Therapeutic Misconception and the Clinical Investigator

Beyond Protocol Deviations

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“Therapeutic Misconception”

- The misconception that participating in research is the same as receiving individualized treatment from a physician.

- “To maintain a therapeutic misconception is to deny the possibility that there may be major disadvantages to participating in clinical research that stem from the nature of the research process itself.” (Appelbaum et al., 1982)

Prevalence of Therapeutic Misconception in Study Subjects (N=88)

- Unaware of randomization assignment 69%
- Expect assignment on the basis of therapeutic needs 40%
- Failed to recognize possibility of getting inactive treatment 44%
- Unaware physician would be blinded to therapy 39%
- Able to identify how protocol would limit treatment options 9%
- Believe dosages would be adjusted to their clinical needs 50%


Even if clinicians and researchers carefully explain the differences between clinical care and research to patient...

and

Even if consent forms prominently state that subjects are not likely to benefit from participating...

Research therapeutic misconception is difficult to eliminate.
A subject enrolls in a clinical trial because she believes that the investigational device is a “new treatment” that is an approved treatment for her condition.
A subject enrolls in a Phase II, randomized, placebo controlled, clinical trial that is presented to him by his primary care physician, who is also a study investigator.

Although the subject is clearly informed about the purposes of the research, he consents to participation because he thinks that the research is going to personally benefit him.

When asked about this, he says, “I know my doctor would only recommend this study for me if he thinks it would help me.”

A participant enters a large epidemiological study because he believes that the screening tests, that will be performed as part of the research, can replace some routine diagnostic testing performed by his physician and, so, will save him some money.

A subject has a serious, rare, life-threatening condition with no known treatment. She hears about an early phase clinical trial and moves her family across country in order to be near a clinical trial site so that she will be eligible for trial participation.
Therapeutic Misconception invalidates the informed consent

(or Illustrates the deficiencies in the ICF)

Average success rate for new drugs approximately 11%

• 20% in cardiovascular trials
• 5% in oncology
• 60% of the time, major reasons drugs didn’t make it to market had to do with efficacy and safety

Minimizing Therapeutic Misconception for Subjects

A key component of informed consent to participate in medical research is the understanding that research is not the same as treatment.
Therapeutic Misconception and the Physician Researcher

• In clinical practice the physician uses scientific knowledge to care for the patient and may experiment therapeutically with the goal of providing that patient with the most effective treatment.

• The purpose of clinical research is to acquire scientific knowledge to promote the medical good of future patients from experimentation with current research participants.
Therapeutic Misconception and the Physician Researcher

Medical research and medical treatment are two distinct forms of activity governed by different ethical principles.

Clinical Equipoise
(Equipoise = the balance of forces or interests)

How can the ethical physician also be an ethical researcher?

There must be a genuine uncertainty that an experimental treatment is beneficial.
Research misconduct means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. – Fabrication is making up data or results and recording or reporting them.

– Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.

Research misconduct does not include honest error or differences of opinion.
Research Misconduct In Clinical Research

**Falsifications:**
- Substitutions of one subject’s record or samples for another’s.
- Altering eligibility dates, test results etc.
- Falsifying dates on Pt. screening logs.
- Selectively eliminating data.
- Purposely not reporting IRB approved protocol deviations in publications and grant applications.

**Fabrications:**
- Not conducting interviews with subjects and creating records of the interview.
- Making up Pt. visits and inserting that record into the medical chart.
- Filling in missing vitals.

- Asking, influencing or intimidating someone to falsify or fabricate.
- Sabotaging the results of an experiment that is recorded in the research record.
Roger Poisson, MD  
St. Luc’s Hospital, Montreal  
National Surgical Adjuvant Breast and Bowel Project (NSABP)

- Poisson fabricated or falsified data related to laboratory tests and dates of procedures in 125 separate instances in 14 projects, involving 99 patients from 1977-1990.
- All falsifications/fabrications led to the enrollment of ineligible.
- There were cases in which women who previously had cancer were reported as cancer-free, cases of breast cancer that were deliberately downgraded or misclassified, dates of treatment that were falsified, and cases in which proper informed consent was never obtained.

CASE STUDY
Post Mastectomy treatment (tamoxifen vs. placebo)
Pt. enrolled despite skin findings that would have made patient ineligible

Physical exam record from Pt. Chart  
Falsified NSABP enrollment form
Protocol requires WBC ≥ 4000

Lab results from Pt. Chart

Roger Poisson, MD
St. Luc's Hospital, Montreal
National Surgical Adjuvant Breast and Bowel Project
(NSABP)

New York Times, April 1, 1994

Doctor Says He Falsified Cancer Data to Help Patients

MONTREAL, MARCH 31 — Dr. Roger Poisson, a prominent Montreal surgeon who has admitted falsifying data in a major North American breast cancer study, said today that he might have broken some rules but did so out of devotion to patients whose inclusion in the research qualified them for state-of-the-art treatment.
Doctor Says He Falsified Cancer Data to Help Patients

Dr. Poisson said that in 30 years of treating breast cancer patients, his goal had been to provide “the best treatment available with the least amount of mutilation possible.”

He asked not to be judged on the discrepancies in his research data but on his larger contributions to patient well-being.

SUMMARY

- Therapeutic misconception is inherent in clinical research trials and efforts should be in place to minimize the idea that a research subject stands to gain from entering into a clinical research trial.

- IRBs and DSMBs should carefully review protocol exception requests and deviations for excesses.

- Be mindful of motivations to enroll ineligible patients and review data during for-cause-audits.

SUMMARY

- The physician and the research team must recognize therapeutic misconception both with regards to themselves and the research subject.

- It is the responsibility of the research team to minimize therapeutic misconception with regard to the research subject.
For questions or concerns regarding any research misconduct issue* contact the ORI

Phone: (240) 453-8800
Email: AskORI@hhs.gov

* ORI only oversees PHS funded research, but can assist with general research misconduct queries.

For questions or concerns regarding human subject protection issues contact the OHRP

Phone: (240) 453-6900
Email: OHRP@HHS.gov

* Common rule requirements