

Improving Informed Consent to Clinical Research

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Therapeutic Misconception (TM) is a major problem in informed consent to clinical trials

TM occurs when a research subject fails to grasp the **distinction between clinical research and ordinary treatment** and attributes therapeutic **intent** to research procedures

Competing Commitments in Clinical Research

- The primary **purpose** of research is to gather **valid data** that will provide an answer to an important research question
- Ethical rules require researchers to protect patients
- Most clinical researchers also are dedicated to good clinical care

Contrasting Clinical Trials and Ordinary Treatment

➤ Treatment

- Individualized Tx decisions
- Physician selects Tx for pt. benefit
- Other treatments used if thought helpful
- Dosage adjusted for maximum benefit

➤ Clinical Trials

- Randomized assignment
- Physician blinded
- Restrictions on other treatments
- Limited adjustment of dosage

Imagine Visiting Your Doctor Who Says

- I have two medications I could give you for this but I don't know which is best so someone else will decide by a coin flip.
- I won't know which one you are getting.
- I have some other medications that might help but I won't let you have them.
- You are going to get this exactly dose unless you have really severe side-effects, whether it helps or not.

These restrictions on treatment are not trivial

- Researchers do not impose these limitations lightly
- They are essential for gathering generalizable data
- Research staff often monitor care better
- **If we take informed consent seriously, subjects should consider these important issues when enrolling**

Illustration: Subject #50

Interviewer: Do you know how treatment in this study is different from ordinary care? Did they say what your treatment would be if you weren't in the study?

Subject: ...No, no, I'll leave that up to them. I want them to give me the best treatment for what I have....if they don't, then I'll drop out.

Interviewer: ...As far as you know if they did have different groups, would the doctors decide which is the best one for you?

Subject: I would assume he would decide which one was the best one for me.

Study 1: Measuring the Therapeutic Misconception

- Text of interviews is coded for two features:
 - the belief that the treatment would be individualized to the subject
 - an unreasonable assessment of benefit (i.e. one precluded by the design of the study)
- Found, conservatively, **62% of a sample of research subjects met one criterion or both**

Understanding of Risks: Qualitative Data from Study 1

- Critical Interview Question: “What, if any, are the risks or disadvantages of being in this study”
- Coded entire text for statements about risks and disadvantages
- N=149

Risks of Treatment

- 23.9% reported no risks or disadvantages
- 2.6% noted only incidental disadvantages
- 14.2% of sample reported only risks associated with standard care
- Largest group (45.8%) reported side effects of the experimental intervention
- None of the above subjects (86.5%) had any apparent awareness of risks associated with the **design** of clinical trials

Risks of the Research Design

- 13.5% of subjects reported some awareness of the risks involved with the research design
- Examples:
 - 12 subjects expressed some concern about possibly getting a placebo (including 4 who reported other concerns about clinical trials)
 - 4 subjects expressed concerns about the double blind design.
 - Others expressed some diffuse concerns e.g. “there are always risks”

What Should We Make of Studies of TM

- Most people join clinical trials because they believe that they will benefit from them
- About half of the subjects have **at least a minimal** understanding that clinical trials are not simply treatment

A Validated Measure of TM

- Recently published new scale
- .Probably should be thought of as a screen not a definitive measure
- Appelbaum PS, Anatchkova M, Albert K, Dunn LB, Lidz CW. Therapeutic misconception in research subjects: development and validation of a measure. Clin Trials. 2012 Dec; 9 (6):748-61

Methods

- 220 participants in clinical trials at 4 medical centers
- Completed 28 item Likert questionnaire
- Thorough semi-structured interview
- Interview coded for three dimensions of TM: **Benefit**, **Purpose**, **Individualization**

Results

- 10 item scale
- 3 strongly correlated factors
- Validated against coded interview
- Positive Predictive Value was 0.65 and Negative Predictive Value was 0.68, with a Positive Likelihood Ratio of 1.89, and a Negative Likelihood Ratio of 0.47.
- That is the simple version of the results
- Copies available

A New Theory of TM

- Humans understand their environment in socially structured cognitive frames
- These frames help us understand each other but they can also lead to misunderstandings when they do not match.



Researcher's Primary Frame: Science

- In designing clinical trials, researchers generally approach the studies from what can be called a “Scientific” cognitive frame.
- Based on an *abstract* concept of how the efficacy of a treatment can be demonstrated.
- This abstract frame regards **cases as units** to be managed according to a protocol that guides the activities of the researcher.

Researcher's Primary Frame

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- A predetermined number of these units need to be studied
- treatments being compared should have equivalent groups and thus participants must “be assigned” treatments at random
- Neither the treating physician nor the participant should know which medication the participant is getting to prevent bias

Researcher's Primary Frame

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- Dosages are restricted to a predetermined range so that the intervention is clearly defined
- other medications that might also affect the outcome are prohibited.
- This frame is **independent of specific patient needs**

Participants' Primary Frame: Personal Needs

- Participants focus on the study from the point of view of the individual units (i.e., themselves) and their medical needs.
- Coming for help with a problem and see the study in that context.
- many participants either ignored design features or made up reasons for them that were consistent with a focus on their own medical needs

An Example of Conflicting Frames - Eligibility

- For researchers, eligibility is built into the design of the trial. Usually trial designs include tightly defined groups to reduce extrinsic sources of variability in response to the intervention.
- Participants tended to see eligibility as a question of whether they personally would be likely to benefit from the experimental intervention. Thus participants reported that the doctor found they were “eligible” and thus would benefit.

The role of secondary frames

- If there were only primary frames, researcher and clinician would quickly be in conflict.
- Secondary frames are one of several ways in which they can continue to misunderstand each other.



Researcher's Secondary Frame

- Particularly prominent among those actively delivering tx to patients.
- Ethical commitments of clinical trials require protecting participants and many of our researcher-interviewees insisted they would never put participants at risk
- Besides: Excellent physicians, more time for pt., better monitoring of condition, possible benefit from new treatment.

Participant's Secondary Frame

- Research is important
- Research is hard to understand and technical
- Researchers are “studying me” and how I respond to treatment. That is, some see the research as a series of single case studies.

Secondary frames & TM

- The researcher's secondary frame allows them to feel comfortable telling participants that they will be very well cared for.
- That reassurance combined with participants own misunderstanding of what research is, allows those in trials to have a sustained therapeutic misconception

How can Informed Consent be saved?

- Subjects need to understand **why** not just how treatment and research differ
 - Need to see their participation in the context of the research design
 - Allows understanding of the elements of the design: e.g., randomization and double-blind
- As much a part of disclosure as risks and benefits of intervention
- **Participants need to frame what they are consenting to as science**

A Test of the New Theory

- Informed consent to mock clinical trials
- Customized to the disorders of real patients
- With diverse medical conditions e.g.,
 - Cancer
 - Cardiac stents
 - Depression
 - Diabetes
- Randomized to mock ordinary consent or enhanced consent to reframe their understanding of trials

Experimental Disclosure

- The experimental disclosure is available on youtube at:
- <https://youtu.be/hlelhbiuTkc>
- You can feel free to use it if it will help you with consents to clinical trials

Does Reframing Reduce TM?

	Control (n = 80)	Scientific Reframing (n= 74)	p value
TM	30.9 (28.3 -33.5)	24.9 (21.8 – 28.0)	0.004

Does it Affect Recruitment?

	Control (n =80)	Scientific Reframing (N = 74)	P values
Willing to Participate	56.3% (45.3-66.6)	52.4% (40.2 – 62.4)	0.603

The costs and benefits of this approach to TM

- In spite of our results, it would probably reduce the flow of subjects slightly
- Might require rethinking of some designs
- Will defend research from critics who simply don't like this type of research.