

Marginalized Populations and Drug Addiction Research: Realism, Mistrust, and Misconception

Celia B. Fisher, Matthew Oransky, Meena Mahadevan, Merrill Singer, Greg Mirhej, and Derrick Hodge

Making a reasoned decision to participate in a randomized controlled trial requires, among other factors, understanding of the uncertain efficacy and risks of the experimental treatment, random assignment to interventions, and the use of placebos or other control interventions. Misunderstandings about randomized controlled trials have been characterized as examples of “therapeutic misconception.”¹ According to Appelbaum, Lidz, and Grisso, the therapeutic misconception reflects the incorrect belief that individualized needs will be taken into account when a subject is randomized into a condition assignment, and the unreasonable expectation that research participation will result in individualized medical benefit.² One factor contributing to the therapeutic misconception is that prospective participants don’t understand key features of the experimental process.³

Hornig and Grady have proposed that many instances identified as therapeutic misconception are better understood as cases either of therapeutic misestimation (i.e., underestimation of risk, overestimation of benefit, or both) or therapeutic optimism (i.e., hope for the best personal outcome).⁴ In this regard, patients with more severe medical conditions may be more likely to overestimate therapeutic gains from participating in a randomized controlled trial.⁵ As typologies for therapeutic misconception continue to evolve, empirical research has supported its expression across a range of disorders.⁶ This has led to growing concern that the therapeutic misconception and related barriers to understanding may compromise the quality of informed consent.⁷

Although individuals from all socioeconomic backgrounds are potentially susceptible to the therapeutic misconception, most studies that assess understanding of clinical trial information have involved middle income patients with cancer, cardiac diseases, or psychiatric conditions.⁸ Yet individuals who lack medical insurance, are poor, and are from marginalized populations may assess information presented in the informed consent process differently than individuals who have access to effective medical care and have health disorders that do not compromise their understanding of their medical condition. For our study, we examined comprehension of clinical trial information and expectations about randomized controlled trials in a population of active and recent drug users who might be recruited to participate in addiction research. This focus reflects our commitment to a relational ethic that views economically and socially disadvantaged persons as experts on their own lived realities and interpretations of research risks and benefits.⁹ Such an approach is also consistent with past research involving at-risk, ethnic, and sexual minority populations, demonstrating that participant and community perspectives on research ethics can differ from the assumptions of seasoned scientists and bioethics scholars.¹⁰

Research Methods

Data for this study were collected as part of a larger study sponsored by the National Institute on Drug Abuse (NIDA) that explored participant perspectives on ethical issues in drug use and HIV-related research. A total of 11 focus groups were conducted. Two focus groups each of African American males and females and gay/bisexual males of mixed ethnicity were conducted in New York City. One Hispanic female group, two Hispanic male groups, one non-Hispanic male group, and one non-Hispanic female group were conducted in Hartford, Connecticut. The Institutional Review Board (IRB) at both sites approved the study, and all participants gave written informed consent.

One-hundred self-described active or recent drug users (68% male, aged 22–70 years, mean age 43 years) were recruited through street outreach in Hartford and agency referral in New York City. Participants were excluded if they showed signs of mental disorder or cognitive impairment. Participants identified themselves as black (33%, African American or Caribbean descent), Hispanic (37%, predominantly Puerto Rican descent), non-Hispanic white (22%), and other (8%); 24% as gay/homosexual or bisexual; and 39% as HIV positive. Most participants (61%) were unemployed and reported welfare or social security benefits as their only income; 32% reported disabilities that interfered with full-time employment; and 79% had no more than a high school education. The most commonly reported drugs they used

were powder cocaine (45%), heroin (44%), crack (32%), marijuana (29%), illicit methadone (18%), speedball (a combination of heroin and cocaine) (13%) and Xanax/Ativan/Valium (11%). The sample for this study was not recruited from an active drug abuse randomized controlled trial; however, 75% had previously participated in research on drugs, alcohol, or HIV, and 43% had participated in a treatment study for these disorders.

Focus group discussions were stimulated by three four-minute videotaped vignettes depicting drug research scenarios portrayed by ethnically diverse professional actors speaking English and Spanish. Each focus group watched videos in which the “participant” was the same gender as group members and the investigator was of the opposite gender. Discussions were audiotaped. To protect confidentiality of focus group participants, we obtained a Certificate of Confidentiality from the National Institutes of Health and used participant pseudonyms. Participants were paid \$25 plus transportation costs. An advisory board of drug abuse advocates, social workers, and addicts assisted in deciding what constituted fair compensation and on the final content and format of the informed consent and video scripts.

The vignette of interest for this analysis depicted an informed consent conference for an eight-week randomized controlled trial testing a new medication to reduce cocaine cravings. The investigator wore a doctor’s coat, and the conference appeared to take place in his or her office. The video began with a narrator’s overview, followed by the investigator’s explanation of the study interspersed with participant questions. Key elements of the study described in the vignette included: 1) the uncertain efficacy and possible side effects of the experimental treatment (short-term nausea, dizziness, constipation, or weight gain, and unknown long-term effects); 2) the use of a placebo (sugar pill), random assignment to conditions (based on a flip of a coin), and double-blind nature of the study; 3) supportive services for all participants that would include “weekly psychological counseling to help stay off drugs and regular medical checkups”; 4) postexperimental availability of the medication for those in the placebo condition if it were found to be effective; and 5) postexperimental treatment and counseling to “wean you off of it and help you keep off cocaine.” (The full script is available from the first author upon request.) A codebook was developed integrating themes emerging from the participants’ own words and themes based on the literature on research ethics. The final set of codes was catalogued in a software program (Atlas.ti) that was then used to recode the transcripts and generate the final themes and subthemes.

Study Results

We found support for previously reported components of the therapeutic misconception, as well as for two core concepts that differentially influence comprehension of informed consent information for the drug users in our study. We labeled the first concept “experimental realism,” defined as participants’ ability to understand ethically relevant components of randomized controlled trials, including the uncertain efficacy and risks of the experimental treatment, random assignment, and the nature and rationale for placebo controls. We labeled the second concept “experimental mistrust,” defined as participant fears of exploitation and objectification at the hands of investigators they believe to be disingenuous or incompetent. In addition, some participants voiced beliefs about the nature of drug addiction and substance abuse recovery that influenced their conceptions of the role of placebo controls. We investigate these themes below as they apply to treatment uncertainty and treatment risks, randomization, and the use of placebo controls.

Treatment Uncertainty and Treatment Risks

In this section we highlight participant statements about the uncertain efficacy and risks of randomized controlled trials for drug addiction that reflect components of experimental realism, experimental mistrust, therapeutic misconception, and related concepts.

Experimental realism

There aren’t any guarantees. The majority of focus group members comprehended both treatment uncertainty and the experimental nature of participation, as typified by the following comments: “There aren’t any guarantees. You don’t know if it’s gonna work or not. It’s just a chance you’re taking.” (black female) “Like we saw in the video, we don’t know what the effects are when you use it. It may affect you badly or it may help you. Who knows? Right now it’s just an experiment. The word says it all.” (Hispanic male)

Participants’ comments also suggested that a lack of guaranteed medical benefits made the decision to participate more difficult. “I don’t think he [the participant] was confused about what she [the investigator] was saying. He was confused

whether he should participate in the experiment or not.” (Hispanic male)

I'd take a chance. Participants asserted that those addicted to illegal drugs might participate out of hope that the treatment would work, reflecting how experimental realism can be consistent with “therapeutic optimism.”¹¹ “I would take the chance, too. If I wanted to really get off of this mess, this other drug, I would take it.” (black female) Another participant said, “If somebody told me that this drug might stop me from using cocaine, I think I'd let it be tested on me because I want to stop using cocaine.” (white male)

Others argued that treatment uncertainty may be unacceptable: “What he [the addict] wanted was to kick the habit or getting help in kicking the habit, so again that goes back to him maybe deciding not to go along with the study because it wasn't guaranteed.” (black male)

Experimental mistrust

Some focus group members struggled with a desire to view the treatment as potentially effective (perhaps a tendency toward therapeutic optimism), but expectations of benefit were undercut by their skepticism about the investigator's honesty or ulterior motives. Furthermore, participants often linked their personal experience with unfavorable and exploitative medical care to the clinical trial context.

He just wanna make some money. For some participants, experimental mistrust was reflected in cynical and unflattering statements about practitioners and clinical researchers as mercenary and opportunistic, as illustrated in this comment by a black female respondent:

He just wanna make some money. It's based on money, and I found that in a lot of these studies. A lot of these studies, they would give you input on getting in this study, and they'll make the study sound so challenging, but then as you get in the study, the study ain't what they was challenging for. Because they just want to get you in there so they could get paid.

Treating the participant like a guinea pig. Informed consent procedures highlighting the unknown efficacy and negative side effects of a treatment for drug addiction also tapped into marginalized drug users' feelings of objectification and exploitation. Group members also expressed concern about being used as “guinea pigs,” a fear well documented in ethnic minority groups that have a history of race-based abuse in research.¹²

It's like she's [the investigator] more interested in if their study gonna work. That's what we need you for. We need you to be a guinea pig, to take this stuff and see if it works for you. And if it do, then we gonna help you. I'm gonna give you all the help you need. (black male)

All I kept seeing were my friends dying. Personal and collective histories of health care neglect and abuse appeared to reinforce a sense of distrust for clinical researchers. In many focus groups, participants' discussion of research risks prompted tales of perceived negligence and deception by practitioners. As one gay male expressed it:

That's what I've been experiencing with the AZT aspect . . . we didn't know, I mean, all I kept seeing was my friends dying, and they were guinea pigs in a certain sense, too. And they didn't realize that they were being overdosed and I didn't know that they were being overdosed either until . . . that was more or less like research also until they finally got the dosage correct . . . Nobody was being informed.

A white female voiced a similar outlook: “Don't you think that every time you go in the doctor's office and get those samples, that they're just testing it out on you?”

As suggested by the following comment, participants' negative health care experiences, particularly with medication side effects, appear to contribute to their distrust of investigators:

My doctor keeps sending me to the dermatologist, and I'm getting frustrated because now the dermatologist is putting me on this cream, that cream—I'm to the point where I just don't want to be bothered now . . . But my doctor didn't tell me that until she saw the black marks and the spots on my skin. And when she realized how bad it was getting, that's when she decided to be honest with me. (black female)

Therapeutic misconception

While many participants who distrusted research demonstrated experimental realism in regard to the uncertain efficacy of the experimental medication, for some participants, experimental mistrust contributed to a therapeutic misconception (conflation of research with personal care) characterized by the belief that the investigator was being incompetent or disingenuous when stating the unknown efficacy of the experimental treatment.

She should have been better prepared. These participants reasoned that since, as one Hispanic male put it, “Doctors know everything and always have an answer for the questions,” the investigator must really know—or should know—whether the treatment will be effective. To reconcile the informed consent information with their belief that “doctors know everything,” some respondents attributed the investigator’s uncertainty about treatment outcomes to incompetence.

I was wondering, when he went to see her [the investigator] looking for help, I don’t understand why she was not sure about . . . whether the medicine was going to work or not. Because if I go there to see her and she tells me that she doesn’t know, that this and that, I don’t know, I will doubt, I think she has the responsibility to know. (Hispanic male)

This woman is not saying everything to me. While most group members understood that the investigator had said treatment efficacy was unknown, as these comments from the Hispanic male group illustrate, some thought the statement was intentionally deceptive:

Because someone comes looking for help . . . and if what they hear is that she [the investigator] was neither sure about the information she was giving him nor the reason was for saying it, that person will not believe her.

Because the woman [the investigator] was there as if she knew something and she did not want to say it to him, you see.

Therapeutic misestimation

Aware that the experimental treatment posed risk, focus group participants emphasized the possibility of negative side effects. As one gay male explained: “I don’t want anything that’s not FDA approved, and I’m scared of what’s FDA approved. You know what I’m saying? Because of all these side effects.”

It may just kill you. In some cases, group discussions turned to concerns about treatment risks that were more serious than those described in the video—evidence of what Horng and Grady have described as therapeutic misestimation.¹³ This perspective is illustrated in comments from black female participants:

Who’s to say that after the eight weeks [of the randomized controlled trial], you’re gonna be alive to tell the story? It may kill you . . . the drug may kill you. Nobody knows what your body can withstand. You don’t know. That’s dangerous.

Any medication that’s up for research, that ain’t gonna work and it may just kill you. Because number one, it’s not FDA approved. They’re not even really sure what it does. Her head could blow off, her arm could fall off, she could not wake up . . . They’re not even sure if it works.

[The research can affect] the chance to have kids, you know what I mean? A whole lot of factors. Sterilization, you know. Just a number of things.

I know what the cocaine does to me. While it may seem ironic that someone who knowingly exposes themselves to the harmful effects of illicit drugs balks at the idea of side effects from an experimental medication, some participants said they preferred the known side effects of their addictive drugs of choice over the potential harms of an unknown treatment. As one participant stated:

At least with my cocaine I know what the effects are . . . Why would I take a chance at hurting myself? Three times she [the investigator] said there could be long-term effects. Why would you do that when I can just do my coke and I don’t have to worry about the long-term effects. I know what the coke does to me. (white male)

Random Assignment to Treatment and Control Conditions

Understanding random assignment to treatment and control conditions is a critical criterion for consent

comprehension of randomized controlled trials. In this section we describe how such understanding is influenced by experimental realism and experimental mistrust.

Experimental realism

That is the only way they can compare. The majority of group members indicated they understood the meaning of random assignment and its methodological rationale. Some, like the Hispanic male quoted below, had a rather sophisticated understanding of both the process and rationale for randomization:

This is called . . . I don't know the name in Spanish but it is a double blind test. That is the name that it has: double blind. So not even the doctors who are part of the study . . . don't know. At the end of the experiment, when the medication runs out, well, they compare and that is when they find out who had what. So they compare how efficient the pill was or the placebo. They find out who made progress and with what: either with the placebo or the medicine. So that is what they compare, you know.

Although not as articulate, most other participants understood that "There's a possibility you might get the real thing, and there's a possibility you might get the sugar pill." (black male)

Some focus group members, responding to the drug user depicted in the video, were highly attuned to the anxieties of research subjects and the responsibilities of investigators regarding randomization. As one participant noted:

I think that when he [the participant] first arrived he was more motivated to get into the program, but as soon as she [the investigator] told him that she didn't know what the effects of the pill were, and when she said that they had sugar pills and real pills and some people will take one and some the other, then he stepped back and didn't want to do it. (Hispanic male)

Another stated:

He's trying to get a guarantee and he's trying to get her [the investigator] to say what he really wants to hear. And she is professional enough to explain to him that over and over, repeatedly, and he needs to hear it over and over and get it through his head that there's no guarantee here. This is a trial. You may not end up with the medicine. I think she covered everything. (gay male)

The tension between the desire to get well and understanding the nature of random assignment is illustrated in these comments from the white female group: "But I think she [the participant] had misunderstood, and she thought this was gonna be a cure-all for her," and "if you sign up for it and you know it can be a placebo or not, and if you're willing to take that and accept that, then it's all good."

Experimental mistrust

Although most participants understood the premise of randomization because they suspected that the investigator might be disingenuous or opportunistic, many did not believe that random assignment would actually occur. This mistrust is illustrated in the following comment regarding the presumed state of mind of the video participant: "He doesn't know whether to believe her and to proceed with the study . . . He is thinking, you know, 'Do I do it or not?'" (Hispanic male) Participants, especially men in the two black male focus groups, suspected that the investigator's statements about randomization were a ruse.

Who's to say that everybody ain't getting [the placebo]? Although respondents understood that the investigator was telling subjects they would be randomly assigned to a treatment or a placebo group, some did not believe that researchers would follow through on this promise. A number of respondents believed that all subjects in the vignette study would be assigned to the placebo group, as demonstrated by the following comments: "Who's to say that everybody ain't getting it? You see what I'm saying? Don't nobody know and there ain't nobody saying nothing. They give everybody the placebo for the first eight weeks just to see if they'll come back." (black male); and, "The crazy part about that, everybody could be getting the placebo from the beginning." (black male)

One participant explained that he thought all participants would get the placebo because the experimental medication didn't exist at all: "I think that placebo is the thing. Because she never said nothing about the name of the real thing." (black male)

As illustrated in another comment, some respondents thought the investigator was intentionally or inadvertently confusing participants:

The risk is that . . . let's say that she receives the medication . . . but in her mind she is going to say to herself that they are just giving her sugar water and this is not going to have an effect because her mind works with what she knows. (Hispanic female)

She'll be giving him the real medicine. Mistrust of the investigator's description of random assignment led some respondents to believe that subjects would be purposely given the medication to serve the investigator's own scientific interest:

I think he learned about the study, and he states that he wants to get off [of cocaine]. So you know they had clinical trials and stuff, but the information that she was giving to him . . . come on, what you gonna give me, a sugar pill? And I won't know if I'm taking the real medicine. But most likely she'll be giving him the real med, to see his reaction within eight weeks. (black male)

She reeled him in. Furthermore, although focus group members often understood the methodological rationale of randomization and that experimental treatment differed from medical care, they still perceived the informed consent conference and the behavior of the investigator as being manipulative or disingenuous, as seen in the following comment:

He [the participant] was very funny about wanting to get the real thing. I mean, first when he came in, she [the investigator] reeled him in and said there's a possibility you might get the real thing, and there's a possibility you might get the sugar pill, placebo . . . in his mind he wanted to get the real thing, he wanted to be straight, when I say straight, I mean, like, kick the habit. (black male)

Addiction Beliefs and Understanding the Purpose of Placebo Control

The majority of participants appeared to understand that the placebo was a "sugar pill" that differed from "the real one," and that it would not effect biological mechanisms that might influence addiction, fitting within the general theme of experimental realism. Despite this understanding, some perceived the placebo condition as either a disguised test of or a therapeutic opportunity to apply the willpower necessary to cure their addiction. Indeed, many researchers have commented on how drug users reject the idea that addiction has a biological basis and instead insist they can stop at any time. Some have argued that denying physiological dependence on drugs is itself related to neurocognitive "disease" factors associated with drug dependence.¹⁴ Whether an emphasis on willpower reflects an underlying disease state or a collective health belief, it represents a serious challenge to informed consent. As the focus group comments reveal, the notion of willpower can reinforce experimental mistrust in the scientific validity of placebo controlled trials or the therapeutic misconception that the placebo condition is designed to provide personal benefit to participants.

Experimental mistrust

Many focus group members commented on how the video participant had come to the consent conference in hopes of getting off cocaine. As a consequence, they believed that irrespective of the condition to which they were randomly assigned, participants would attempt to exert the willpower necessary to quit their habit. For some this meant the study lacked scientific validity. Others believed that the placebo was being used to test their personal resolve or to assess the role of willpower in addiction recovery.

You will never know if the medicine actually works or not. The addiction-willpower belief led some to question the placebo control's scientific validity. They thought investigators would be unable to distinguish improvements caused by the experimental treatment from positive outcomes produced by participants' strong desire to get off of drugs, as suggested by this comment from a Hispanic male: "Because you will not know if he quit because he had willpower or because of the placebo. People who were taking the medicine could or could not give up using cocaine. You will never know if the medicine actually works or not."

You have to put some energy into it. Others believed that participation in the clinical trial presented a personal challenge they would have to overcome: "For me the key is if the guy decides to change the situation what the problem is, maybe 50% is the pill they use or the sugar pills . . . and the rest is you have the need to change." (gay male) Another

participant said, “You have to put some energy into it. You have to use your willpower because in reality you have no idea what you are taking in, you know. It may be the sugar pill, and it may also be that you feel better than the person who is taking the real one.” (Hispanic male)

Therapeutic misconception

As illustrated below, some participants thought the placebo was a potentially effective treatment for strengthening the willpower necessary to fight the addiction. Some also thought that it was being used to assess the role of willpower in addiction recovery, as mentioned above.

They are checking to see if you have willpower. Participants’ health beliefs about the nature of addiction and the centrality of willpower in stopping drug use led some to assume the placebo condition was in fact a test of willpower and/or that it was expected to have a therapeutic effect that might even be greater than the experimental treatment. According to one Hispanic male, “Well, what I getting about this video is that they are doing an experiment to find out about what kind of attitude people have in the program, if it works psychologically with the placebo or if it works with the real medicine. What I see is that this is a way of knowing if the person had a psychological will . . . a mental response, or if he had a true reaction.” And a white female said, “She could even get the placebo and psychologically help her get clean.”

Discussion

Consistent with concepts of therapeutic misconception, therapeutic misestimation, and therapeutic optimism, focus group members in our study sometimes conflated research and personalized care, overestimated participation benefits and risks, and thought overcoming addiction might be worth taking a chance on a clinical trial. At the same time, focus group members’ statements were realistic about features that distinguish randomized controlled trials from clinical care and reflected experimental mistrust of investigator integrity and competence.

Experimental Realism. Cognitive deficits from long-term substance abuse, HIV/AIDS-related dementia, comorbid psychiatric disorders, or psychological symptoms associated with addictive disorders, such as cravings and impulsivity, can compromise informed, rational consent. The level of sophistication about research methodology from which the theme experimental realism emerged in our sample was therefore unanticipated in this undereducated, impoverished, and drug abusing population. There are at least two explanations for this finding. First, we designed the consent conference vignette to be as informative and jargon-free as possible. In addition, drawing upon the expertise of our community advisory board, the video “subject” asked the type of questions that a potentially confused participant might wish to ask. For example, the video “investigator” explained random assignment to the placebo and experimental groups as being decided through a process similar to “flipping a coin,” very directly stated that s/he did not know whether the treatment would work, and underscored the nature and reason for the placebo. These findings not only highlight the importance of clear communication during consent conferences, but also that poorly educated street drug users from largely impoverished backgrounds are able to make important distinctions between research and clinical care.

It is important to note that a large portion of our sample (75%) had previously participated in some form of research involving surveys, drug exposure studies, harm reduction interventions, or treatment protocols directed at drug use or HIV. We gleaned from focus group comments that many individuals regularly sought out research participation opportunities as a means of obtaining “honest” money, passing the time, enhancing their knowledge, or doing something that might help others.¹⁵ Future studies will determine the extent to which research experience is typical of street drug users in other cities with active research institutions, and the degree to which the experimental realism observed in our study is tied to such experiences.

Experimental Mistrust. The marginalized drug users in our focus groups had no shortage of mistrust toward the individual investigators portrayed in the video and toward the research enterprise in general. Ironically, experimental mistrust framed the way the therapeutic misconception expressed itself among our participants. For those who conflated research and personal care, the video investigator’s declarations that s/he did not know if the experimental treatment would work were perceived as either disingenuous or a sign of practitioner incompetence.

Addiction Beliefs. Some have argued that denial and other psychological characteristics of illicit drug users—

especially those who do not seek treatment—are evidence that they lack the information or decision-making capacity to make an informed decision about research participation.¹⁶ Yet at least one study showed injection drug users are as competent to consent to an HIV vaccine trial as those who do not use drugs.¹⁷ For some drug users in our sample, beliefs about addiction and recovery shaped their perspectives on the nature of the placebo control. One who has an addictive personality often denies substance dependence and contends that she can quit the habit at any time if she just exerts the necessary willpower.¹⁸ For some focus group participants, this form of addiction denial compromised their ability to fully understand the nature of the placebo as an inert comparison condition. When combined with experimental mistrust, this led some to believe that the true nature of the study was to test their willpower, while for others it led to a therapeutic misconception that both arms of the trial were designed to produce patient benefits.

Is Experimental Mistrust Ethically Tolerable? Horng and Grady argued that both therapeutic misconception and therapeutic misestimation are rarely or only sometimes ethically tolerable because they jeopardize fully informed, autonomous participation decisions.¹⁹ They suggest that when individuals accurately assess research risks and benefits, therapeutic optimism is ethically acceptable because it can be therapeutically beneficial to them. Jansen takes issue with this last position, arguing that false beliefs based on unrealistic optimism lead individuals to enroll in a trial under the erroneous assumption that it will produce desired health outcomes.²⁰

Drawing on these arguments, we believe that experimental mistrust is ethically tolerable when it coexists with or increases adequate comprehension, but not when it compromises the integrity of informed consent for research participation. Experimental mistrust is ethically acceptable when it promotes a healthy skepticism regarding experimental treatment benefits. Such skepticism can motivate participants to ask clarifying questions during the informed consent process that will help them to acquire the information necessary to mitigate the possibility of therapeutic misestimation. Experimental mistrust can also balance therapeutic optimism by encouraging a realistic weighing of participation risks against potential benefits. Experimental mistrust is ethically unacceptable when it inspires subjects to agree to participate because they have assumed that the information given to them is intentionally deceptive, and then based their beliefs about research benefits on this assumption. For example, comments from our respondents suggested that experimental mistrust would lead some to assume that contrary to the investigator's claims during the informed consent interview, random assignment to a placebo was a ruse and that all participants would actually receive treatment, or that the placebo was the condition the investigator believed would result in benefit.

Experimental mistrust may also contribute to fears that research participation will result in the worst personal outcome, concerns that research participation will be frustrating and dispiriting, and skepticism about whether assignment to different conditions is an adequate test of treatment efficacy. This form of experimental mistrust is also ethically intolerable. Deciding whether to participate in a randomized controlled trial must be based on comprehension and acceptance of research risk, as well as a healthy skepticism of potential personal benefits. However, overemphasizing risk can compromise decision-making, especially when combined with participants' unrealistic expectations of placebo benefit. Because this kind of experimental mistrust is based on false premises and discourages participation, it jeopardizes distributive justice by depriving marginalized populations of the benefits of clinical research.

Minimizing Experimental Mistrust. How can investigators minimize experimental mistrust? Educational efforts aimed at improving comprehension of research procedures and reducing confusion about medical care and medical research have been suggested.²¹ While clear and culturally sensitive informed consent dialogues are essential first steps, they cannot remedy distorted appraisals based upon mistrust of the clinical investigator who is providing the information, nor pessimism about health care outcomes in general. Our findings suggest that we may need to build upon the capacity of individuals from economically disadvantaged, uninsured, and socially marginalized populations to be realistic about the nature, purposes, and risks of randomized controlled trials. We must also anticipate and effectively address the personal and collective history of abuses they may have experienced as patients and research subjects.

Study Limitations

Several limitations of these data should be noted. First, analysis of focus group discussions does not lend itself to generalization to other populations with the same degree of confidence as quantitative studies using well-defined samples. The size of each focus group must be small to facilitate discussion, selection of participants is not random and reflects the unique community history of group members, and participant comments cannot be isolated from either the

influence of other group members or the responses of facilitators.²² Rather, themes derived from focus groups—especially when drawn from underrepresented populations—produce valuable heuristic concepts that can be tested in other populations and with other methods.²³

Second, the experimental realism and experimental mistrust themes emerged in response to a hypothetical scenario. While many group members spontaneously drew upon their personal medical and research histories to comment on how they might react to being recruited to participate in a randomized controlled trial, their appraisals might be different if they were actually being recruited to participate in a study.

Third, while we conducted focus groups that were homogeneous with respect to gender, ethnicity, and sexual orientation, this methodology is not conducive to analyses of the role these demographic factors play independently or interactively in appraisals of information about randomized controlled trials. In addition, members of focus groups do not speak with one voice. Individual attitudes can change as focus group members discuss with one another multiple ethical dimensions of the research dilemma presented. Recognition of what Fisher has termed the “opinions in progress” nature of focus group discussions is essential if we are to respect that ethics-in-research decision-making among research participants is as contextually based and contemplative as the ethical deliberations we expect from our professional colleagues.²⁴

Finally, we sought to expand bioethics discourse on the therapeutic misconception to include concepts held by poorly educated, economically disadvantaged, and socially marginalized populations. To begin this exploration, we gathered the opinions of one such population: current or recently active illicit drug users. This population was selected because aspects of drug addiction are controversial, and significant questions have been raised about the consent capacities of drug users recruited to participate in research. Future research with disadvantaged groups who have other disorders is necessary to determine whether the themes that emerged through participants’ appraisal of consent information are a product of their economic and social status, their substance abuse, their hypermarginalized and stigmatized position in society, or all of these factors in tandem.

Acknowledgments

This research was supported by NIDA grant #1 R01 DA015649-01A2 to Fordham University, Principal Investigators, Celia B. Fisher and Merrill Singer. Both teams contributed to data collection, data analysis, and the preparation of this paper. We are grateful for the staff and clients of Housing Works, in New York City, for their advice and participation.

Celia B. Fisher, PhD, is Director, Center for Ethics Education, and Marie Ward Doty Professor of Psychology, Fordham University, Bronx, NY; **Matthew Oransky, MA**, is Research Assistant, Center for Ethics Education, Fordham University, Bronx, NY; **Meena Mahadevan, PhD**, is Research Associate, Center for Ethics Education, Fordham University, Bronx, NY; **Merrill Singer, PhD**, is Director, Center for Community Health Research, Hispanic Health Center, Hartford, CT; **Greg Mirhej, MA**, is Research Scientist, Hispanic Health Council, Hartford, CT; and **Derrick Hodge, PhD**, is Research Scientist, Hispanic Health Council, Hartford, CT.

References

1. Appelbaum PS, Roth LH, Lidz C. The therapeutic misconception: Informed consent in psychiatric research. *International Journal of Law and Psychiatry* 1982;5:319-329; 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(2):20-24.
2. Appelbaum PS, Lidz WL, Grisso T. Therapeutic misconception in clinical research: Frequency and risk factors. *IRB: Ethics & Human Research* 2004;26(2):1-8.
3. Davis TC, Holcombe RF, Berkel HG, 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.
4. Horng S, Grady C. Misunderstanding in clinical research: Distinguishing therapeutic misconception, therapeutic misestimation, and therapeutic optimism. *IRB: Ethics & Human Research* 2003;25(1):11-16.
5. See ref. 2, Appelbaum et al. 2004; Schaeffer SH, Krantz DS, Wichman A, et al. The impact of disease severity on the

informed consent process in clinical research. *The American Journal of Medicine* 1996;100:261-268.

6. Advisory Committee on Human Radiation Experiments. *Final Report*. Washington DC: U.S. Government Printing Office, 1995, chap. 16; Gordon EJ, Yamokoski AH, Kodish E. Children, research, and guinea pigs: Reflections on a metaphor. *IRB: Ethics & Human Research* 2006;28(5):12-19; Kodish E, Eder M, Noll RB. Communication of randomization in childhood leukemia trials. *JAMA* 2004;291(4):470-475; Lidz CW, Appelbaum PS. The therapeutic misconception: Problems and solutions. *Medical Care* 2002;40(9, suppl.):V-55-V-63.
7. National Bioethics Advisory Commission. *Research Involving Persons with Mental Disorders that May Affect Decisionmaking Capacity*, vol. I, *Report and Recommendations*. Rockville, MD: National Bioethics Advisory Commission, 1998.
8. Joffe S, Cook EF, Clear PD, et al. Quality of informed consent in cancer clinical trials: A cross-sectional survey. *Lancet* 2001;358:1772-1777; See ref. 2, Appelbaum et al. 2004; Hochhauser M. "Therapeutic misconception" and "recruiting doublespeak" in the informed consent process. *IRB: Ethics & Human Research* 2002;24(1):11-12; Waggoner WC, Mayo DM. Who understands? A survey of 25 words or phrases commonly used in proposed clinical research consent forms. *IRB: A Review of Human Subjects Research* 1995;17(1):6-9.
9. Fisher CB. A relational perspective on ethics-in-science decision-making for research with vulnerable populations. *IRB: A Review of Human Subjects Research* 1997;19:1-4; Fisher CB. Relational ethics and research with vulnerable populations. *Reports on Research Involving Persons with Mental Disorders That May Affect Decision-Making Capacity*. Rockville, MD: National Bioethics Advisory Commission, 1999, p. 29-49; Fisher C. Ethics in drug abuse and related HIV risk research. *Applied Developmental Science* 2004;8(2):91-103.
10. Fisher CB. Participant consultation: Ethical insights into parental permission and confidentiality procedures for policy relevant research with youth. In: Lerner RM, Jacobs F, Wertlieb D, eds. *Handbook of Applied Developmental Science*, vol. 4. Thousand Oaks, CA: Sage, 2002, p. 371-396; Fisher CB, Wallace S. Through the community looking glass: Reevaluating the ethical and policy implications of research on adolescent risk and psychopathology. *Ethics and Behavior* 2000;10(2):99-118; Grady C, Hampson LA, Wallen GR, et al. Exploring the ethics of clinical research in an urban community. *American Journal of Public Health* 2006;96: 1996-2001; Melton GB, Levine RJ, Koocher GP, et al. Community consultation in socially sensitive research: Lessons from clinical trials of treatments for AIDS. *American Psychologist* 1988;43:573-581.
11. See ref. 4, Horng and Grady 2003; Jansen LA. The problem with optimism in clinical trials. *IRB: Ethics & Human Research* 2006;28(4):13-19.
12. Corbie-Smith G, Thomas S, Williams M, Moody-Ayers S. Attitudes and beliefs of African Americans toward participation in medical research. *Journal of General Internal Medicine* 1999;8:23-30; see ref. 10, Fisher and Wallace 2000; Friemuth VS, Quinn SC, Thomas SB, et al. African Americans' views on research and the Tuskegee Syphilis Study. *Social Science and Medicine* 2001;52:797-808; Gwadz MV, Leonard NR, Nakagawa A, et al. Gender differences in attitudes toward AIDS clinical trials among urban HIV-infected individuals from racial and ethnic minority backgrounds. *AIDS Care* 2006;18(7):786-794; Sengupta S, Strauss RP, Devellis R, et al. Factors affecting African American participation in AIDS research. *Journal of Acquired Immune Deficiency Syndromes* 2000;24:275-284.
13. See ref. 4, Horng and Grady 2003.
14. Kleiman M. The "brain disease" idea, drug policy and research ethics. *Addiction* 2003;98:871-874; Leshner AI. Introduction to the special issue: The National Institute on Drug Abuse's (NIDA's) Drug Abuse Treatment Outcome Study (DATOS). *Psychology of Addictive Behaviors* 1997;11:211-215.
15. Mahadevan M, Fisher CB, Bonet L, et al. Risks and benefits of participating in drug abuse research involving HIV testing: Views from the street. Conference presentation, Society for Applied Anthropology, Tampa, FL, March 28, 2007.
16. Adler MW. College on problems of drug dependence, special report: Human subject issues in drug abuse research. *Drug and Alcohol Dependence* 1995;37:165-175; Charland LC. Cynthia's dilemma: Consenting to heroin prescription. *American Journal of Bioethics* 2002;2:37-47; Cohen PJ. Untreated addiction imposes an ethical bar to recruiting addicts for nontherapeutic studies of addictive drugs. *Journal of Law, Medicine & Ethics* 2002;30:73-81; see ref. 9,

Fisher 2004.

17. Harrison K, Vlahov D, Jones K, et al. Medical eligibility, comprehension of the consent process, and retention of injection drug users recruited for an HIV vaccine trial. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* 1995;10:386-390.

18. See ref. 14, Kleiman 2003, Leshner 1997.

19. See ref. 4, Horng and Grady 2003.

20. See ref. 11, Jansen 2006.

21. See ref. 2, Appelbaum et al. 2004; see ref. 4, Horng and Grady 2003.

22. Krueger RA. *Analyzing and Reporting Focus Group Results*. Thousand Oaks, CA: Sage, 1998.

23. Guba EG, Lincoln YS. Epistemological and methodological bases of naturalistic inquiry. *Educational Communication and Technology Journal* 1982;30:233-253.

24. See ref. 10, Fisher and Wallace 2000.

Celia B. Fisher, Matthew Oransky, Meena Mahadevan, Merrill Singer, Greg Mirhej, and Derrick Hodge, "Marginalized Populations and Drug Addiction Research: Realism, Mistrust, and Misconception," *IRB: Ethics & Human Research* 30, no. 3 (2008): 1-9.