 = 2.79, p < .10$
Pressure:
$X^2 = 2.78, p < .10$

Better Monitoring is Reason for Participation (Yes/No)

There were 3 variables that were significantly related to citing better monitoring as a reason for participation in the trial: 1 patient variable, 1 parent variable, 1 clinician variable, and 0 social network variables. Two additional clinician variables approached significance.
Table 35: Factors Related to Citing Better Monitoring as a Reason for Participation in the Trial

<table>
<thead>
<tr>
<th>Independent Variables (% Within Variable)</th>
<th>Better Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Yes</td>
</tr>
<tr>
<td>Total Prognosis – Death/Recurrence</td>
<td></td>
</tr>
<tr>
<td>None (43.8%)</td>
<td>23.1</td>
</tr>
<tr>
<td>&gt;=1 (56.2%)</td>
<td>8.0</td>
</tr>
<tr>
<td>Religion</td>
<td></td>
</tr>
<tr>
<td>Protestant (50.6%)</td>
<td>22.2</td>
</tr>
<tr>
<td>Other (49.4%)</td>
<td>6.8</td>
</tr>
<tr>
<td>Increased Toxicity – Unlikely</td>
<td></td>
</tr>
<tr>
<td>None (68.5%)</td>
<td>8.2</td>
</tr>
<tr>
<td>&gt;=1 (31.5%)</td>
<td>28.6</td>
</tr>
<tr>
<td>Decision-Making Preference</td>
<td></td>
</tr>
<tr>
<td>Doctor Decides (30.3%)</td>
<td>25.9</td>
</tr>
<tr>
<td>Shared/I Decide (69.7%)</td>
<td>9.7</td>
</tr>
<tr>
<td>Pressure</td>
<td></td>
</tr>
<tr>
<td>None (78.7%)</td>
<td>18.6</td>
</tr>
<tr>
<td>Some/Much (21.3%)</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Patient and Parent Factors:

Parents were more likely to cite better monitoring as a reason for their decision to participate in the trial if they reported their Religion as Protestant. Parents were less likely to say that better monitoring was a reason if the physician made at least one Prognosis – Death/Recurrence statement during the ICC.

Clinician Factors – Doctor/Parent Relationship:

Parents were more likely to list better monitoring as a reason for participation if they preferred the doctor to be the primary decision-maker (Decision-Making Preference).
Clinician Factors – Physician’s Recommendation:

Parents were less likely to list better monitoring as a reason for participation in the trial if they felt some or much Pressure to enroll their child on the trial.

Clinician Factors – Presentation of Risks and Benefits:

Parents were more likely to cite better monitoring as a reason if the physician made at least one Increased Toxicity – Unlikely statement during the ICC.
**Logistic Regression**

Variables found to be significantly associated with the decision itself or the reasons for participation were subsequently entered into a forward stepwise logistic regression model to determine whether they remained significant after controlling for the effects of the other variables. *Strength of Recommendation (Parent)* was excluded from the regression model for Doctor because there was no variability in one category of the variable (see Table 34). *Pressure* was excluded from the regression model for Better Monitoring for the same reason (see Table 35). A probability for entry of .05 and a probability for removal of .10 were used. It was necessary to run separate logistic regressions for each category of the dependent variable because they are not discrete (parents could give multiple reasons for their decision).

The results of the logistic regression analyses are shown in Table 36 below. The Nagelkerke R Square value reported in Table 36 indicates the percentage of the dependent variable that can be explained by all the independent variables in the model. The table lists the variables that had an independent effect on each of the dependent variables, as well as the odds ratio for each of the relationships. Within each dependent variable, the independent variables in the model are presented in descending order according to the odds ratio.
Table 36: Results of Logistic Regression Analyses

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>R for Model</th>
<th>Independent Variables</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>On/Off Trial Decision</td>
<td>.46</td>
<td>Parent-Directed Decision (Doctor)</td>
<td>12.92</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Network Members Present</td>
<td>5.19</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Network Facilitation of Communication</td>
<td>4.14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total Explicit Recs for This Child</td>
<td>.15</td>
</tr>
<tr>
<td>Benefit is Reason</td>
<td>.44</td>
<td>Experiment – No</td>
<td>8.34</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total Implicit Recommendations</td>
<td>7.83</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Understanding of Randomization</td>
<td>6.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total Direct Benefit – This Child</td>
<td>.20</td>
</tr>
<tr>
<td>Altruism is Reason</td>
<td>.14</td>
<td>Experiment – Yes</td>
<td>3.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total Positive Illness Severity</td>
<td>.28</td>
</tr>
<tr>
<td>Right to Withdraw is Reason</td>
<td>.25</td>
<td>Patient Age</td>
<td>4.12</td>
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<tr>
<td></td>
<td></td>
<td>Understanding of Randomization</td>
<td>.24</td>
</tr>
<tr>
<td>Comparison to Standard is Reason</td>
<td>.23</td>
<td>Risk Level</td>
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<td>Network Facilitation of Communication</td>
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<td>Safety is Reason</td>
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<td>Allowance for Modification in Trial</td>
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<td>Religion</td>
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<tr>
<td></td>
<td></td>
<td>Increased Toxicity – Unlikely</td>
<td>.18</td>
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Four variables remained significantly related to the on/off trial decision when controlling for the effects of the other variables in the regression model.
The regression for direct benefit resulted in 4 variables in the model, altruism had 2, the right to withdraw had 2, comparison to standard had 3, safety had 5, doctor had 2, and better monitoring had 2. The odds ratio for each pair of variables in Table 36 describes the strength of the relationship. For example, the odds ratio of 5.19 for the relationship between the on/off trial decision and Network Members Present tell us that in cases where no network members were present for the ICC, the odds of the parent participating in the trial is 5.19 times that of those with a network member present for the ICC. The results of the analyses reported in this chapter will be discussed in Chapter 11.
Chapter 11: Discussion and Conclusions

The purpose of this research was to enhance understanding of parental decision-making regarding their child's participation in a randomized clinical trial (RCT) for the treatment of acute leukemia. This was accomplished by 1) describing the reasons parents gave for their decision about their child's participation in a clinical trial for the treatment of acute leukemia, and 2) examining the patient, parent, clinician, and social network factors that influenced parents' decision to participate in the trial.

Discussion: Summary of Results

The following discussion of the results reported in previous chapters is organized by the topics covered in Chapters 3-9. As explained in the Methodology Chapter, all variable names are shown in bold italics for clarity.

Parent Decision-Making

Chapter 3 presented the dependent variables of the study, including the On/Off Trial Decision and the reasons given by parents for their decision to enroll their child in the trial. The 82% consent rate for the trial in the sample of 108 parents is in line with the high pediatric cancer trial participation rates reported in the literature (Bleyer 1997; Hirschfeld, et al. 2000; Murphy 1995; Ross, et al. 1996). Although most parents did decide to participate in the trial, these parents reported many different reasons for their decision.
As in other studies of parental decision-making about trial participation (Harth and Thong 1990; van Stuijvenberg, et al. 1998; Zupancic, et al. 1997), Direct Benefit and Altruism were the two most frequently cited reasons for participation in the trial. Eighty percent of parents listed benefit to their child as a reason for their decision to participate. Because there is very little, if any, chance of benefit to an individual child from participation in a phase III cancer trial, an argument could be made that parents who cited Direct Benefit to their child did not make a rational decision. From this standpoint, parents acting as rational decision-makers would only list benefit to others (Altruism) as a reason for participation. However, it is important to bear in mind the context of this decision, in which parents may grasp any chance, however small, to benefit their child with cancer. The majority of reasons given by parents in the Direct Benefit category mentioned unconditional benefit rather than just a chance for benefit. This suggests that most parents who decided to enroll their child on the trial committed to the trial being the best treatment for their child, leaving uncertainty behind.

Altruism was the second most often cited reason for participation, with 67% of parents listing this reason. Other studies of parental decision-making about trial participation found higher rates of altruistic motivation (Harth and Thong 1990; Zupancic, et al. 1997). This difference could be due to the fact that parents in this study were not prompted for specific reasons, thereby omitting the social desirability of responding affirmatively to a question about helping others. The majority of reasons given in the Altruism category
mentioned benefit to other patients or children rather than science, knowledge, or treatment in general. This points to the parents’ desire to help others like their child more than a general or impersonal recipient.

Not only did the parents in this study list benefit to their child (*Direct Benefit*) more often than benefit to others (*Altruism*), but those who cited both gave top priority to benefit for their child in their response to the open-ended question. This is in contrast to other studies that showed altruism as the most often cited reason (Harth and Thong 1990; van Stuijvenberg, et al. 1998; Zupancic, et al. 1997), which may, again, be a factor of the research methodology. This difference in the relative importance of altruism may also be an effect of the decision-making context since the other studies did not include children with a life-threatening disease like cancer. Parents who are not faced with a disease as serious as cancer may be more driven by a desire to help others because their child’s life is not at stake.

A significant finding from this study is that parents frequently gave reasons for their decision other than *Direct Benefit* or *Altruism*. The *Right to Withdraw, Comparison to Standard,* and *Safety* were all reported by roughly one-fourth of the parents who decided to participate in the trial. These reasons are absent from previous decision-making studies, probably because they were not included in the list of reasons parents were asked to choose from. By allowing parents to respond in their own words, without prompting for particular reasons, the interviews produced reasons that are not typically considered in the decision-making literature.
In comparison to many studies of adult patients' decision-making that found the doctor to be an important reason for trial participation (Bevan, et al. 1993; Dehlinger 1986; Jenkins and Fallowfield 2000), the Doctor was only cited as a reason for participation by 16% of parents in this study. This difference could be a result of the adult versus pediatric contexts. The infrequency with which the Doctor was cited as a reason may also be due to parents' perception that they made the decision without the influence of the doctor. These same parents, however, may have responded affirmatively to a question prompting specifically for whether the doctor was a reason for their participation for the same reasons relating to social desirability mentioned above with respect to altruism.

Patient Factors

The patient factors analyzed and described in Chapter 4 were gender, age, risk level, prognosis, and illness severity. Patient Gender was not significantly associated with any of the dependent variables. Patient Age was related to the Right to Withdraw as a reason for participation in the trial, with parents of younger children being more likely to cite the Right to Withdraw as a reason. One potential explanation for this is that parents are more concerned about the potential for unexpected toxicities when their child is very young, and the right to withdraw gives them reassurance that they have some control over stopping their child's participation in the trial if it were harmful.
The child’s Risk Level was related to the Comparison to Standard and Safety reason categories, with parents of lower risk children being more likely to cite Comparison to Standard or Safety as a reason for their decision to participate. The Numerical Prognosis given during the ICC was also significantly associated with the Comparison to Standard and Safety categories, with parents of children given a higher chance of cure being more likely to cite Comparison to Standard or Safety as a reason. A likely reason for these findings is the lesser risk of the trials that children with a lower risk and higher prognosis are treated on. These lower risk trials involve experimental arms that are very similar to the standard treatment. Because all the treatments on the trial are similar to standard, they pose very little risk in terms of additional side effects or receiving inferior therapy.

Although there was a more or less even number of low and high risk patients, there were more than twice as many Positive Illness Severity statements by physicians than Negative Illness Severity statements. This optimistic framing of illness severity most likely represents physicians’ desire to maintain hope for parents who have just been given a devastating diagnosis of cancer for their child. Similarly, physicians’ propensity to focus on the bright side of the situation is revealed by the fact that the child’s Prognosis is framed in terms of Cure/Survival more than three times as often as it is framed in terms of Death/Recurrence. Although physicians were honest with parents about the child’s Numerical Prognosis, disclosing the same number to parents in the ICC as they reported on a questionnaire for our study, the positive
framing of the prognosis in terms of cure/survival may serve to maintain hope for parents.

The physician’s presentation of the child’s illness severity influenced parental decision-making in several ways. Positively framed discussions of Illness Severity were related to the Direct Benefit and Altruism reason categories. Parents who were involved in ICCs with more than one Positive Illness Severity statement were less likely to cite Direct Benefit as a reason for participation in the trial, but were more likely to cite Altruism as a reason. Perhaps parents whose child’s illness severity is framed in a positive light view their child as relatively well off and therefore focus on the potential benefit to others in their decision-making. Negatively framed discussions of illness severity were related to the Safety reason category, with parents involved in ICCs with at least one Negative Illness Severity statement being less likely to list Safety as a reason. Parents who are presented with a negative statement about their child’s illness severity may perceive the trial as riskier to their child because their child is doing relatively poorly, and thus be less inclined to say safety is a reason for their decision.

The doctor’s presentation and framing of the child’s Prognosis also impacted parental decision-making. When the physician made more than two prognosis statements framed in terms of Cure/Survival, parents were less likely to cite Safety as a reason for their decision. The reason for this relationship is unclear, but the high number of discussions about the child’s chance of cure must somehow shift parents’ focus away from the safety of the
Parents involved in ICCs with at least one discussion of the chance of
Death or Recurrence were less likely to list Better Monitoring as a reason for
their decision to participate in the trial, although more research is needed to
explain this relationship.

Parent Factors
The parent variables included in this research were gender, age, ethnicity,
socioeconomic status, education, religion, understanding of randomization, and
the parent's perception of the riskiness of the trial. The Gender of the parent
interviewed was not related to parental decision-making. Parent Age was
significantly associated with the Direct Benefit and Doctor reason categories,
with parents over the Age of 35 being more likely to cite Direct Benefit or the
Doctor as a reason for their decision. It may be that the decision-making of
older parents is influenced more by the doctor because of the trend for earlier
generations to have greater respect for and deference to authority figures such
as doctors. The tendency for older parents to focus more on benefit to their
child may be related to their view of the importance of the doctor. Older parents
may be more prone to feel that the trial must be of benefit to their child if the
doctor presented it as an option. Further research is needed to test these
possible explanations for the relationship between parent age and decision-
making about trial participation.

Parents with higher Education and Socioeconomic Status were more
likely to list the Right to Withdraw as a reason for their decision to participate
in the trial. Parents with higher *Education* were also more likely to cite *Safety* as a reason for their decision. These relationships may merely be a reflection of these parents' higher understanding of their right to withdraw and safety issues related to the trial. It is also possible that parents with higher education and socioeconomic status are more concerned about their ability to control aspects of trial participation such as the right to withdraw. These parents may also engage in more balanced decision-making, considering the risks (or lack of risks) in addition to the benefits of trial participation, and thus cite safety as a reason more often than parents with less education.

Parents' reported *Religion* also played a significant role in decision-making, with Protestants being more likely to participate in the trial (*On/Off Trial Decision*) and cite *Better Monitoring* as a reason for participation, but less likely to cite the *Right to Withdraw*. More research is needed to uncover the ways in which *Religion* impacts decision-making. One potential avenue to explore is suggested by Butow's finding that religion has a significant influence on patient attitudes toward decision-making, with those believing God controlled the outcome of disease desiring less decision-making responsibility (Butow, et al. 1997). Are Protestants more likely to place control in the hands of God compared to Catholics and non-Christians, thereby lessening their desire for power over stopping participation? Do Protestants have a higher degree of faith in God to take care of the child regardless of the treatment received, and does this result in Protestants being more likely to participate in the trial?
Interestingly, the finding that Protestant parents were more likely to participate in the trial runs contrary to the classic pediatric research ethics debate between Paul Ramsey and Richard McCormick. Using a Protestant perspective of ethics, Ramsey argued that any research on children was unethical unless the goal is strictly therapeutic (Ramsey 1976). He maintained that parental consent was invalid because parents can only ethically choose treatments for their children that are geared toward their individual care. On the other hand, McCormick, a Catholic theologian, stressed the importance of social justice or altruism, and contended that parental consent is validated by the fact that the child should choose to participate in minimal risk research if s/he could in order to contribute to the health of others (McCormick 1976). Future research is needed to determine whether and how these religious differences in ethical perspectives play out in actual parent decision-making. Such research will need to expand the assessment of religion beyond a simple label to include other measures such as church attendance.

Parent Ethnicity also impacted parental decision-making, with minority parents being less likely to cite the Right to Withdraw or Safety as reasons, but more likely to list Direct Benefit. As discussed in the literature, people of different ethnic groups may place more or less emphasis on autonomous decision-making, the doctor/patient relationship, and trust in physicians (Fox and Swazey 1984; Kaufert and O'Neil 1990). Further research is needed to explain how ethnicity affects decision-making in this context. Can these relationships between minority status and decision-making be explained by
higher trust or decision-making power given to doctors? In other words, are minority parents more likely to think that their child will benefit from the trial because it was presented by the doctor as an option, and are they less likely to consider the safety of the trial or the right to withdraw because they placed responsibility for these things in the doctor’s hands? Do minority parents sense more of a power differential between themselves and the physicians, and does this perception play a role in their decision-making process?

A comparison of parent and physician views of the riskiness of the trial showed that parents rated the trial as riskier than doctors did. Parents’ Perception of the Riskiness of the Trial was related to the Comparison to Standard reason category, with parents being more likely to mention Comparison to Standard as a reason if they rated the trial as less risky. This relationship may be due to a link in parents’ minds between the similarity of the trial to standard treatment and the riskiness of the trial, such that parents view the trial as less risky because of its similarity to standard treatment.

Parental Understanding of Randomization influenced parental decision-making in many ways. Parents who understood randomization were less likely to mention Direct Benefit, but more likely to cite Altruism as a reason for their decision to participate in the trial. Parents who understood randomization may have a better overall understanding of the trial. If so, these findings may represent the parents’ understanding of the unlikelihood of benefit for their child and the purpose of the trial as helping children in the future. Parents who understood randomization were also more likely to cite the Right
to Withdraw, Comparison to Standard, or Safety as reasons for participation in the trial. This may again reflect a more nuanced understanding of the risks and benefits of the trial, or consideration of more factors during decision-making as a result of their higher understanding.

Social Network Factors

Chapter 5 presented the analysis of the support given by network members during the informed consent conference and during the parents' decision-making process. A comparison of the network members present during the ICC and the network members from whom parents sought advice shows that parents received support from different network members in these two contexts. While the network members present during the ICC were almost exclusively extended family members, parents reported seeking advice after the ICC from friends and family who had some medical background or experience with cancer, as well as other parents of children with leukemia and doctors from outside the hospital.

This finding points to the different types of support given by various network members, as described in the literature on social networks (Berkman, et al. 2000; Horwitz 1978; Thompson 1995). More specifically, support given during the ICC by family members in the categories of Questions About Trial, Non-Trial-Related Questions, Comments About Child/Family, and Facilitation of Communication all fall under Berkman's definition of instrumental support (Berkman, et al. 2000). Network support in the
**Statements of Solidarity** category is representative of emotional support (Berkman, et al. 2000; Thompson 1995), while support in the **Offers of Advice/Opinion** category is a type of informational support (Berkman, et al. 2000). Berkman defines the appraisal type of support as help with decision-making and giving feedback (Berkman, et al. 2000), which is the primary type of support parents' sought from friends, family, and doctors with particular expertise after the ICC. This research shows that parents receive diverse kinds of support from many different network members during their decision-making about enrolling their child on a clinical trial. In addition, the support provided by the network members during the ICC is evidence of the network impacting the content of the discussion by being present at the doctor-family encounter, as described by McKinlay (McKinlay 1981).

The **Presence of Network Members** during the ICC was significantly related to parents’ decision about whether or not to participate in the trial (**On/Off Trial Decision**). Specifically, parents who had at least one network member accompany them in the ICC were less likely to participate in the trial. Similarly, parents were less likely to participate in the trial when there was at least one instance of a network member **Facilitating Communication**, asking a **Non-Trial-Related Question**, or providing support of any kind during the ICC (**Total Network Questions/Comments**). The presence of a network member during the ICC may offset the typically unequal power relations during the meeting by increasing the number of people who are viewed as advocates for the parents and child. Parents may feel more comfortable actively refusing the
trial when they are empowered by having others “on their side”. In the same way, parents who are provided support in the form of questions or facilitation of communication may feel more in control of the situation via better understanding and thus more qualified to make a decision they might view as contrary to the physician’s wishes.

The actual support provided by network members who were present during the ICC also influenced decision-making in several ways. All types of support provided by network members during the ICC (Trial Questions, Non-Trial-Related Questions, Facilitation of Communication, Comments About Child/Family, and Total Questions/Comments) were associated with the Comparison to Standard reason category. Parents were more likely to cite Comparison to Standard as a reason for their decision to participate in the trial when a network member provided any type of support during the ICC. This may, again, reflect a better understanding of the trial, and in particular its similarity to standard treatment, as a result of instrumental support of network members.

Finally, parents were more likely to list the Doctor as a reason for their participation in the trial when a network member asked a Non-Trial-Related Question or provided support of any kind (Total Network Questions/Comments). One possible explanation for this finding is that the network members’ question asking and other support during the ICC may prompt the doctor to provide more information that is perceived as helpful to
parents’ decision-making, thus making them more likely to cite the doctor as important.

Clinician Factors: Doctor/Parent Relationship

Chapter 6 described two aspects of the doctor/parent relationship: trust and level of shared decision-making. Parents’ level of Trust in the physician was very high. Parents with higher levels of Trust in their child’s doctor were more likely to cite Direct Benefit as a reason for their participation in the trial, most likely because they trust the doctor to present a treatment that would be in their child’s best interests. As expected, parents with higher levels of Trust in the physician were also more likely to cite the Doctor as a reason for their decision.

The analysis of shared decision-making outlined in Chapter 6 showed that 30% of ICCs had no evidence of shared decision-making, and there was only an average of 2 instances of Shared Decision-Making in the 108 ICCs. Those parents who were involved in ICCs with more than one instance of Shared Decision-Making were more likely to say Direct Benefit was a reason for their decision to participate in the trial. It is likely that parental sharing of their opinions or decision-making process during the ICC may be the driving force behind this relationship since it was by far the most common type of shared-decision-making. Perhaps parents who discussed their concerns about the trial with the doctor during the ICC were more likely to come to the conclusion that their child would benefit from the trial, although the reason for this is uncertain. One potential explanation is that clinicians may emphasize the
potential for benefit to the child in response to parents’ expressed concerns about the trial.

Parents’ Decision-Making Preference was associated with the Better Monitoring reason category. Parents who reported a preference for the doctor being the primary decision-maker were more likely to list Better Monitoring as a reason for participation in the trial. Parents who prefer less decision-making responsibility may be inclined to believe for some reason that the doctor will watch their child more closely if they participate in the trial. On the other hand, parents may abdicate decision-making responsibility to the doctor because they believe that the doctor will watch their child more closely.

Table 11 in Chapter 6 shows that parents and doctors both tend to rate themselves as the most important in influencing the decision about trial participation. In cases where the physician rated him or herself as the most important in making the decision about trial participation (Doctor-Directed Decision (Doctor)) or the parent rated the doctor as most important (Doctor-Directed Decision (Parent)), parents were more likely to participate in the trial (On/Off Trial Decision). In contrast, in cases where the physician rated the parents as the most important in making the decision (Parent-Directed Decision (Doctor)), parents were less likely to participate in the trial (On/Off Trial Decision). It seems, then, that the decision to participate in the trial is seen as a doctor-directed decision, while the decision to not participate in the trial is seen as a parent-directed decision. It could be that doctors and parents alike view the decision to decline participation as one that requires the active
refusal of the parents, while participation in the trial may be perceived as parents' passive acceptance of the physician's decision to enroll the child in the trial.

This finding suggests that physicians may be moving in the direction of using an "opt-out" approach to informed consent in this setting. The opt-out approach to research subject recruitment typically involves obtaining a signature to indicate refusal to participate rather than a signature for accepting participation, and the default assumption is that people prefer to participate in the research.

The opting out approach to informed consent has been used to increase participation rates in less than minimal risk research such as: review of medical records (Heaney, et al. 2001), an observational study involving a questionnaire, cardiovascular exam, blood tests, and follow-up (Junghans, et al. 2005), school-based survey research (Eaton, et al. 2004), and primary care follow-up for high-risk infants (Rogers, et al. 1998). In addition, in 1999, the US Institute of Medicine recommended implementation of the opt-out approach to prenatal HIV testing to increase uptake of testing (De Cock, et al. 2003; Stringer, et al. 2001). Using this method of consent, women in prenatal care are tested for HIV unless they actively refuse. Several European countries have adopted the opt-out system to increase rates of organ transplantation (Gundle 2005; Kennedy, et al. 1998; The Council on Ethical and Judicial Affairs 1994), and many have called for switching to this approach in order to increase organ donation in the US (Berry 1999; Gill 2004; Gundle 2005).
Some caution that the opt-out approach could cause people to feel pressure not to opt out because it is socially unacceptable (Kennedy, et al. 1998). This is a valid concern, however very few parents in this study reported feeling any pressure to participate in the trial. Although physicians in this study did seek a signature from parents to indicate their consent to participate, the manner in which the physicians presented the trial is in many ways indicative of an opt-out approach. Along with viewing refusals as parent-driven decisions, physicians rarely initiated shared decision-making and made frequent use of implicit recommendations that presented the trial as the primary treatment option or the standard of care that parents needed to passively accept or actively refuse.

These findings raise many questions regarding physicians’ approach to informed consent for Phase III pediatric cancer trials. Do clinicians use an opt-out approach to the consent process because they consider the decision about the trial to be a burden for parents? Is the opt-out approach preferred because it only burdens the few who choose to decline the trial? Does it in fact reduce the burden on already anxious parents? Is the greater burden on refusers justified by the higher accrual rates that may be attributable to the opt-out approach? Who should bear the greatest burdens – accepters or decliners? Is it worse to burden more parents with having to actively decide to participate or to give a greater burden to fewer parents who actively decline the trial?

Do the common beliefs that children benefit from trial participation or that research is the standard of care contribute to the use of the opt-out approach?
Given the similarity of treatment on a Phase III pediatric cancer trial to off-study therapy, is the risk to subjects low enough to judge this approach appropriate in this context? Are the documented high accrual rates for Phase III pediatric cancer trials due to the use of the opt-out approach? Based on high accrual rates in pediatric cancer trials, should the default assumption be that parents prefer to participate? However, just because most parents do ultimately decide to participate doesn't mean that most would favor an opt-out approach to consent. Further research is warranted to answer these questions and explore physician and parent perspectives on this issue.

Along these same lines, parents were less likely to cite the Doctor as a reason for their decision when they rated themselves as most important in influencing the decision (Parent-Directed Decision (Parent)), but were more likely to cite the Doctor as a reason when they rated the doctor as most important in influencing the decision (Doctor-Directed Decision (Parent)). Parents who rated the doctor as most important in influencing the decision (Doctor-Directed Decision (Parent)) were also more likely to list Direct Benefit or Comparison to Standard as reasons for their decision.

Clinician Factors: Physician Recommendation

As described in Chapter 7, the physician's recommendation of the trial was measured in several ways. Table 13 in Chapter 7 shows that the majority of physicians reported the trial as the treatment they most strongly recommended during the ICC (Trial Most Recommended by Doctor Report). In comparison,
less than a third of parents said the trial was the most strongly recommended treatment (*Trial Most Recommended by Parent Report*). Physicians may be driven to recommend the trial, and report recommending it, by the culture of pediatric oncology which is very research-oriented. Parents, on the other hand, may equate a recommendation of the trial with coercion, leading them to report that no recommendation was made regardless of the data in Chapter 7 which shows that explicit recommendations for the trial were given in the majority of ICCs. Parent and physician report of the trial as the most strongly recommended treatment were not related to parental decision-making.

Physician recommendations of the trial were grouped into three types: *Implicit Recommendations, Explicit Recommendations for All Children,* and *Explicit Recommendations for This Child.* This analysis shows that more than half of ICCs contained at least one *Implicit Recommendation* of the trial. *Implicit Recommendations* were related to the *Direct Benefit* and *Comparison to Standard* reason categories. Parents who were given at least one *Implicit Recommendation* for the trial during the ICC were less likely to cite *Direct Benefit* as a reason for their decision, but more likely to cite *Comparison to Standard* as a reason. Further research is needed to uncover the reasons behind these influences of *Implicit Recommendations* on parental decision-making, but these findings point to the necessity to consider implicit language in assessments of recommendation. Implicit language used in presenting the trial may have more potential to influence parental decision-making in the newly diagnosed pediatric cancer context because of parents’

247
vulnerability in terms of the shock of the diagnosis, the severity of the illness, and their unfamiliarity with the environment, disease, and its treatment.

An explicit recommendation was found in 70% of ICCs. Explicit Recommendations for All Children had no impact on parental decision-making. On the other hand, parents who were given at least one Explicit Recommendation for Their Child were more likely to participate in the trial (On/Off Trial Decision). In addition, parents who were given at least one Explicit Recommendation for Their Child were less likely to cite the Right to Withdraw as a reason for their decision to participate in the trial. Thus, parents were more swayed by recommendations made in reference to their child, choosing participation in the trial more often and being less likely to report consideration of the right to withdraw in their decision-making. Parents may cite the Right to Withdraw less frequently because they don't feel the need for control over stopping participation when the doctor explicitly recommended the trial as the best treatment for their child.

A Recommendation Score was computed for each ICC using the number of implicit and explicit recommendations made by the physician. Only 15% of ICCs had a Recommendation Score of 0, representing a completely neutral presentation of the trial. The Recommendation Score was significantly related to the On/Off Trial Decision, with parents involved in an ICC with a higher Recommendation Score being more likely to participate in the trial. This finding further validates the powerful effect that the physician's recommendation has on parental decision-making.
The Parent Advisory Group on Informed Consent suggested that the offer of the trial contains an implicit recommendation. These parents advocated against physicians making an explicit recommendation for the trial unless the parents request one. This analysis of the physician's recommendation during 108 ICCs reveals a mismatch between actual practice and the suggestions made by the PAGIC members. In summary, there were few cases where the trial was presented neutrally, and the majority of ICCs contained explicit recommendations for the trial, 88% of which were unsolicited by parents.

The parents' rating of the Strength of the Recommendation was associated with the Comparison to Standard and Doctor reason categories. As expected, parents who gave a stronger rating of the physician's recommendation were more likely to cite the Doctor as a reason for their decision. In addition, parents who gave a stronger rating of the physician's recommendation were more likely to list Comparison to Standard as a reason for participation in the trial. The link between these two variables is not obvious, but parents may feel that the doctor strongly recommended the trial because of its similarity to standard treatment. Although the recommendation variables discussed above did have an influence on parental decision-making, the majority of parents reported feeling no Pressure to participate in the trial. It is possible that parents do not feel pressure because they are unaware of the effects of the physician's recommendation on their decision-making.
Clinician Factors: Presentation of Benefits

The physician's presentation of direct benefit and altruism was described in Chapter 8. In the 108 ICCs, there were twice as many physician statements of benefit that were framed generally (Total Direct Benefit – General) compared to statements of benefit made with reference to the particular child (Total Direct Benefit – This Child). This may represent a concern on the part of clinicians that parents may interpret statements about potential benefit for their child as a guarantee that the trial will be advantageous. It may also reflect physicians' uncertainty about how the trial will affect any particular child.

A striking finding is that 86% of the 108 ICCs included some type of statement by the physician about the chance for direct benefit to the child from trial participation. This is not surprising in light of the fact that the majority of clinicians who completed our General Clinician Questionnaire expressed the belief that patients do receive direct benefit from participation in trials. However, this finding may be a cause of concern because of the potential for coercion from presenting the trial as beneficial to the child. In the context of pediatric cancer, parents may be particularly susceptible to the influence of such statements. These parents are in a vulnerable position because they are simultaneously faced with the shock of their child being diagnosed with cancer, an unfamiliar hospital environment, and extraordinary amounts of complex medical information. They are likely to seize any option that is presented as potentially improving their child's chances for cure, therefore a simple statement
by the physician about a chance for benefit to the child may unduly persuade them to participate in the trial.

Indeed, parents were more likely to participate in the trial (On/Off Trial Decision) when the doctor discussed the potential for direct benefit to their child during the ICC (Total Direct Benefit – This Child). The physician's discussion of direct benefit was also significantly related to parents' reporting that direct benefit was a reason for their decision to participate. Specifically, parents involved in ICCs where physicians mentioned direct benefit to their child at least once (Total Direct Benefit – This Child), direct benefit in general more than once (Total Direct Benefit – General), or either type of direct benefit more than twice (Total Direct Benefit) were more likely to cite Direct Benefit as a reason for participation in the trial. This finding lends rationality to the decision-making process of these parents because it is logical to participate in the trial for reasons of benefit to your child if the doctor told you there was some chance of benefit. It is not surprising that parents translate physicians’ discussion of the possibility of benefit for child-subjects as a group into absolute conviction that their child will benefit.

The discussion of altruism was found in the majority of ICCs, with physicians most often mentioning science, knowledge, or treatment in general as the recipient of benefit from the child’s participation in the trial (Total Clinicians/Science Recipients). This is in contrast to parental decision-making with respect to altruism since most parents citing Altruism as a reason for participation made reference to other children or patients as the recipient of
benefit. This may represent physicians’ greater interest in the research enterprise as opposed to parents viewing everything from the perspective of their child and others like him/her.

While the discussion of direct benefit by the physician during the ICC significantly impacted parents’ reporting of benefit as a reason, the physician’s discussion of altruism had no influence on parents’ reporting of Altruism as a reason. The only way in which altruism discussion affected parental decision-making was through the discussion of Other Patients/Children as Recipients of benefit from the child’s participation in the trial. Parents were less likely to cite the Doctor as a reason for participation in the trial when the doctor made at least one reference to Other Patients/Children Recipients of benefit from the child’s participation in the trial. Perhaps parents who were presented with the idea that the trial is designed to help other children were inclined to view the doctor’s role in decision-making as diminished because the purpose of the trial was not focused on their child.

Clinician Factors: Presentation of Risks

Chapter 9 described the many aspects of the risks and safety of the trial that were covered by physicians during the ICC, including increased toxicity, decreased cure rate, uncertainty, similarity to standard, experimental nature, and mechanisms of oversight and control.

The possibility of increased toxicity on the trial was commonly discussed in the ICCs (Increased Toxicity – Possible), as was the unlikelihood of a
decreased cure rate (Decreased Cure Rate – Unlikely). Therefore, physicians frequently presented the risks of the trial as being a chance for more side effects, without a negative effect on the chances for survival. Discussions of the possibility for increased toxicity (Increased Toxicity – Possible) were not related to parental decision-making, but parents involved in ICCs with at least one discussion of the safety of the trial in terms of the unlikelihood of increased toxicity (Increased Toxicity – Unlikely) were more likely to cite Better Monitoring as a reason for participation in the trial. Parents who were reassured of the safety of the trial in terms of side effects may be prone to transform this concept of safety into additional supervision of their child.

Parents were more likely to cite Safety as a reason for their decision when the physician made at least one statement about the unlikelihood of a decreased cure rate on the trial (Decreased Cure Rate – Unlikely). It is possible that parents were more convinced about the safety of the trial, and thus cite it as a reason for their decision, when the physician assured them that it would not negatively impact their child’s survival. Parents involved in ICCs with at least one Decreased Cure Rate – Unlikely statement were also more likely to list the Right to Withdraw as a reason for participation in the trial. A potential explanation for the connection between these two variables relates to an alternative interpretation of the Decreased Cure Rate – Unlikely variable from the perspective of parents. Although these statements point out the improbability of a decrease in cure rate, these statements may cause some parents to consider the possibility that the trial may be inferior for the first time.
These parents may be concerned about the potential for something to go wrong, and weigh the importance of the right to withdraw more heavily during decision-making.

Discussion of the uncertainty related to the trial was a common feature of the ICCs, with most of these discussions framed in terms of doubt about the benefits of the trial (Uncertainty About Benefit). Physician statements of Uncertainty about Benefits were not related to parental decision-making, however parents were less likely to cite the Doctor as important to their decision when the doctor made at least one statement of Uncertainty about Risks during the ICC. This may indicate that uncertainty about the risks of the trial is a bigger concern for parents than uncertainty about benefits. In addition, parents may be less likely to perceive the doctor as an authority in the decision-making process because the doctor expressed doubts about the risks of the trial. Parents involved in ICCs with more than four statements of uncertainty of any type (Total Uncertainty Discussions) were less likely to cite Direct Benefit as a reason for participation in the trial. This finding is probably due to the statements of uncertainty decreasing the likelihood that parents would view the trial as beneficial to their child.

Only a little more than half of the ICCs contained a discussion of the trial’s Similarity to Standard treatment, a defining feature of phase III pediatric cancer clinical trials. These discussions had a significant influence on parental decision-making, with parents being more likely to participate in the trial (On/Off Trial Decision) if the physician mentioned the trial’s Similarity to Standard at
least once during the ICC. The thought of enrolling their child on a clinical trial was probably less frightening, and therefore more acceptable, for parents who were told that it would not differ a great deal from the treatment they would receive if they did not participate in the trial. Parents involved in ICCs that contained an explanation of the trial’s *Similarity to Standard* were also more likely to cite *Altruism* as a reason for their participation in the trial. Parents may be more likely to consider the purpose of the trial as helping others when they understand that it is almost the same as what they would get outside of the trial and is therefore unlikely to have a significant effect on their own child.

The examination of how the word “experiment” was used during ICCs revealed that the trial was most often discussed as not being experimental, but some form of the word “experiment” was used in 70% of the ICCs (*Experiment Total*). Research has shown that parents have a negative connotation of the word “experiment”, therefore the use of the word in any context could influence decision-making about the trial (Advisory Committee on Human Radiation Experiments (ACHRE) 1995; Slevin, et al. 1995). Parents involved in ICCs containing at least one positive assertion that some aspect of the trial is experimental (*Experiment - Yes*) were less likely to cite *Altruism* as a reason for participation in the trial. Parents were less likely to say that *Direct Benefit* was a reason for their decision when the physician made at least one statement during the ICC negating the experimental nature of the trial (*Experiment - No*). It is not clear why these relationships between the experiment variables and parental decision-making exist, but it is likely that more in-depth interviews with
parents about their views of the experimental nature of the trial could elucidate the issue.

Four types of oversight or control mechanisms were described in Chapter 9, including family right to withdraw, data safety and monitoring, allowance for modification within trial, and physician right to withdraw. Parents were more likely to cite *Altruism* as a reason when the *Physician’s Right to Withdraw* the child from the trial was discussed during the ICC. Interestingly, parents were less likely to say the *Doctor* was a reason for their decision when the *Physician’s Right to Withdraw* was discussed. Parents were less likely to cite *Safety* as a reason for their decision when there was some discussion during the ICC of the ability to modify the child’s treatment within the trial (*Allowance for Modification Within Trial*). Finally, parents were less likely to participate in the trial (*On/Off Trial Decision*) when more than two kinds of oversight/control mechanisms were discussed during the ICC (*Total Oversight/Control Mechanisms*).

Further research is needed to uncover potential explanations for these unexpected findings. It is possible that although doctors and researchers tend to think of discussion of these oversight and control mechanisms as providing reassurance of the safety of the trial, parents may just be hearing the possibility that something could go wrong. Presentation of the need for these mechanisms may be primarily anxiety-provoking for parents, and thus influence their decision-making in complex and unexpected ways.
Conclusions

Anthropologists have long been interested in describing health and illness behavior, including decision-making about treatment. Decisions about participation in clinical research are becoming a common part of treatment seeking for many diseases, therefore it is important that we develop an understanding of how these decisions are made. This dissertation informs anthropological understanding of decision-making by providing information about how decisions are made in the relatively new decision-making context of clinical research.

The methodology employed in this dissertation draws on the strengths of both the predictive and descriptive approaches commonly used by anthropologists in decision-making research. By testing the hypothesized relationships in the decision-making model (Figure 1) that guided my analyses, this study bears some resemblance to the decision modeling approach utilized by Young and Garro (Young 1981b). However, Young and Garro described their approach as an attempt to describe and test shared standards of treatment choice in the Mexican communities in which they conducted their fieldwork (Young 1981b). The ability of my model to predict treatment decision-making is compromised by the heterogeneity of the parents in my sample. In other words, American society is more heterogeneous, compared to a small Mexican village, in terms of beliefs that influence treatment decision-making, which complicates the prediction of decision-making behavior. Along the lines of Young and Garro's research, this study provides preliminary exploration of the variables
that influence or predict decision-making in the context of pediatric cancer trials. Refinement and expansion of the variables included in the model will be necessary in order to take the analysis one step further by formalizing the model into a decision tree and testing it in another sample of parents following Young and Garro’s methodology.

The context of decision-making constitutes a major difference between the work of Young and Garro and the research reported here. Young and Garro studied treatment decisions for routine illness episodes, which increased the likelihood that standards of treatment choice would be shared and predictable (Young 1981b). The uncommonness and severity of childhood cancer adds complexity to the decision-making context examined in this dissertation. In this sense, the research might be more closely aligned with the work of John Janzen, who focused on treatment decisions for unusual illnesses in Zaire (Janzen 1978). In the context of uncommon illness episodes, Janzen employed a thick descriptive approach to examining decision-making (Janzen 1978). While I did not adopt his case study technique, my analysis did incorporate rich, in-depth description of the variables hypothesized to influence decision-making. This dissertation has demonstrated the value of using open-ended methods and qualitative textual analysis to study decision-making. A more robust picture of decision-making was made possible by allowing parents to present their reasons for participation in their own words and by analyzing the language used by physicians in presenting the clinical trial.
The testing of the model in Figure 1 revealed many significant influences on parental decision-making regarding trial participation. All four factors that were hypothesized to impact decision-making (patient, parent, clinician, and social network factors) were in fact shown to be related to decision-making. In other words, all participants in the informed consent process, including patients, parents, clinicians, and social network members, were found to shape parental decision-making in some way. Two themes resulted from the analyses that have important implications for decision-making and communication research: the physician's influence and the role of social networks.

The Physician's Influence:
This study provides evidence that the physician influences parental decision-making in many ways that are largely unexplored in other research. Measurement of the physician's role in trial decision-making is often limited to explicit recommendations. This study demonstrates the significant impact of physicians' use of language that implicitly recommends the trial. In addition, it shows the importance of analyzing the language used by the physician in describing the risks and benefits of the trial to families. Parents' decision about trial participation, as well as their reasons for participating, varied according to how the doctor presented the trial.

In addition, results of the qualitative analyses of the informed consent conferences confirm the significance of framing for decision-making illustrated previously in the literature (Kayser-Jones 1995; O'Connor 1989; Siminoff and
Fetting 1989; Tversky and Kahneman 1981). For instance, discussions relating to illness severity, prognosis, and the experimental nature of the trial were framed by physicians either positively or negatively, and these different ways of framing the discussions had a differential impact on decision-making. Statements about direct benefit and explicit recommendations for the trial were framed by physicians in reference to the particular child, or more generally for all children, and this framing influenced parental decision-making in a variety of ways. In her research on treatment decision-making in nursing homes, Kayser-Jones found a similarly strong effect of physician framing of alternatives on decision-making (Kayser-Jones 1995). A greater understanding of the physician’s role in the research decision can help physicians recognize the influence they have and use this influence in a way that aids parents in making their decision.

The Role of Social Networks:
The significant roles played by social networks both during and after the informed consent conferences indicate that the social reality of decision-making for many parents includes their network members. This finding contributes to a growing body of anthropological knowledge regarding the role of lay referral networks in treatment decision-making (Chrisman 1977; Janzen 1978; Kayser-Jones 1995; McKinlay 1973; McKinlay 1980). The considerable influence of social network factors on parent decision-making illustrates the need to broaden the list of variables examined in decision-making research. Many
anthropologists have argued that doctors need to be sensitive to the role played by network members in treatment decision-making, and this sensitivity can lead to improved doctor-family interactions (Chrisman 1977; Janzen 1978; Kayser-Jones 1995). By describing how parents utilize their social networks when faced with a decision about trial participation, this research supplies physicians with useful information to guide their communication practices. For example, the influence of network members on parental decision-making points to the need for physicians to broaden the informed consent process to include education of network members about the trial.

Practical Implications:
An understanding of how these research decisions are made by parents also informs bioethics and clinical practice. The increasing prevalence of clinical research trials for disease treatment has led to an ongoing discourse among researchers regarding the quality of informed consent for such research. In an effort to comply with ethical codes of conduct, such as those of disclosure and autonomy, clinicians often present the information they feel people need to make a decision about trial participation, and leave them to make the decision completely on their own. As Patricia Marshall argues, the general ethical principles that clinicians use to guide their informed consent practices are often too far removed from the actual experience of those involved in ethical decision-making (Marshall 1992). A focus on real-life situations and how they are dealt
with is necessary in order to explain the pluralism of decision-making that exists in the research context.

This study supplies clinicians with the types of information that parents find most important when making this difficult decision. If doctors are aware of the factors that influence parental decision-making, they will be better able to provide the information that parents need and support them during the decision-making process. In short, this research provides the description of parental decision-making that doctors and bioethicists need to improve informed consent because “good facts make good ethics” (Crigger 1995).

Future Directions

The results of this research suggest many potential avenues for future research. Although the list of variables analyzed in this study is quite extensive, there are several variables that were not measured, such as parents’ general attitude toward and experience with trials, social network experience with trials, parity, and parents’ general risk taking behavior. The effects of these factors on decision-making should be addressed in future research and would be a valuable contribution to the study of parental decision-making in the context of pediatric cancer trials.

Future studies would benefit from asking parents to identify the sequence in which they considered factors and the weight they gave to each one in order to further clarify the relationships between the different reasons parents gave for their decision. A bigger sample that includes more parents
who declined participation in the trial would allow similar analyses of the
different reasons for declining participation in the trial.

One next step might be to gather more information about the role of
social networks, including what kind of advice or other decision-making support
was received and why parents sought advice or help from certain network
members and not others. Information such as the proximity of relatives and
friends and the frequency of contact with different network members could
increase our understanding of who parents turn to for support (McKinlay 1973).
Data on why certain parents seek support could answer the question of whether
a more negative attitude toward doctors, hospitals, or clinical research leads
parents to seek support from their social network.

Another interesting direction the research could be taken in is to explore
the factors that influence how the physician presents the trial to parents, using
interviews with physicians to examine why they use certain language in
describing the trial or how their background and beliefs shape the way they
conduct informed consent conferences. Similar research with a larger sample
size would allow for comparison of multiple ICCs led by the same doctor to
determine whether doctors are consistent in their framing and presentation of
information or are influenced by factors specific to each family.

This dissertation has focused on description of how the independent
variables influenced parent decision-making. Further investigation of the
relationships between the independent variables would enhance understanding
of how interrelationships between these variables impact decision-making.
These analyses could also answer questions about the informed consent process, such as Do clinicians frame presentation of illness severity and prognosis differently according to the child's risk level? Is prognosis only framed in terms of death/recurrence for high risk children? How do clinicians use positive framing of illness severity for high risk patients?

Finally, some relationships discovered in this dissertation can only be explained by gathering more information about the variables involved. For instance, in-depth interviews to uncover parent perspectives of the role their religious beliefs played in decision-making will be necessary to understand why Protestants were more likely to participate in the trial and cite better monitoring as a reason for participation, but less likely to cite the right to withdraw.
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267

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