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Evaluating the quality of information about alternatives to research participation in oncology consent forms

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ABSTRACT

A careful consideration of the alternatives to research participation is an essential element of making an informed choice to enroll in a biomedical research study. While there is general agreement on the importance of informing prospective subjects about alternatives to research participation, little is known about how investigators communicate this information. The purpose of this study was to attempt to assess the quality of information about alternatives contained in informed consent documents in oncology randomized controlled trials. Our study indicates that there is room for improvement concerning the discussion of alternatives to research participation in informed consent documents in oncology randomized controlled trials. Though most of the documents in our study met the minimal disclosure standard found in the U.S. federal regulations, less than a third met the reasonable person standard, a widely accepted principle endorsed by the common law and various ethics guidelines and documents. There was a statistically significant difference between the alternative discussions in local and model forms ($P<0.0014$). The alternatives discussions in local informed consent documents were more likely to receive higher scores than those in model consent documents, with an odds-ratio of 3.5 to 1.

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1. Introduction

A careful consideration of the alternatives to research participation is an essential element of making an informed choice to enroll in a biomedical research study [1]. Many regulations and guidelines hold that investigators should provide prospective research subjects with information about alternatives. U.S. federal research regulations require that the informed consent process include "disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject" [2]. The Council for the International Organizations of Medical Sciences (CIOMS) guidelines state that investigators should inform subjects about "any currently available alternative interventions or courses of treatment" [3]. It is especially important for investigators to discuss alternatives when prospective subjects have several treatment options for their medical condition, some of which may be preferable to participating in a research study [4].

While there is general agreement on the importance of informing prospective subjects about alternatives to research participation, little is known about how investigators communicate this information. While many studies have been conducted on informed consent in research, few of these examine the discussion of alternatives [5]. In 2003, Horng et al published a study on informed consent documents in Phase I oncology studies that included some data on the description of alternatives to research participation. They found that 88% of the consent forms mentioned standard treatments as alternatives to research participation, 65% mentioned the option of receiving no treatment, 56% mentioned palliative or supportive care, and 52% mentioned other experimental treatments [6]. This study provided some useful data about

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the content of information contained in oncology consent forms, but it did not attempt to assess the quality of that information.

A more recent study conducted by two of us (and three other authors) suggested that there may be some cause for concern about the quality of alternatives discussions in informed consent documents. We found that only 17.4% of consent forms for oncology randomized controlled trials (RCTs) in which all of the treatments being investigated were available to the subjects without participating in the study actually informed subjects that they could receive these treatments off-study [7]. Information about the option of obtaining a treatment off-study is important for making a well-reasoned decision to participate in an RCT [4]. The purpose of our present study was to attempt to assess the quality of information about alternatives contained in informed consent documents in oncology RCTs.

2. Materials and methods

The consent forms were drawn from the sample used in our previous study of alternatives, which was obtained by requesting consent forms from Phase II, III, or IV non-pediatric U.S. oncology RCTs registered in Clinicaltrials.gov, a clinical trials registry supported by the National Institutes of Health (NIH) containing over 75,000 studies [4]. Studies registered at this website are sponsored by government agencies, private industry, and private foundations and take place in all 50 states and 140 countries. Our initial search on Clinicaltrials.gov yielded 1794 studies that met our search criteria. This list was pared down to 749 studies in which all of the treatments were commercially available at the initiation of the study and there were no placebo control groups. We did not include RCTs that examined the effectiveness of surgical procedures or radiation therapy. Consent forms were requested from a random sample of 250 of these studies, and 104 consent forms were acquired. The NIH Office of Human Subjects Research determined that the federal regulations for protection of human subject did not apply to our study because we did not obtain private information about human subjects or interact with human subjects.

We developed a scoring system to measure the quality of the alternatives discussion and coded all of the consent documents using this system. The system is based on (1) the U. S. federal regulations, and (2) the reasonable person standard. The U.S. federal regulations mention 14 different types of information that investigators should disclose to subjects (where appropriate), including alternative procedures or courses of treatment. While this list is useful, it omits important types of information that most people would want to know [8], such as financial interests related to the research [9] and the disposition of biological samples [10].

A widely recognized principle for disclosure that goes beyond the minimum regulatory requirements is the reasonable person standard, which has been adopted by most states in the U.S. and has been mentioned in various ethical guidelines, such as the Belmont Report [1,11]. According to the reasonable person standard, physician/investigators should disclose information that a reasonable person would want know to make an intelligent choice [1,4]. A strong argument can be made that a reasonable person would want to know something about the different alternatives in order to decide whether to choose one of the alternatives or participate in research, because to make an intelligent choice one must be able to evaluate the different options [4,12]. Simply knowing what the alternatives are does not necessarily help one decide whether to choose any of the alternatives.

Table 1
Scoring system for alternatives discussions.

Score	Definition
0	Document does not include a discussion of alternatives
1	Document mentions that alternatives exist but does not list or describe alternatives
2	Document lists or describes alternatives
3	Document lists or describes alternatives and provides information that could be useful in deciding whether to choose any of the alternatives

With these two different legal standards in mind, we defined the scores as follows (see Table 1). We gave a consent form a score of "0" if it contained no discussion of alternatives; a "1" if it mentioned that alternatives exist but did not list or describe any alternatives; a "2" if it listed or described alternatives; and a "3" if it listed or described alternatives and provided some information that could be helpful in deciding whether to choose one of the alternatives, such as (a) potential benefits or risks of alternatives, (b) availability of alternatives, or (c) the nature of the alternatives, such as the procedures used, etc. Consent forms that scored a 0 did not even meet the minimum regulatory requirements, while forms with a score of 1 possibly met the regulatory requirements, depending on how "disclosure" is interpreted. Forms with a score of 2 or above met the regulatory requirements, and forms with a score of 3 met the regulatory requirements and the reasonable person standard. Two of us, DR and DP, independently scored all of the documents according to the measures we developed. DR and DP agreed on the initial coding of over 95% of the documents and resolved disagreements following further discussion.

In addition to rating the quality of the alternatives discussion, we also counted the number of words in the alternatives discussion and the number of words in the entire consent document, which gave a measure of the percentage of the document devoted to the discussion of alternatives. In counting the number of words in the alternatives discussion, we did not include some statements that were placed in the section marked "alternatives" (or some similar marking) which did not have anything to do with alternatives, such as statements informing subjects that they have a right to withdraw at any time or statements about compensation for research injuries or liability.

We also collected information on the age of the consent document, which was based on the approval date for document; source of funding for the study (private vs. public); and the type of consent document, i.e. model vs. local. A local form was defined as a form approved by a particular IRB, while a model form was defined as a document drafted by a committee, such as an Oncology Cooperative Group, which could be implemented at different sites and approved by local IRBs. We were able to identify model forms because we requested them from Oncology Cooperative