

# THERAPEUTIC MISCONCEPTION:

What is it, Why it matters, and How to minimize it

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## Objectives

- Define therapeutic misconception and its importance;
- Distinguish between therapeutic misconception and other factors that may inhibit the informed consent process;
- Develop useful criteria to identify and minimize instances of therapeutic misconception and apply these criteria to cases

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## Definitions

- When clinical research subjects fail to recognize the ways in which research participation may involve the sacrifice of some degree of personal care, they are said to manifest a "therapeutic misconception."
  - Appelbaum, Lidz and Grisso. "Therapeutic Misconception in Clinical Research." *IRB Ethics & Human Research* 26 (2004): 1-8

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## Definitions

- Therapeutic Misconception is not equivalent to mere failure to understand the nature and purpose of the research study or the procedures involved.
  - Lidz and Appelbaum. "The therapeutic misconception: Problems and solutions." *Medical Care* 40 (2002, 9, suppl):V55-V63.
- Conversely, understanding the goals and methods of a research project does not mean that subjects will not necessarily avoid endowing them with therapeutic intent.

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## Definition

- Therapeutic Misconception seems to involve interactions among several phenomena:
  - Presumptions acquired by individuals in clinical treatment and brought with them to the research setting;
  - Subjects' hopes for benefiting from research participation; or
  - Shortcomings of the informed consent process
    - Dresser R. "The ubiquity and utility of the therapeutic misconception." *Social Philosophy and Policy* 19 (2002): 271-294

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*The power of the [research subject's] mind to hear only that which fits its preconception cannot be over-estimated. In addition, it is questionable whether investigators would be willing to be...brutal about shattering subjects' therapeutic misconceptions. The perception of potential benefit, after all, is one of the most powerful incentives for subjects to agree to take part in research projects.*

Appelbaum, Roth and Lidz. "The Therapeutic Misconception: Informed Consent in Psychiatric Research." *International Journal of Law and Psychiatry* 5 (1982): 319-29.

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### Why Therapeutic Misconception Matters...

- Since the initial description of TM in a study of consent of psychiatric research two decades ago, TM is still not uncommon in research:
  - Subjects appear frequently to overestimate the likely benefits of entry into research studies;
    - Daugherty, Banik, Janish, et al. "Quantitative analysis of ethical issues in Phase I Trials: A survey interview study of 144 advanced cancer patients." *IRB: Ethics & Human Research* 22 (2000): 6-14
  - Underestimate risks;
    - Joffe, Cook, Cleary, et al. "Quality of informed consent in cancer clinical trials: A cross-sectional survey." *Lancet* 358 (2001): 1772-1777
  - Confused about randomized assignment;
    - Featherstone and Donovan. "Why don't they just tell me straight, why allocate it?" The struggle to make sense of participating in a randomized controlled trial." *Social Science and Medicine* 55 (2002): 709-719
  - Generally conflate research with ordinary treatment.
    - Cox. "Informed consent and decision-making Patients' experiences of the process of recruitment to phases I and II anti-cancer drug trials." *Patient Education and Counseling* 46 (2002): 1-38

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### Why Therapeutic Misconception Matters...

- Subjects appear frequently to overestimate the likely benefits of entry into research studies:
  - Of 225 participants in 44 different studies, 51.1% manifested an unreasonable belief in the nature or likelihood of benefit;
  - Examples (participant interview)
    - "I think it's a win-win for anybody. I don't think they would ask you to do this or present this to you if they didn't think it was going to help you."
    - "That's the only reason. They're concerned with helping the people. You know, they are helping the people."
    - Interviewer: "So do you think that they are giving everyone the best treatment?"
    - Participant: "I don't think they'd be in this if they didn't. You know it's just like being a doctor with a sign on the door. You know, they're healers."
  - Appelbaum, Lidz and Grisso, "Therapeutic Misconception in Clinical Research." *IRB Ethics & Human Research* 26 (2004): 5.

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### Why Therapeutic Misconception Matters...

- Confused about randomized assignment:
  - Of 225 participants in 44 different studies, 31.1% of participants expressed inaccurate beliefs regarding the degree of individualization of their treatment
    - Examples (participant interview)
      - Interviewer: Agree or disagree: Doctors are not allowed to choose the treatment I receive based on my needs.
      - Participant: Um, disagree
      - Interviewer: So you think in the study they are allowed to pick which group you're going to be in?
      - Participant: I think so.
    - Interviewer: So you're definitely going to get [the active medication]?
    - Participant: Well, I told them this is what I want. I don't have that long to go through researches. Do that on younger people, you know.
    - Interviewer: So [the choice of treatment] does depend on what each individual needs?
    - Participant: I think so, yes. I think they do take into account what each person needs.

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### Why Therapeutic Misconception Matters...

- Generally conflate research with ordinary treatment:
- Phase I Oncology Trails:
  - One-third said that their main reason for participating was to seek a cure or remission;
  - Three-fourths of the patients joined their studies because they hoped the relevant agent under the study would produce some anticancer effect
  - Nearly 90% said their goals in joining a Phase I study were the same as their goals in undergoing established cancer treatments.
- In response to an open-ended question about their motivation for enrolling, *not one person cited a desire to help future patients.*
  - Daugherty et al., "Quantitative Analysis of Ethical Issues in Phase I Trials." *IRB* 22 (2000): 6-14.

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### Why Therapeutic Misconception Matters...

- Generally conflate research with ordinary treatment:
  - Clinical trial "branding" which may contribute to a subject's therapeutic misconception by biasing his or her assessment of the experimental drug
    - *ALIVE* (Adenosine Lidocaine Infarct zone Viability Enhancement trial)
    - *BEST* (Beta-blocker Evaluation of Survival Trial)
    - *MAGIC* (Magnesium In Coronaries)
    - *MIRACL* (Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering)
    - *PROVED* (Prospective Randomized study of Ventricular failure and the Efficacy of Digoxin).
- Mark Hochhauser, "Therapeutic Misconception and Recruiting Doublespeak in the Informed Consent Process." *IRB: Ethics & Human Research* 24 (2002): 13-32.

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### Why Therapeutic Misconception Matters...

- Generally conflate research with ordinary treatment:
  - Advertising of clinical trials
    - "Cancer patient and health care providers have access to these clinical research trials as part of the latest in cancer care"  
<http://www.cancer.uwn.edu/page/protocol/index.html>
    - Chosen for their interdisciplinary nature and potential benefits to patients, these programs range from fundamental investigations of the origin of disease to advanced clinical trials in which patients have access to the latest and most promising treatments.  
<http://www.ucsf.edu/presscl/2001/10/12.50.html>
    - Participants are among the first to receive new treatments before they are widely available.  
<http://www.hawaii.edu/crch/SerCTBenefits.htm>
    - Clinical trials offer high quality cancer care  
<http://www.clevelandclinic.org/cancer/tril/default.htm>
    - If you have cancer, you may want to think about taking part in a clinical trial. Clinical trials are a treatment option for many people with cancer.  
<http://www.cancer.gov/clinicaltrials/Taking-Part-in-Cancer-Treatment-Research-Studies>

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*Why Therapeutic Misconception Matters...*

- Participant and Study Characteristics Associated with the Therapeutic Misconception
  - Increased age;
  - Lower levels of education;
  - Less optimism about one's current health;
  - Greater optimism about one's health in 6 months.
  
- In general, the worse one's self-described health and functional status, the higher one's level of therapeutic misconception
  - Appelbaum, Lidz and Grisso, "Therapeutic Misconception in Clinical Research." *IRB Ethics & Human Research* 26 (2004): 5.

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*Why Therapeutic Misconception Matters...*

*If Therapeutic Misconception is not avoided, it smuggles the virtues accorded exclusively to the sacredness of the patient physician relationship into the researcher subject relationship...*

*"...in order that physician-researchers may continue to see [themselves] as compassionate physicians in the midst of service of dispassionate science."*

Matthew Miller, "Phase I Cancer Trials: A Collusion of Misunderstanding," Hastings Center Report 30 (2000): 41.

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*How to Minimize Therapeutic Misconception*

- Edward Fried Model
  1. Forbidding any physician from referring a patient into a protocol in which he or she has a financial interest and forbidding any physician from conducting research on any patient of his or hers, whether or not for gain.
  
  2. Requiring immediate dismissal from the protocol of all subjects who show unexpected or expected and disabling side effects. This would probably require regular independent assessment of subjects

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## How to Minimize *Therapeutic Misconception*

3. Consent procedures must require all physician researchers to explain to their subjects in comprehensible language,
  1. That they are releasing said researchers from any fiduciary duty they might have them to have as a physician and that the researchers they meet will not be acting in that capacity to them;
  2. That the financial and other interests of the researchers' clients may be more important to them than the interest of the subject in his or her health;
  3. That the most important risks of participation are unforeseeable, and the belief many subjects have that their personal situation "can not get any worse" is false; and
  4. That most subjects who consent to research do not believe these things when they are told them; they are under the impression that its purpose is to help them personally.

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## How to Minimize *Therapeutic Misconception*

- Joffe, Cook, Cleary et al., Model Quality of Informed Consent (QuIC)

Does the evaluative tool itself fail to be sensitive to the therapeutic misconception?

A1. When I signed the consent form for my current cancer clinical trial, I was agreeing to participate in a clinical trial.	Disagree	Unsure	Agree
A2. The main reason cancer clinical trials are done is to improve the treatment of <u>my</u> cancer patients.	Disagree	Unsure	Agree
A3. I have been informed how long my participation in this clinical trial is likely to last.	Disagree	Unsure	Agree
A4. All <u>of</u> the procedures in my clinical trial are standard for my type of cancer.	Disagree	Unsure	Agree
A5. In my clinical trial, one of the researchers' major purposes is to compare the effects (good and bad) of two or more different ways of treating patients with my type of cancer, in order to see which is better. <sup>1</sup>	Disagree	Unsure	Agree
A6. In my clinical trial, one of the researchers' major purposes is to test the safety of a new drug or procedure.	Disagree	Unsure	Agree
A7. In my clinical trial, one of the researchers' major purposes is to find the highest dose of a new drug or procedure that can be given without causing serious side effects. <sup>2</sup>	Disagree	Unsure	Agree

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## How to Minimize *Therapeutic Misconception*

- Joffe, Cook, Cleary et al., Model Quality of Informed Consent (QuIC)

Can an assessment of the adequacy of informed consent do enough to minimize therapeutic misconception?

	I Didn't Understand This at All	1	2	3	4	5	I Understood This Very Well
B1. The fact that your treatment involves research	1	2	3	4	5		
B2. What the researchers are trying to find out in the clinical trial	1	2	3	4	5		
B3. How long you will be in the clinical trial	1	2	3	4	5		
B4. The treatments and procedures you will undergo	1	2	3	4	5		
B5. Which of these treatments and procedures are experimental	1	2	3	4	5		
B6. The possible risks and discomforts of participating in the clinical trial	1	2	3	4	5		
B7. The possible benefits <u>to you</u> of participating in the clinical trial	1	2	3	4	5		

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## How to Minimize *Therapeutic Misconception*

- Integrate a “neutral discloser” into the informed consent process
  - Trained to teach patients about how research participation would differ from clinical care;
  - Has no involvement with the research projects that were seeking participants; and
  - Has no involvement with the patients’ medical care.

Appelbaum et al., “False Hopes and Best Data.” *Hastings Center Report* 17 (1987): 23.

- Physician-researcher who recruit own patient would open IC forms with statement stressing the distinction between research and care:

- Ex.: “... research is an intervention with little evidence suggesting whether effects will be beneficial or harmful.”
- Ex.: “This medical research project is not expected to benefit you.”

Jonathan Moreno et al., “Updating Protections for Human Subjects Involved in Research,” *JAMA* 280 (1998): 1954.

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## How to Minimize *Therapeutic Misconception*

- Use of community member as center of authority assessing *therapeutic misconception*:
  - Similar to Section 46.107(a) of the Common Rule related to Community consultation to prevent group harm:
    - Specific accountability;
    - Education and awareness re: *therapeutic misconception* in research;
    - Barometer of misconception as it relates to a potential subject;
    - Recognize patient enrolling as research subject as a vulnerable population where community members would understand not just IC form, but recruitment process;
    - Community members as secondary reviewer in a primary/secondary reviewer model.

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## Resources

- Rebecca Dresser. “The Ubiquity and Utility of the Therapeutic Misconception.” *Social Philosophy & Policy Foundation* 19 (2002): 271-94;
- Steven Joffe, E. Francis Cook, Paul D. Cleary, Jeffrey W. Clark, Jane C. Weeks. “Quality of Informed Consent: A new measure of understanding among research subjects.” *Journal of the National Cancer Institute* 93 (2001): 139-47;
- Edward Fried. “The Therapeutic Misconception, Beneficence, and Respect.” *Accountability in Research* 8 (2001): 331-48;
- W. Glannon. “Phase I Oncology Trials: why the therapeutic misconception will not go away.” *Journal of Medical Ethics* 32 (2006): 252-55;
- Paul S. Appelbaum and Charles W. Lidz. “Re-Evaluating the Therapeutic Misconception: Response to Miller and Joffe.” *Kennedy Institute of Ethics Journal* 16 (2006): 367-373;
- Franklin G. Miller and Steven Joffe. “Evaluating the Therapeutic Misconception.” *Kennedy Institute of Ethics Journal* 16 (2006): 353-366;
- Charles W. Lidz, Paul S. Appelbaum, Thomas Grisso and Michelle Renaud. “Therapeutic misconception and the appreciation of risks in clinical trials.” *Social Science & Medicine* 58 (2004): 1689-1697;
- Paul S. Appelbaum, Charles W. Lidz, and Thomas Grisso. “Therapeutic Misconception in Clinical Research: Frequency and Risk Factors.” *IRB Ethics and Human Research* 26 (2004): 1-9;
- Gary S. Belkin. “Misconceived bioethics?: The misconception of the “therapeutic misconception”” *International Journal of Law and Psychiatry* 29 (2006): 75-85;
- Mark Hochhauser. “Therapeutic Misconception and “Recruiting Doublespeak” in the Informed Consent Process.” *IRB: Ethics and Human Research* (2002): 11-12;

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