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An Intervention to Improve Cancer Patients' Understanding of Early-Phase Clinical Trials

Nancy E. Kass, ScD,
Phoebe R. Berman Professor of Bioethics and Public Health, Bloomberg School of Public Health and Berman Institute of Bioethics, Johns Hopkins University, Baltimore, MD

Jeremy Sugarman, MD, MPH,
Harvey M. Meyerhoff Professor of Bioethics and Medicine, Department of Medicine, Berman Institute of Bioethics, Johns Hopkins University, Baltimore, MD

Amy M. Medley, MPH, PhD,
Behavioral Scientist, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA

Linda A. Fogarty, PhD,
Director, Results and Knowledge Management, Capacity Project, Chapel Hill, NC

Holly A. Taylor, PhD, MPH,
Assistant Professor, Department of Health Policy and Management, Bloomberg School of Public Health and Berman Institute of Bioethics, Johns Hopkins University, Baltimore, MD

Christopher K. Daugherty, MD,
Associate Professor, University of Chicago Medical Center, Chicago, IL

Mark R. Emerson, BS,
Research Associate, Department of Population, Family and Reproductive Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

Steven N. Goodman, MD, MHS, PhD,
Professor of Oncology, Berman Institute of Bioethics and Johns Hopkins School of Medicine, Johns Hopkins University, Baltimore, MD

Fay J. Hlubocky, MA,
Research Ethicist/Professional, University of Chicago Medical Center, Chicago, IL

Herbert I. Hurwitz, MD,
Associate Professor of Medicine, Duke University Medical Center, Durham, NC

Michael Carducci, MD, and
Associate Professor of Oncology and Urology, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD

Annallys Goodwin-Landher, BA
Research Assistant, Pathways Study, Duke Center for Palliative Care, Duke University Medical Center, Durham, NC

The consent process for human subjects research educates potential participants about research risks, benefits, and procedures so they can make an informed decision about whether to enroll in a clinical trial. Yet numerous studies demonstrate that trial participants sometimes have difficulty distinguishing research from clinical care—i.e., they believe the experimental innovation is therapy.[1] This "therapeutic misconception" is widespread,[2] including among research participants in oncology clinical trials. For instance, Joffe and colleagues found that

30% of oncology trial participants believed that the investigational therapy was proven to be the best treatment for their cancer.[3] In another study, Daugherty et al. found that 73% of 144 participants in a phase I trial joined the study seeking an "anticancer response" including cure or remission, and 61% reported the main purpose of the trial was to determine efficacy.[4] In a study we conducted, 17% of cancer patients recruited for phase I trials believed the trials promised a cure, 60% reported a purpose related to efficacy, and only 17% mentioned a purpose related to dosing, safety, or side effects.[5] If these reports regarding participants' beliefs about clinical trials reflect a true *misconception* that investigational interventions are actually proven *treatments*, this is ethically troubling, particularly for early phase clinical trials where the primary purpose is to determine toxicity and dosing rather than efficacy.

Our own work has further documented that oncologists often couple discouraging statements about research benefit with longer encouraging ones. They also sometimes emphasize the chance of a great breakthrough and suggest that the decision regarding trial enrollment depends on whether the patient likes to "play the lottery," or wants to "try for the home run."[6] Yet other studies have shown that phase I oncology consent forms do not overestimate the benefit of early phase clinical trials.[7] Such work, when taken together, suggests that consent interventions may be useful as a means of providing supplemental or more detailed information to patients being recruited to participate in these types of trials.

Traditionally, however, most empirical research testing different interventions to improve individuals' understanding of clinical research[8] has been conducted in simulated research and treatment settings, rather than in actual clinical trials. Studies have measured the effects of simplifying consent forms[9] and/or of giving quizzes with "corrected feedback"[10] for respondents imagining hypothetical studies. Some intervention studies showed an increase in understanding. Two studies gave oncology patients a simplified consent form for actual trials, though neither found that the patients' level of understanding differed from that achieved through the consent process that used a standard consent form.[11]

Multimedia interventions have also been tested to see whether they improve patients' understanding of a clinical trial, with mixed results.[12] Participants who were shown a video about a hypothetical clinical trial, quizzed about what they learned from it, and then provided corrected feedback understood more than control subjects.[13] Other studies, however, have found that an interactive computer tool did not increase oncology patients' understanding of a hypothetical trial.[14] Cancer patients randomized to a video or computer instructional program did not improve their understanding when compared to patients using a standard consent process.[15] Studies supplementing standard consent with videos have also shown an increase in understanding too small to be significant.[16]

One criticism of multimedia interventions is that they repackage the same information provided in traditional consent documents. It might be more important, then, to test how different information is given to prospective subjects. Thus, we developed a computer-based multimedia intervention that distinguished purpose and benefits of early-phase clinical trials from that of later trials and used video clips of patients and oncologists to explain clinical trials and enrollment decisions. We tested this computer-based tool against an informational pamphlet with cancer patients who were considering whether to enroll in an actual early-phase clinical trial.

Study Methods

Cancer patients at the Johns Hopkins Medical Institutions (JHMI), Duke University Medical Center (DUMC), and the University of Chicago Pritzker School of Medicine (UCSM) were eligible to participate in our study if they had been referred for evaluation with an oncologist

regarding possible participation in an early-phase clinical trial, and if they and their oncologists were willing to have appointments audiotaped. At JHMI and DUMC, patients were referred by oncologists for our study when because of their clinical history, participating in the early-phase clinical trial might be discussed at their clinical appointment. UCSM patients were eligible if they were being treated in the Advanced Solid Tumor Clinic, which clinic staff and patients commonly refer to as the "phase I clinic."

Our prospective trial randomly assigned participants to an intervention or control group. Participants in the intervention group watched a 20-minute computer-based presentation on early-phase clinical trials, while those in the control group received an informational pamphlet developed by the National Cancer Institute (NCI) called "Taking Part in Clinical Trials: What Cancer Patients Need to Know."[17]

The intervention was a self-directed, narrated, computer-based presentation that participants viewed in an empty room or private area before meeting with oncologists. It described the three phases of drug testing, including the different purpose of each; explained that early-phase clinical trials are designed to collect information to benefit future patients and that medical benefits to participants are unusual; described ways that patients might benefit from trial participation other than medically; urged patients to discuss a trial's risks and benefits with oncologists; and emphasized that the decision to participate in a clinical trial is completely voluntary. Benefits from clinical trial participation described in the computer-based tool included helping others by making a contribution to improve cancer treatment; exploring every opportunity to fight the cancer diagnosis; obtaining extra attention from clinicians and extra tests as part of the clinical trial; and having a renewed sense of hope.

Participants in the intervention group could also view embedded video clips of five actors portraying patients who decided to enroll in a clinical trial (three) or not to enroll (two) and clips of two oncologists (one actual, one actor) describing the purpose and benefits of early-phase clinical trials. At relevant points, pictures of patients or oncologists would appear on the screen. Observers could then start a clip by touching a picture. After each section, observers were provided a suggested question to ask their doctors (e.g., "What benefits, other than medical, have other patients experienced from being in trials like this?"). The last screen listed all the questions, and the observers could receive the entire list to take to an appointment with the oncologist.

The NCI pamphlet covered similar topics, including the three phases of clinical drug testing. However, the NCI pamphlet included information on postmarketing trials, which the multimedia presentation did not. It also covered the information presented in a research protocol; the process of randomization; common protections for research participants, such as informed consent and institutional review boards (IRBs); and the potential benefits and drawbacks of participating in an early-phase clinical trial. Benefits described included high-quality care, the possibility of medical benefit, the ability to take an active role in making personal medical decisions, and the chance to help others. The pamphlet also provided a set of suggested questions that control group participants might want to ask their doctors. The control group participants reviewed the pamphlet on their own with no further engagement by research staff.

While oncologists were not formally told whether the cancer patients enrolled in our study had received the pamphlet or had viewed the computer-based tool, this information was not kept secret, either. That is, if participants in our study chose to discuss with oncologists something they viewed in the computer tool or something they read in the pamphlet, they were free to do so. We do not know how many study participants discussed something they read or viewed in

our study with their oncologists; thus, we do not know how many oncologists were aware of the arm of our study to which their patients had been assigned.

The written and narrated information in the computer-based tool came from the NCI pamphlet and discussions with oncologists. Scripts for video clips were drawn primarily from in-depth interviews conducted earlier in this project. Because of confidentiality concerns, "standardized patients" (actors portraying patients) represented the cancer patients in the video clips. The computer-based tool was viewed individually by 10 cancer patients (recruited in the oncology waiting room), and by a focus group of eight cancer survivors from a support group (seven women and one man). They provided feedback on each screen and on overall effectiveness, ease of use, clarity of presentation, adequacy of information, and satisfaction. Three oncologists (separately) and three nurses (together) viewed each screen and video clip and also provided feedback. Based on this feedback, several changes were made, including a modification of the navigational tools, the inclusion of four additional illustrations of the reasons for joining or not joining early-phase trials, the addition of one question to ask the doctor, and a few minor word changes. We also refilmed two of the "patient clips," keeping the script the same, but swapping the actors playing each role.

Survey Data

After the oncology appointment in which enrolling in an early-phase clinical trial was discussed with participants in our study, a trained interviewer then interviewed them for 30–40 minutes using a structured questionnaire that contained multiple-choice questions in addition to a few open-ended ones. Responses to the items were recorded directly on the survey instrument. The questionnaire elicited beliefs about the purpose of the research, expected benefits and risks, and intended decision about enrollment. Some items on the questionnaire came from previous studies.[18] In addition, two group meetings were held with oncologists (at Johns Hopkins and Duke) to review the instrument, which was revised accordingly. The survey was administered to eligible patients after the clinical appointment or, if they preferred, within the week by telephone. Respondents in our study who had not yet decided whether to join an early-phase clinical trial were contacted again one to two weeks later. Although they were free to view the tool or read the pamphlet with a surrogate, they were interviewed alone. Written informed consent was obtained from all study participants prior to randomization and before the interview. Institutional review boards at JHMI, DUMC, and UCSM reviewed and approved this study.

On the questionnaire, respondents provided information about the trial they were invited to join. This information was then given to study nurses, who matched it with a trial and gave us a copy of the trial's blank consent form. This enabled us to confidently classify trials by phase. Respondents were classified as phase I if offered participation in phase I trials *only* and phase II if offered participation in a phase II or both phase I and II trials. Anyone offered enrollment in a phase III trial and those for whom the trial phase could not be determined were excluded from the analyses involving trial phase.

Data Analysis

Univariate, descriptive statistics were generated. Bivariate analyses (using chi-square) tested the association between demographic and dependent variables and between intervention and control groups. Logistic regression assessed differences between intervention and control groups in enrollment decision; purpose as safety rather than efficacy; and believing long-term benefit and/or cure results from participation. Model covariates were generated based on variables that were significantly related to at least one of the three outcome variables in bivariate analysis and/or variables that were deemed potential confounders.

The safety and efficacy variables were calculated in two ways. For Model One, in which efficacy and safety are entered as separate independent variables, efficacy was positive if any of the following purposes were selected: “To see if the drug works,” “To see if the drug will help me,” or “To cure my cancer.” If none of these three purposes was chosen, efficacy was considered to be negative. Safety was positive if any of the following purposes were selected: “To see if the drug is safe” or “To figure out the best dosage.” If neither of these two was chosen, it was considered negative. For Model Two, efficacy/safety is a dichotomous outcome variable and was positive if efficacy (as described above) was the only reported purpose; it was considered negative if safety was reported as a purpose of the study, regardless of reported efficacy status. Anyone who did not report either efficacy or safety as a purpose of the study was dropped from Model One. Since participants from UCSM were recruited from a dedicated phase I clinic, regression models were adjusted for trial phase (phase I or phase II) and site (UCSM, DUMC, JHMI), as well as for age, education level, previous enrollment in a research trial, and agreement with the statement, “I do whatever the physician recommends.”

Study Results

We randomized 288 participants to receive the consent intervention or the brochure; 130 completed the survey. Of the participants who completed the survey and were thus included in our sample, 70 were randomly assigned to receive the computer-based tool, and 60 were assigned to the pamphlet. Participants in the control group reported slightly higher family income, and intervention participants were more likely to report prior trial participation (demographic data available from authors). For logistical reasons, participants were recruited at JHMI and DUMC first. When enrollment at UCSM began, the earlier randomization scheme already had two-thirds of JHMI participants randomized to the control arm. The randomization scheme for UCSM, therefore, used a 2:1 ratio oversampling assignment to the intervention group.

Most participants (85.1%) completed the survey by phone. There was no significant difference between the intervention and control groups in terms of completing the survey by phone or in person. There were also no significant differences between those who completed the survey by phone or in person in terms of planning to enroll in a trial, knowing that the purpose of an early-phase clinical trial is to look at safety and not efficacy, or expecting long-term treatment or cure.

Understanding Trial Purpose

Respondents in the intervention group were significantly more likely to state correctly that the purpose of an early-phase trial related to safety (34.4%), compared to 16.7% of the control participants ($p = 0.03$; Table 1). In addition, intervention participants were more likely to state that the purpose of an early-phase trial related to dosing ($p = 0.075$). There was no difference between groups in believing the purpose related to efficacy. Of note, a majority of participants from both groups (57.4%) reported that the main purpose of an early-phase trial was “to see if the drug works,” and 15.3% said the purpose was “to cure my cancer.”

Intervention participants were more likely to believe that the oncologist talked to them about joining an early-phase trial because they “might benefit from the drug” (46.8% vs. 25.9%, $p = 0.02$). The majority of participants (94.4%) reported that they did not have to participate in the trial. Ultimately, 76.4% of participants in our study decided to enroll in an early-phase trial. There were no significant differences in likelihood of enrollment between the intervention and control groups.

Multivariate analysis of responses shows that respondents in the intervention group were 32 times more likely to believe that the purpose of an early-phase trial was to examine safety, as

opposed to efficacy, of study drugs (OR = 32.31, p = 0.005; data available from authors). Respondents recruited from JHMI and UCSM were also more likely when compared to respondents from DUMC to report that the purpose of an early-phase trial was to test safety of study drugs (OR = 121.97, p = 0.009; OR = 23.423, p = 0.041, respectively). Multivariate analysis also reveals that intervention group respondents were 60% less likely to believe there would be a long-term benefit and/or cure from enrolling in an early-phase trial than respondents in the control group (p = 0.041). Additionally, respondents from JHMI and UCSM were less likely to report an expectation of long-term benefit than those from DUMC (OR = 0.16, p = 0.027; OR = 0.13, p = 0.007, respectively).

Trial Benefits

Respondents were asked about benefits from participation for "most cancer patients" and for themselves (Table 2). There was no significant difference between the intervention or control group regarding beliefs about how trial participation would affect their or other patients' cancer. In addition, there was no significant difference between the two groups regarding expected side effects for "most cancer patients" or themselves. However, many more respondents believed *they* would experience long-term benefit or cure if they enrolled in an early-phase cancer trial than believed this to be true for "most cancer patients" (41.7% vs. 12.6%, p = 0.04; data not shown). Similarly, more respondents believed they would experience no or minor side effects (86.5%) than believed this to be true for "most cancer patients" (73.1%, p = 0.002). Respondents who decided not to enroll were significantly more likely to expect their cancer to get worse or experience no change than those who enrolled in an early-phase trial (21.7% vs. 2.5%, p = 0.006). Furthermore, 50.0% of respondents who enrolled in an early-phase trial said they would experience a long-term improvement or cure, compared to 13.0% who did not enroll (p = 0.002).

Reasons for Participating in an Early-Phase Trial

Table 3 shows that respondents in the intervention group were significantly more likely to report that they had enrolled in an early-phase trial because their physician thought it would be a good idea (70.2% vs. 48.6%, p = 0.045). No other reasons for enrolling were significantly different between respondent groups. Reasons most frequently reported as "contributing a lot" to enrolling were: "I wanted to feel like I'd done everything I could" (97.6%); "joining the investigational study gave me hope" (90.4%); and "I trust the physician who presented the study to me" (90.4%). Other factors significantly associated with deciding to enroll included expectation of long-term benefit, older age, and being offered a phase I, rather than phase II, trial. Respondents expecting long-term improvement or cure from trial participation were 17 times more likely to decide to enroll in an early-phase trial than respondents expecting short-term improvement or no change (OR = 17.6, p = 0.019). Respondents recruited for phase I trials were almost 10 times more likely to join compared to those recruited for a phase II trial (OR = 9.6, p = 0.04). There was no difference between intervention and control groups in enrollment decision.

Discussion

The *moral* mandate in clinical research—to ensure that patients are informed about and *understand* the research—becomes particularly acute in certain settings where we know from previous studies that patients may have unrealistic expectations about the therapeutic efficacy of investigational interventions. This is especially true for patients who participate in early-phase oncology trials. The results of our use of a computer-based informed consent intervention suggest that this tool can modify some cancer patients' beliefs about a trial's purpose and benefit. We know of no other studies that have tested the efficacy of an informed consent intervention in this way.

While our consent intervention changed cancer patients' reported understanding of the purpose of clinical trials and moderated their expectations for long-term benefit from participating in research, their likelihood of enrolling in an early-phase clinical trial did not change. This may be because they had already decided about enrollment before the intervention; they also may have felt the need to try everything possible, even if believing personal benefit was remote. Indeed, the reason most respondents in both arms of our study gave for enrolling was "I wanted to feel like I'd done everything I could."

While understanding of purpose and benefit was modified by the intervention we tested, many other aspects of understanding remained unchanged. First, no differences were seen between intervention and control participants in terms of reasons they enrolled in an early-phase trial or side effects expected. Second, while intervention participants were twice as likely to report a study purpose related to toxicity or dosing, the majority of respondents in both arms continued to report a belief that the purpose of on early-phase trial related to efficacy. Thus, regardless of the arm to which they were randomized, most of the participants in our study believed that the early-phase clinical trial they had the option to participate in was designed to examine whether the investigational drug would treat their cancer. Further, while intervention participants were significantly less likely to believe they would have long-term benefit or cure from enrolling in an early-phase clinical trial, essentially half of *all* respondents in our study continued to believe this.

That most cancer patients join early-phase trials believing they will experience long-term benefit is consistent with results from other studies.[19] Participants in our study also believed that their own outcomes in an early-phase clinical trial would be better than those of "most cancer patients," consistent with the distinction between "frequency expectation" (understanding that, statistically, most patients do not benefit from trial participation) and "belief expectation" (believing "it will be me" who is in the small minority that does benefit).[20] Further, higher expectations of benefit are associated with optimism, monetary risk-seeking, better health-related quality of life, and poorer ability to reason numerically, perhaps explaining why interventions simply targeted at imparting knowledge have limited impact on participants' understanding of trials.[21]

An interesting finding is that intervention participants were more likely to believe the physician talked to them about joining an early-phase clinical trial because they "might benefit from the drug" (46.8% vs. 25.9%, $p = 0.02$). This finding is unexpected, and it is not clear why respondents believed this since it was not mentioned in the actual intervention. It would be worth examining this finding in future research to see if it is a recurring theme and to explore why these views might be held.

An important question for researchers, ethicists, and oncologists is the degree to which patients' beliefs about research at the end of life can or should be modified. While recent research suggests that the chance of therapeutic response from a phase I trial is greater than previously thought,[22] the overwhelming likelihood is that "long-term benefit or cure" will not be the result.[23] In such a context, being able to better distinguish a true therapeutic *misconception* from a simply optimistic outlook would be useful.[24] However, regardless of patients' own outlook, ensuring that the differences among phase I, II, and III trials are described and that risk/benefit information is clear seems to be critical; that patients then process this information in different ways leading to various expectations of research benefit may be ethically legitimate.

Our study had many limitations. First, at the request of the Johns Hopkins Cancer Research Committee, participants in the control group were provided with an NCI pamphlet, rather than hearing information exclusively from oncology staff, which would have been a "true" control. The NCI pamphlet provided information about differences among phase I, II, and III trials and

included sample questions. Thus, the control group may have changed beliefs and behaviors as a result of reading the pamphlet, which might have moderated the effect of the computer-based intervention. It is possible that results would have been more dramatic if a true control group (nonintervention arm) had been used.

Another limitation is that oncologists were not formally blinded as to whether participants received the pamphlet or viewed the computer-based tool. It is very likely that participants may have mentioned something they saw or read through the intervention or pamphlet, thus alerting oncologists to whether they had received the intervention. We cannot know whether oncologists' awareness, if present, might have systematically changed their behavior toward those known to be in the intervention group.

Additionally, this study was conducted at three academic medical centers where patients may seek access to the latest research interventions. Findings likely are more generalizable to patients at academic centers that conduct early-phase clinical trials than to cancer patients broadly. Moreover, one center (UCSM) has a dedicated phase I clinic, and patients recruited there may have been particularly likely to have decided to join an early-phase trial in advance of our study. Because participants recruited at USCM also were more likely to be randomized to the intervention group, this may have created bias, although multivariate analysis indicated that findings were consistent across institutions.

Another limitation is that most of the participants in our study were white. However, this may correctly reflect the population of adults who consider enrolling in cancer trials, since there is evidence that African Americans—particularly African American men—enroll in cancer research at lower rates than whites do.[25] More research is needed on the possible interaction between the computer-based tool and race.

Further limiting the study is the fact that consent studies are challenged to distinguish measurement of understanding from recall. The intervention stressed that early-phase trials were designed to measure safety and dosing rather than efficacy, and intervention participants reported this more often. Whether they understood that distinction or its implications is less clear, although their tempered expectation of benefit suggests some change in understanding. Also, it is reasonable to assume that the "false hope" felt by some participants may be inversely related to their life expectancy, and this may have affected their willingness to join an early-phase trial. The current data do not allow examination of this question, so the relationship between life expectancy and willingness to participate in clinical trials should be further explored.

This study also had a relatively small sample size that may have affected the degree of specification in the regression models. With a larger sample size, perhaps other variables would have risen to significance. And finally, survey data—while revealing important trends across a group of respondents—are not well suited to capturing how people think about complicated topics. Qualitative interviews may contribute additional understanding of complex, nuanced issues—for example, how cancer patients with advanced disease view clinical research, and how their ability to accurately weigh the pros and cons of trial participation is affected by their often terminal diagnoses.[26]

Despite these limitations, our study suggests that a computer-based tool can modify the beliefs of some cancer patients regarding the purpose and benefit of an early-phase clinical trial. Further research is needed that examines whether this tool, or other tools that also provide more detail about the purpose and benefits of early-phase cancer trials, provide similar or greater changes in beliefs about these types of trials. While recent reports suggest that the chance of therapeutic response from a phase I trial is greater than previously thought,[27] the overwhelming likelihood is that "long-term benefit or cure" will not be the result.[28] Although we recognize

that being direct in the recruitment process about the benefits and risks of clinical trials may be difficult,[29] the information provided in the recruitment process should be accurate and complete so that patients can make *informed* decisions about whether to participate.

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References

1. Riecken HW, Ravich R. Informed consent to biomedical research in veterans administration hospitals. JAMA 1982;248:344–348. [PubMed: 7045434] RodenhuisSVan Den HeuvelWJAAnnyasAAPatient motivation and informed consent in a phase I study of an anticancer agentEuropean Journal of Cancer and Clinical Oncology198420457462Joffe S, Cook E, Cleary P, et al. Quality of informed consent in cancer clinical trials: A cross-sectional survey. Lancet 2001;358:1772–1777. [PubMed: 11734235] Kass NE, Sugarman J, Faden R, Schoch-Spana M. Trust: The fragile foundation of contemporary biomedical research. Hastings Center Report 1996;26:25–29. [PubMed: 8891706]
2. See ref. 1, Joffe et al. Appelbaum PS, Roth LH, Lidz CW, et al. False hopes and best data: Consent to research and the therapeutic misconception. Hastings Center Report 1987;17:20–24. 2001. [PubMed: 3294743] Lesko LM, Dermatis H, Penman D, et al. Patients', parents', and oncologists' perceptions of informed consent for bone marrow transplantation. Medical and Pediatric Oncology 1989;17:181–187. [PubMed: 2664440] Howard JM, DeMets D. How informed is informed consent? The BHAT experience. Controlled Clinical Trials 1981;2:287–303. [PubMed: 6120794] Snowdon C, Garcia J, Elbourne D. Making sense of randomization: Responses of parents of critically ill babies to random allocation of treatment in a clinical trial. Social Science and Medicine 1997;45:1337–1355. [PubMed: 9351153] Benson P, Roth LH, Winslade W. Informed consent in psychiatric research: Preliminary findings from an ongoing investigation. Social Science and Medicine 1985;20:1331–1341. [PubMed: 2862705] Robinson EJ, Kerr CE, Stevens AJ, et al. Lay public's understanding of equipoise and randomization in randomized controlled trials. Health Technology Assessment 2005;9(8):1–196. [PubMed: 15763039] Henderson GE, Churchill LR, Davis AM, et al. Clinical trials and medical care: Defining the therapeutic misconception. Public Library of Science 2007;4(11):e324.
3. See ref. 1, Joffe et al. 2001.
4. Daugherty CK, Banik DM, Janish L, et al. Quantitative analysis of ethical issues in phase I trials: A survey interview study of 144 advanced cancer patients. IRB: Ethics & Human Research 2000;22(3):6–14. [PubMed: 11697385]
5. Kass N, Sugarman J, Taylor H, et al. Purpose and benefits of early phase clinical trials: What do oncologists say? What do patients hear? Journal of Empirical Research on Human Research Ethics 2008;3(3):57–68. [PubMed: 19385771] Meropol NJ, Weinfurt KP, Burnett CB, et al. Perceptions of patients and physicians regarding phase I cancer clinical trials: Implications for physician-patient communication. Journal of Clinical Oncology 2003;21 (13):2589–2596. [PubMed: 12829680]
6. See ref. 5, Kass et al. 2008.
7. Horng S, Emanuel EJ, Wilfond B, et al. Descriptions of benefits and risks in consent forms for phase I oncology trials. NEJM 2002;347(26):2134–2140. [PubMed: 12501226]
8. Flory J, Emanuel E. Interventions to improve research participants' understanding in informed consent for research: A systematic review. JAMA 2004;292(13):1593–1601. [PubMed: 15467062]
9. Agre P, Rapkin B. Improving informed consent: a comparison of four consent tools. IRB: Ethics & Human Research 2003;25:1–7. [PubMed: 15035248] Epstein LC, Lasagna L. Obtaining informed consent: Form or substance. Archives of Internal Medicine 1969;123:682–688. [PubMed: 5771055] Dresden G, Levitt A. Modifying a standard industry clinical trial consent form improves patient information retention as part of the informed consent process. Academic Emergency Medicine 2001;8:246–252. [PubMed: 11229946] Murphy DA, O'Keefe ZH, Kaufman AH. Improving comprehension and recall of information for an HIV vaccine trial among women at risk for HIV: Reading level simplification and inclusion of pictures to illustrate key concepts. AIDS Education and Prevention 1999;11:389–399. [PubMed: 10555623] Campbell F, Goldman B, Boccia M, et al. The effect of format modifications and reading comprehension on recall of informed consent information

by low-income parents: A comparison of print, video, and computer-based presentations. Patient Education and Counseling 2004;53:205–216. [PubMed: 15140461] Bjorn E, Rossel P, Holm S. Can the written information to research subjects be improved? An empirical study. Journal of Medical Ethics 1999;25:263–267. [PubMed: 10390684]

10. Davis TC, Holcombe RF, Berkel HJ, et al. Informed consent for clinical trials: A comparative study of standard versus simplified forms. Journal of the National Cancer Institute 1998;90:668–674. [PubMed: 9586663] Taub H, Baker M. A reevaluation of informed consent in the elderly: A method for improving comprehension through direct testing. Clinical Research 1984;32:17–21. [PubMed: 6544180] Taub H. Comprehension of informed consent for research: issues and directions for future study. IRB: Ethics & Human Research 1986;8:7–10. [PubMed: 11649821] Stiles P, Poythress N, Hall A, et al. Improving understanding of research consent disclosures among persons with mental illness. Psychiatric Services 2001;52:780–785. [PubMed: 11376225] Wirshing D, Wirshing W, Marder S, et al. Informed consent: Assessment of comprehension. American Journal of Psychiatry 1998;155:1508–1511. [PubMed: 9812110] DCCT Research Group. Implementation of a multicomponent process to obtain informed consent in the Diabetes Control and Complications Trial. Controlled Clinical Trials 1989;10:83–96. [PubMed: 2467781] Wadey V, Frank C. The effectiveness of patient verbalization on informed consent. Canadian Journal of Surgery 1997;40:124–128.
11. See ref. 10, Davis et al. 1998; Coyne C, Xu R, Raich P, et al. Randomized, controlled trial of an easy-to-read informed consent statement for clinical trial participation: A study of the Eastern Cooperative Oncology Group. Journal of Clinical Oncology 2003;21:836–842. [PubMed: 12610182]
12. See ref. 9, Agre and Rapkin 2003; see ref. 9, Campbell et al. 2004; Dunn L, Lindamer L, Palmer B, et al. Enhancing comprehension of consent for research in older patients with psychosis: A randomized study of a novel consent procedure. American Journal of Psychiatry 2001;158:1911–1913. [PubMed: 11691700] Llewellyn-Thomas H, Thiel E, Sem F, et al. Presenting clinical trial information: A comparison of methods. Patient Education and Counseling 1995;25:97–107. [PubMed: 7659635] Fureman I, Meyers K, McLellan AT, et al. Evaluation of a video-supplement to informed consent: Injection drug users and preventive HIV vaccine efficacy trials. AIDS Education and Prevention 1997;9:330–341. [PubMed: 9376207] Weston J, Hannah M, Downes J. Evaluating the benefits of a patient information video during the informed consent process. Patient Education and Counseling 1997;30:239–245. [PubMed: 9104380] Benson P, Roth L, Appelbaum P, et al. Information disclosure, subject understanding, and informed consent in psychiatric research. Law and Human Behavior 1988;12(4):455–475. [PubMed: 11659248] Strevel EL, Newman C, Pond GR, et al. The impact of an educational DVD on cancer patients considering participation in a phase I clinical trial. Supportive Care in Cancer 2007;15(7):829–840. [PubMed: 17177040]
13. See ref. 12, Dunn et al. 2001.
14. See ref. 12, Llewellyn-Thomas et al. 1995.
15. See ref. 9, Agre and Rapkin 2003.
16. See ref. 12, Fureman et al. 1997; Weston et al. 1997; Benson et al. 1988.
17. National Cancer Institute. Taking part in clinical trials: What cancer patients need to know. 1998. http://www.cancer.gov/PDF/a559d304-f6d9-492a-ab1b-875644f29be2/whatcancerpatients.pdf
18. See ref. 1, Rodenhuis et al. 1984.
19. See ref. 4, Daugherty et al. 2000; see ref. 5, Kass et al. 2008.
20. Weinfurt K, Castel L, Li Y, et al. The correlation between patient characteristics and expectations of benefit from phase I clinical trials. Cancer 2003;98:166–175. [PubMed: 12833469]
21. See ref. 20, Weinfurt et al. 2003.
22. Roberts TG, Goulart BH, Squitieri L, et al. Trends in the risks and benefits to patients with cancer participating in phase I clinical trials. JAMA 2004;292(17):2130–2140. [PubMed: 15523074] Horstmann E, McCabe MS, Grochow L, et al. Risks and benefits of phase 1 oncology trials, 1991 through 2002. NEJM 2005;352(9):895–904. [PubMed: 15745980]
23. Decoster G, Stein EE, Holdener EE. Responses and toxic deaths in phase I clinical trials. Annals of Oncology 1990;1:175–181. [PubMed: 2148104]
24. Henderson GE, Churchill LR, Davis AM, et al. Clinical trials and medical care: Defining the therapeutic misconception. PLoS Medicine 2007;4(11):e324. [PubMed: 18044980]

25. Sateren W, Trimble E, Abrams J, et al. How sociodemographics, presence of oncology specialists, and hospital cancer programs affect accrual to cancer treatment trials. Journal of Clinical Oncology 2002;20:2109–2117. [PubMed: 11956272]

26. See ref. 1, Kass et al. 1996.

27. See ref. 22, Roberts et al. 2004; Horstmann et al. 2005.

28. See ref. 23, Decoster et al. 1990.

29. Buckman, R. How to Break Bad News: A Guide for Health Care Professionals. Baltimore, MD: Johns Hopkins University Press; 1992.

Table 1

Respondents' Beliefs about the Purpose of the Clinical Trial and Their Decision Regarding Participation

	N	Computer-Based Tool %	NCI Pamphlet %	Total %	p-value
What do you think is the purpose of the investigational study?					
To see if the drug works	122	57.8	56.9	57.4	0.919
To see if the drug is safe	115	34.4	16.7	26.1	0.030[a]
To figure out the best dosage	115	29.0	15.1	22.6	0.075
To see if the drug will help me	119	25.0	29.1	26.9	0.616
To cure my cancer	118	17.2	13.0	15.3	0.525
Why do you think the physician talked to you about joining the study?					
I might benefit from the drug	116	46.8	25.9	37.1	0.020[a]
I don't have any other standard treatment options	113	24.6	17.3	21.2	0.345
I am a good candidate for the trial	112	21.7	26.9	24.1	0.517
S/he thought I might be willing to help	113	3.3	11.3	7.1	0.144
Other drugs had stopped working	113	13.1	21.2	16.8	0.255
Did you feel like you had the option to refuse to be in the investigational study?					
Yes	119	95.6	93.1	94.4	
No	7	4.4	6.9	5.6	0.544
Did you decide to enroll in the current study?					
Yes	84	78.3	74.0	76.4	
No	26	21.7	26.0	23.6	0.594

[a] $p < 0.05$

Note: Some variables may add up to greater than 100% as respondents could choose all options that apply.

Table 2

Respondents' Perception of the Benefits and Side Effects of the Investigational Study to Both Themselves and Other Cancer Patients

	N	Computer-Based Tool %	NCI Pamphlet %	Total %	p-value
Perceived Benefits and Side Effects of Investigational Study for Other Cancer Patients					
Most cancer patients who enroll in investigational studies like the one presented to you:					
Have cancer get worse/experience no change in their cancer		13.2	6.8	10.2	
Experience some short-term improvement in their cancer	127	35.3	40.7	37.8	
Experience long-term improvement/complete cure		10.3	11.9	11.0	
Don't know		41.2	40.7	40.9	0.659
Most cancer patients who enroll in investigational studies like the one presented to you experience:					
No side effects		4.5	0.0	2.4	
Minor side effects	126	65.7	72.9	69.0	
Major side effects		7.5	6.8	7.1	
Don't know		22.4	20.3	21.4	0.398
Perceived Benefits and Side Effects of Investigational Study for Respondents Themselves					
While participating in the investigational study, do you expect:					
For those who decided to enroll in the clinical trial:					
To have your cancer get worse or experience no change		4.3	0.0	2.5	
To experience some short-term improvement in your cancer	80	39.1	32.4	36.3	
To experience some long-term improvement or cure		41.3	61.8	50.0	
Don't know		15.2	5.9	11.3	0.181
For those who decided not to enroll in the trial:					
To have your cancer get worse or experience no change		36.4	8.3	21.7	
To experience some short-term improvement in your cancer	23	36.4	33.3	34.8	
To experience some long-term improvement or cure		9.1	16.7	13.0	
Don't know		18.2	41.7	30.4	0.336
While participating in the investigational study, do you expect to experience:					
For those who decided to enroll in the clinical trial:					
No side effects		4.3	5.6	4.9	
Minor side effects	82	84.8	88.9	86.6	
Major side effects		2.2	0.0	1.2	
Don't know		8.7	5.6	7.3	0.764

	N	Computer-Based Tool %	NCI Pamphlet %	Total %	p-value
For those who decided not to enroll in the trial:					
No side effects		0.0	0.0	0.0	
Minor side effects	23	81.8	58.3	84.2	
Major side effects		9.1	16.7	15.8	
Don’t know		9.1	25.0	17.4	0.462
Do you think joining an investigational study will have any impact on your prognosis?					
Yes	100	80.8	85.4	83.0	
No		19.2	14.6	17.0	0.536
If yes, do you think it will have a positive or negative impact on your prognosis?					
Positive	81	97.6	97.5	97.5	
Negative		2.4	2.5	2.5	1.000

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Table 3

Participants' Self-Reported Reasons for Deciding to Participate in an Investigational Study

Computer-Based Tool	%	NCI Pamphlet %	Total %	p-value
How much did the following reasons contribute to your decision to join an investigational study?				
Contributed a lot	100.0	94.6	97.6	
Contributed a little/did not contribute	0.0	5.4	2.4	0.191
Joining the investigational study gave me hope.				
Contributed a lot	87.0	94.6	90.4	
Contributed a little/did not contribute	13.0	5.4	9.6	0.289
I trust the physician who presented the study to me.				
Contributed a lot	91.5	88.9	90.4	
Contributed a little/did not contribute	8.5	11.1	9.6	0.722
Because it might help me fight my cancer.				
Contributed a lot	93.6	83.8	89.3	
Contributed a little/did not contribute	6.4	16.2	10.7	0.173
The investigational study gave me the best chance medically.				
Contributed a lot	84.8	83.3	84.1	
Contributed a little/did not contribute	15.2	16.7	15.9	0.858
The investigational study was a way to help others.				
Contributed a lot	71.7	64.9	68.7	
Contributed a little/did not contribute	28.3	35.1	31.3	0.502
The physician who presented the investigational study thought it would be a good idea to join.				
Contributed a lot	70.2	48.6	60.7	
Contributed a little/did not contribute	29.8	51.4	39.3	0.045

Note: These questions were only asked of the 76% of participants who decided to participate in an investigational study.