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Method for a Study of Therapeutic Misconception

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Objectives of the Working Paper

This paper describes the Method for a study of therapeutic misconception performed at the University of Massachusetts Medical School during 1998-2002. The research was supported by a grant from the National Institute of Mental Health (1-R01-MH58097) to Charles Lidz (principal investigator) and Paul S. Appelbaum and Thomas Grisso (co-investigators).

In preparing for publication of the study, it became apparent that most publication venues would not provide sufficient opportunity to describe the Methods for the study in adequate detail. This CMHSR Working Paper, therefore, has been prepared as a document that can be supplied to other researchers who seek more information about the Method than journal publications are likely to provide.

The Study of Therapeutic Misconception

In treatment settings, clinicians owe primary allegiance to their patients' well being. Typically patients can expect that this will offer personal care designed specifically to treat their own disorder in a manner that is consistent with their own needs.

In contrast, clinicians engaged in medical research cannot always provide the personalized care that is the tradition of medicine. They experience a sometimes conflicting set of obligations to protect the validity of the data they generate. This often necessitates the use of techniques, such as randomized assignment, placebo control groups, double-blind procedures, and fixed treatment protocols, that usually do not allow for modifications to meet individualized needs of participants in clinical research.

A number of past studies have described a phenomenon, called *therapeutic misconception* (TM), in which clinical research subjects fail to recognize the ways in

which research participation may involve the sacrifice of some degree of personal care. Most research protocols must fully disclose the conditions of participation to prospective subjects, which necessitates an explanation of the risks of participation, including any ways in which the study's procedures differ from ordinary medical care. But it has long been known that some patients, whether because of socialization to ordinary medical care and the role of doctors or for some other reason, continue to believe that as research subjects they will receive individualized care that is intended for their benefit. This is of concern because it means that some patients volunteer for clinical research with a distorted notion of the benefits and risks, thus failing to meet essential criteria for informed consent

While TM has been observed and described for several decades, there have been few empirical studies to document its nature, prevalence, and correlates. Indeed, there have been no objective measures of TM or TM-like dimensions with which to perform systematic research on the phenomenon. Developing methods to assess TM, and thereby documenting the prevalence of TM in a range of clinical research studies, were among the general objectives of the present study.

Participants in the Study

Description of Participants

Participants (n = 243) were recruited from among 263 persons (20 refused) who were approached in the context of their recruitment to participate in 44 clinical research studies being conducted at two academic medical centers. Of the 243, 18 subjects were excluded from this report due to inadequate data. The resulting sample (n = 225) included 9 participants from 26 studies at one center and 126 from 18 studies at the other. The disorders that served as the focus for each of these studies are characterized in Table 1.

Table 1
Disorders Targeted in Research Projects Examined in this Study

Disorders	Number of Studies	Number of Participants
Asthma	1	13
ADHD	1	19
Cancer	13	38
Depression	8	51
Heart Disease	6	27
Hepatitis C	2	4
Osteoarthritis	3	16
Rheumatoid Arthritis	2	21
None	1	19
Other*	9	17
TOTAL	44	225

* Includes acute respiratory distress syndrome, diabetes, hemophilia, HIV infection, plantar warts, polycystic ovary syndrome, and Sjogren's syndrome

The number of participants drawn from each study ranged from 1 to 20 (mean = 5.1, S.D. = 5.4), with 60.1% (n = 137) obtained from 10 studies. Participants ranged in age from 18 to 82 years (mean = 53.1, s.d. = 15.5), including 68 males (30.2%) and 157 females (69.8%). Ninety-one percent (90.5%) were non-Hispanic whites, 5.4% African-American, 1.3% Hispanic, and 2.7% other. Subjects were highly educated with a mean of 14.2 years of schooling.

When interviewed for the present study, almost all of the participants either had not yet begun their participation in the medical research studies for which they had volunteered or were in the very earliest stages of participation. Only a small proportion of them had experienced the medical research procedures involved in the studies for which they had volunteered. Past participation in at least one medical research study was reported by 30% of the participants.

Description of Medical Research Studies

The medical research studies from which participants were obtained included a very heterogeneous mix of medical research topics, objectives, and interventions. In twenty-four of the studies, at least one of the interventions was an FDA-approved drug. Risks of the procedures ranged from minimal in both likelihood and seriousness to procedures with more than a small chance of serious harmful consequences.

Tools and Measures

The procedure described later included a *Therapeutic Misconception Interview* (TM Interview). This semi-structured interview consisted of questions that require the participant to describe and reflect on the nature, purpose, demands, and potential consequences of the clinical research study for which they have recently volunteered. The interview was designed to provide information that could be scored for two purposes: a measure of their *understanding* of the information that was in disclosure forms for obtaining informed consent, and a measure of the degree to which they manifested *therapeutic misconceptions* regarding the nature of the medical research study. Understanding was measured by using responses to the interview to obtain the participant's score on the Understanding scale of the MacArthur Competence Assessment

Tool-Clinical Research (MacCAT-CR). Therapeutic misconception was assessed by using the interview responses to obtain ratings on the Therapeutic Misconception Index (TMI). These tools and instruments are described below.

Consent Form Analysis (CFA)

Preliminary to interview and scoring, it is necessary to document the design, procedures, benefits, and risks of the clinical research study for which individuals' understanding and therapeutic beliefs will be assessed. For this purpose, a *Consent Form Analysis* (CFA) was developed. This form provides a standardized way of identifying and documenting various elements of the clinical research study about which participants have been informed prior to the present procedure. A copy of the CFA is included in this Working Paper (see *Appendix A*).

Therapeutic Misconception Interview(TM Interview)

This structured interview consists of two parts. A set of introductory questions orients the participant to the task of talking about the clinical research study for which the person has volunteered (e.g., How did you first hear about the research study? What led you to sign up for it?). This set of questions is important for scoring TM because it provides the participant a chance to describe the project uncontaminated by the more specific framing of the project that is contained in the subsequent, more structured questions. It is here, for example, that participants sometimes revealed that they were unaware that their "treatment" was part of a research project. The second, more extensive set of questions elicits responses with which MacCAT-CR Understanding and the Therapeutic Misconception Index could be scored. All questions are asked in the same sequence and wording for every interviewee. Interviewers, however, are encouraged to

probe for clarification of answers when a participant's original responses are vague or otherwise difficult to understand.

The second set of questions was drawn in part from the manual for the MacCAT-CR (Appelbaum & Grisso, 2001). They elicit the individual's grasp of the nature and purpose of the research study, its procedure as the participant will experience it, its potential benefits and risks/discomforts, and matters of confidentiality and voluntariness associated with the study.

Other questions were constructed to focus on the two primary dimensions of therapeutic misconception as described earlier: perceptions of potential benefits of participation, and perceptions of the degree to which the study was focused on general vs. individualized care. Among these questions were some that were phrased in an open-ended format; others requested a yes-no answer but encouraged explanation of the answer. A copy of the TM Interview is included in this Working Paper (see *Appendix B*).

MacCAT-CR Understanding

The *MacArthur Competence Assessment Tool for Clinical Research* (MacCAT-CR: (Appelbaum & Grisso, 2001) was designed to assess the degree to which individuals understand and appreciate the significance of information that has been disclosed to them in the process of obtaining their informed consent to participation in any clinical research study, and can use the information to reason about their choice. Only the "Understanding" scale of the MacCAT-CR was used in the present study. The Understanding scale focuses on participants' factual understanding of what they have been told about a research study, and 11 questions in the MacCAT-CR procedure (all employed in the TM Interview) elicit responses for scoring factual understanding.

While the MacCAT-CR allows for assessment of similar *elements* found across studies (e.g., purpose of the study, procedure, benefits, and risks), the specific *information* that must be understood regarding each of those elements will be different from one study to another. For this reason, scoring of the MacCAT-CR first requires identification of the specific information associated with each of the elements: for example, the specific risks associated with the particular study in question.

There are three ways to define the specific conditions of a study within these elements:

- as described in the research protocol that is written for purposes of Human Subjects committee review
- as described in the participant consent form, and
- as it was disclosed to individuals verbally by researchers during the process of obtaining their informed consent.

(One cannot presume that these three versions of a study's conditions will always be in agreement with each other, and, in our experience, often they were not.) For the present study, we chose to use the consent form as the criterion for defining such matters as a study's purpose, procedure, risk, and benefits, because (a) what they were told verbally when their research studies were proposed to them was not documented, and (b) they could not be expected to have knowledge of information that was in the Human Subjects protocol if it was not in the consent form. Therefore, each study's elements are translated into specific content for the scoring of Understanding, using the information already documented in the CFA for the clinical research study for which a participant has volunteered.

After the study's elements have been translated for specific content, participants' responses to the relevant questions are scored (2 = adequate understanding, 1 = partial understanding, 0 = inadequate understanding) according to the standardized criteria in the MacCAT-CR manual to be applied to the specific facts of the research study in which they are participating. Scores on MacCAT-CR Understanding may range from 0 to 26.

The MacCAT-CR is published commercially and may be obtained from Professional Resource Press, Sarasota FL (1-800-443-3364).

Therapeutic Misconception Index (TMI)

The TMI involves scoring a participant's TM Interview material for evidence associated with two *belief concepts*. Unlike the MacCAT-CR process, no specific interview questions are scored. The scorer examines the individual's responses throughout the whole interview protocol to identify evidence in any part of it for presence of any of the four belief concepts. Participants receive a "Y" if the belief is present, "N" if it is absent, and "0" if the participant's responses do not allow an opinion to be formed. The two concepts and the nature of the scoring criteria for each of them are defined as follows. Materials further describing the TMI concepts and demonstrating the scoring criteria are included in this Working Paper (see *Appendix C*).

Unreasonable Belief about Benefit

This refers to the fact that a medical benefit the individual anticipates is not "reasonable" to expect. Whether an expectation of benefit is unreasonable, of course, requires a consideration of: (a) the specific design, procedures, and benefits described in the study's consent form, (b) the participant's description of the benefit, and (c) the participant's expressed likelihood of the benefit. Beliefs in medical benefit were

considered unreasonable if, in the context of a particular research project, the participant's description of the benefit was *medically impossible or inconsistent with the design of the study*. The TMI scoring procedure first asks the scorer to identify whether the individual has indicated a belief that participation may involve some personal medical benefit. If this is present, then the scorer identifies whether this belief is unreasonable, according to criteria in the manual (see *Appendix C*) that assist in making this judgment.

Belief in Individualized Care

The second index of TM involves evidence that the participant believes that his or her own needs will dictate individualized adjustments (e.g., of medications or experimental assignments) that the study design does not in fact allow. Criteria for identifying this in the participant's record is provided in the TM scoring manual (see *Appendix C*).

Participants receive a score of 0 (not present) or 1 (present) for both types of beliefs. A total TM score is also calculated as the sum of ratings on Benefit and Individualized Care

SF-36

Participants were administered the SF-36 (Ware, 1993), a measure of general health that includes items on physical/medical conditions as well as functioning.

Procedure

Data were collected for this study from September 22, 1998 to June 28, 2000. The study first required identifying ongoing clinical research studies from which participants for the present study could be obtained, then identifying potential participants as they volunteered for the clinical research studies, and administering the present study's tools and measures.

Selecting and Recruiting Clinical Research Studies

Projects were recruited initially by meeting with the Chairs of all clinical departments at the University of Massachusetts Medical School and the Chairs and Division Heads of the most research-active departments at the University of Pittsburgh Medical School. They were asked to name the researchers who did the most clinical research in their department or division. These researchers were then contacted and, almost without exception, they agreed to participate. We selected the projects that the researchers identified as most likely to recruit significant numbers of participants.

Identifying Clinical Research Participants

Each clinical research study had a person associated with that research team who was responsible for recruiting, informing, and obtaining consent from potential volunteers for that study. We arranged with those individuals in the various clinical research studies to notify us whenever they obtained consent for participation in their research study from anyone who was willing to participate in our study, was able to consent to it, and with whom an appropriate time for an interview could be arranged.

When such notifications were received, we contacted the participant. This was accomplished in varied ways across studies. If the research staff person was able to contact us while the participant was still at the research site, this was done in person. If the participant had already left the site, arrangements were made to interview the participant either at his or her home, a mutually convenient meeting place or, if necessary through a telephone interview.

Participant Interviews

Of those persons contacted, 7.9% refused to participate in the interview. In most cases the interview occurred the same day that the participants consented to participate in the clinical research study from which they were recruited, but in some cases the interviews were as late as one week after consent. The present study was described to the individual as a project to learn more about people's voluntary participation in clinical research studies. In other words, individuals were told that they were being interviewed because they had volunteered for a clinical research study, that we wished to talk to them about their willingness to be in that study, but that the present study was not related to the one for which they had volunteered. If they consented to participate, they were asked for demographic identifying information. They were then administered the TM Interview, which typically required 30 to 45 minutes. Participants were given $10 to thank them for their participation.

References

Appelbaum, P., & Grisso, T. (2001). *MacArthur Competence Assessment Tool for Clinical Research.* Sarasota, FL: Professional Resource Press.

Ware, J. (1993). *SF-36 Health Survey: Manual and Interpretation Guide*. Boston: The Health Institute, New England Medical Center.

APPENDIX A

CONSENT FORM ANALYSIS FORM

Title: _____

_____

_____

(Study ID)

Benefits to Subjects

_____ Consent form states no benefit(s)

_____ Consent form states possible benefit(s)

_____ Consent form states benefit(s)

_____ Possible benefits include:

- _____ Tests only FDA approved drugs for this condition
- _____ Standard care (drugs, tests, etc.)
- _____ Diagnosis
- _____ Evaluation
- _____ Tests only
- _____ Information about one's medical condition
- _____ Other: _____

Lethal Risk(s)

_____ Death has occurred as a possible outcome of participation

_____ Death has occurred as a possible outcome of drug administration

_____ Death may occur as possible outcome of participation

Design

Total no. of drugs/treatments: _____ Total no. of conditions: _____

_____ Data collection study

_____ Safety and efficacy study

_____ Tests one (1) FDA approved drug

_____ Tests one (1) FDA approved drug for this condition

_____ Tests one (1) FDA approved drug for this condition, but not at this dose

_____ Tests one (1) FDA approved drug for another condition

_____ Tests two (2) FDA approved drugs

_____ Tests two (2) FDA approved drugs for this condition

_____ Tests two (2) FDA approved drugs for this condition, but not at this dose

_____ Tests two (2) FDA approved drugs for another condition

_____ Tests two (2) FDA approved drugs for this condition, but in combination

_____ Tests three (3) FDA approved drugs for this condition, but in combinations

_____ Tests one (1) “clinically-promising” drug

_____ Tests two (2) “clinically-promising” drugs

_____ Tests one (1) experimental drug

_____ Tests two (2) experimental drugs

_____ Tests two (2) standard care treatments

_____ Tests one (1) “clinically-promising” treatment

_____ Tests two (2) “clinically-promising” treatments

_____ Tests one (1) experimental treatment

_____ Tests two (2) experimental treatments

_____ Standard care (drugs, tests, etc.) a possible condition

Design Features

_____ Randomized

_____ Placebo-controlled

_____ Double-blind

_____ Single-blind

_____ Unblind

Alternatives

_____ Same drug(s)/treatment(s) available outside of study

_____ Same drugs available outside of study though not in combination

_____ FDA approved drug(s) outside of study listed

_____ Standard care outside of study listed

_____ No alternative treatments outside of study listed

_____ No alternative treatments available outside of study

Procedure

_____ Dosage not disclosed

_____ Dosage(s) held constant by a protocol

_____ Dosage(s) increased from subject to subject

_____ Subjects will receive increasing dosages over time

_____ Dosage(s) may be altered in response to a subject's tolerance

_____ Dosage(s) may be altered in response to a subject's tolerance in severe situations

_____ Number of administrations can vary by subject as needed

_____ Number of administrations will vary by subject

_____ Certain previously prescribed drug(s) precluded

_____ Previously prescribed drug(s) precluded

_____ Previously prescribed treatment(s) precluded

_____ Certain adjunctive treatments not allowed

_____ Adjunctive treatments not allowed

_____ Consent states subject will be dismissed from the study if condition worsens

_____ Other: _____

Follow-up

_____ Ongoing research follow-up required

_____ Ongoing research follow-up offered

_____ Ongoing clinical follow-up required

_____ Ongoing clinical follow-up offered

Future Research

_____ Blood or other samples requested for future research

_____ Blood or other samples required for future research

APPENDIX B

Therapeutic Misconception Interview: Part 1

Subject Initial Interview

1. I understand that you have (disease). Can you tell me a bit about it and how it has affected you? *When did you first notice a problem?*

2. Can you tell me a little about the history of your treatment? *Do you have a family doctor? Did s/he discover this or did it happen in another way? How did you get to UMass?*
   How have you (they) treated it up to this point? Has it helped?

3. How did you end up getting to this research project? *Who first contacted you about it? Did you hear about it on your own or did your doctor refer you? Did your doctor tell you why s/he decided to refer you? What made you interested in the project?*

4. What led you to decide to (or not to) sign up for the research project?

5. What does the project involve?

6. Did you talk with anyone else about the project?
   Other patients who are in it?
   Did you read about it anywhere?

Okay, now I am going to ask you some structured questions. Some of these may not quite apply to you or you might think that I should know better than to ask you, but I do need to ask everyone these questions, okay?

APPENDIX B

Therapeutic Misconception Interview: Part 2

MacCAT

U-1
1. Purpose:
What is the purpose of the project? That is, why are the researchers doing it?

2. Duration:
How long will your participation in the project last?

3. Procedural element 1: Pre-intervention
What specifically will you need to do before the treatment can begin?

4. Procedural element 2: Intervention
What, specifically will the intervention involve?

Aside from the intervention, is there anything else that the project will involve?

U-2
1. What is the primary goal of the project? In other words, was the project designed to help people in the future or help the individual participants in the study?

U-3
Individualized Care
1. Will the treatment be the same for everyone in the study? (How will researchers decide who gets the study drug and who doesn't?)

2. Can the treatment be changed if it seems it will help the person to change it?

U-4
Benefits
1. What might the researchers learn if people decide to participate in the study?

2. In what way might you be better off personally by being in this project?

Risks and Disadvantages:
1. What, if any, are the risks or disadvantages of being in this study?

U-5
Withdrawal
What would happen if you decide that you did not want to be in the study anymore?

APPENDIX C

Therapeutic Misconception Index

TM Coding System

General Instructions

For each case, we will search the transcripts to assess two specific dimensions of the subjects understanding.

We are permitted to use all information in the text except the explicit PIRQ answers. They should not be in the transcript but sometimes one gets the idea of what they are from the comments made during the discussion. Such information should not be used. However any questions asked or comments not directly reflective of the answers given on the PIRQ are usable.

In coding these, we need to be careful that the subjects are referring to what is being gained from participating in the research project not from other treatment. Of course if the subjects do not see a distinction between treatment and research, that is TM but sometimes their comments are not clearly directed at a research component of what they are going through.

For each dimension we will review the text coded under one or more codes. We will then use the following information to code the two dimensions into one of three possible categories:

1. Y = evidence of TM present on this dimension. Note that any **clear** evidence suffices. Conflicting evidence should not raise doubts about this since we are assuming that people can have conflicting beliefs. Therefore if the subject believes that the treatment will be individualized but also that it is randomized and double blind, that would still count as a "Y". However ambiguous statements or statements that can be interpreted in multiple ways should not count as a "Y" unless it seems **more likely that not** that TM is present

2. N = there is evidence present that the individual does not have TM on this dimension. This does not have to be conclusive evidence that there is no TM anywhere. It will do to have evidence that the subject has some areas of understanding with no TM if there is not enough evidence to code a "Y".

3. 0 = no evidence present or ambiguous evidence which makes use of one of the first two codes impossible. In general, conflicting or uncertain evidence should result in a group review of the instance.

The dimensions are:

1. **Unreasonable Benefit**: This is a two stage judgment. First we assess:

Any Personal Benefit - The question here is whether or not the subject sees any personal benefit to participation other than financial benefits, which is different than his/her participation in the society or being a member of an at risk class. Thus we do not count this as Y if the subject says "In this study doctors will learn more about cancer and I have cancer." or "This study will help learn about depression and my children are at risk for depression therefore I want to participate" However we do include such things as "I will learn more about my disease"

Unreasonableness- Y's in this code are a subset of Y's in **Any Benefit**. What is reasonable is not an easy thing to assess. A few hints:

a. If the result suggested cannot possibly happen, that is Y
b. If the methods of the study preclude the perceived benefit from being correct, that is a Y
c. If we are dealing with a clinical trial where two medications are tested and one is unproven and the other is available on the market, this is a Y unless the subject has a substantial reason to believe that the available treatment will not work or has very significant undesirable side effects.

d. If the consent form says "no benefit" and the subject sees a benefit this is a good indication that we should code Y.

2. **Treatment individualization**: *If there is any doubt after reading the consent form, the protocol should be reviewed first to see if it does indeed involve treatment standardization. If not code 0 and continue.*
There are two ways in which we often find this:

a. If the subject believes that assignment to an intervention condition (which is randomized or otherwise not clinically determined) is determined by the patient's needs.
b. The subject believes that treatment specifics (e.g. medication dosage) will be determined by individual need rather than by protocol (of course some protocols allow some of this and we need to be careful that the subject is not just reporting fact)

We have a lot of trouble interpreting statements here because some subjects state that everyone gets the same treatment but mean that they are all getting the best treatment.