

## Interactive Ethics

The Ethics Program and STARS invites comments on the ethics dilemma that follows. Students should send their comments by e-mail to [ethics@utsouthwestern.edu](mailto:ethics@utsouthwestern.edu). We will post your comments with your initials, school name, and class subject (or anonymously if you prefer). At the end of the comment period, we also will post a perspective from the ethics program.

**Case for October-December 2009**  
(case closed-commentary posted)

### Treatment vs. Clinical Research

#### Some definitions for this case:

Clinical research is the science of effective medical care. Clinical research does experiments that compare a standard drug with a new, unproven drug. The scientist observes each patient group over time to see which drug works better. Sometimes, the patients in the study (research subjects) can't tell the difference between ordinary medical treatment and being in the research study. This happens even though all the research subjects are told at the beginning that they are joining a research study.

This misunderstanding is called the "therapeutic misconception"- when research subjects think they are getting standard treatment instead of research. In other words, the therapeutic misconception is when sick people participating in a research study believe they are getting standard medical treatment.

A **clinical trial** is a comparison of a standard drug, against a new, unproven, drug ( the **study drug**). How can the researcher be sure that patients getting each drug (standard drug and the study drug) are equally sick? One way is to give all the research subjects the study drug, one at a time. For the first part of the study, half of the subjects are given the standard medicine. The other half get the study drug. In the second half of the study, the drugs are switched around. The scientists then observe which medicine works better over the duration of the study. This kind of study is called a "**crossover**" study, because the each drug is "crossed over" to different subjects over the study period. The study subjects don't know which drug they get. Not only that, but the study doctors don't know which drug the subjects get. This is called a "**double-blind**" study. "Blind" because the person doesn't know which drug is given. "Double" because the subjects AND the doctors don't know which drug is given. The double-blind method prevents **bias** from interfering with the study results. Bias is when the doctor or subject wants one of the drugs to work better.

#### The Case:

You are a clinical researcher comparing a standard skin cream (Plain P) with a new skin cream, Super X. You want to find out if Super X is better than Plain P for the treatment of psoriasis (a skin disease). You use a crossover, double-blind research design. The subjects are split into two groups. Group A gets Plain P for the first half of the study. Group B gets Super X for the first part of the study. For the second part of the study, Group A gets Super X, and Group B gets Plain P. One researcher does tests that measure the

improvements, but she doesn't treat the subjects, just measure their improvements. The other researcher gives out the creams and follows the research subjects.

Before you start the study, you spend an hour going over the study procedure with each volunteer subject. You have all the subjects sign a consent form that tells all the details of the study. All the subjects say they understand you when you go over the study plan. You emphasize that this is a research experiment and none of the participants will be able to stay on Super X after the study is over. This is because Super X is not yet approved by the government for doctors to prescribe. You have 20 study subjects in the study. All study subjects get both drugs, but at different times in the study.

At the end of the study, many of the study subjects have improved. Fourteen of your 20 subjects ask why they are being taken off Super X. These fourteen subjects thought they were on Super X the whole time.

### **Questions:**

1. Do you think the fourteen subjects had a "therapeutic misconception?"
2. What would you say to them about getting Super X?
3. Do you think the results of the study are invalid?
4. Do you think the study results should be thrown out because so many of the subjects didn't understand the research? Why? not?

Dear Students,

Thank you for your thoughtful and interesting comments. We received responses from over 100 students. Here's the professional response from a UT Southwestern faculty member. We hope you have enjoyed participating in this process.

### **Professional Response**

**Diane Sheppard, RN**  
**Manager, Institutional Review Board**  
**UT Southwestern Medical Center**

It is important to understand the general differences between clinical treatment and clinical research. These differences are often misunderstood by research subjects and can lead to misunderstandings including the therapeutic misconception.

Although individuals may receive treatment in the context of clinical practice and clinical research, the orientation of these activities are very different. In clinical practice, the physician provides individualized care that is intended to be in the best interest of that individual patient. The risks of any diagnostic procedures or treatments are justified solely by the anticipated benefits to the patient. In contrast, clinical research is oriented toward developing knowledge that will help future patients. The investigator follows a written protocol, or plan, that outlines the research objectives, methods and procedures. Clinical

research protocols are not designed to provide individualized treatment options for each participant. Additionally, a research subject is often asked to accept risks without the prospect of direct benefit.

As most of you noted in your responses, the investigator spent an hour with the potential subject to carefully explain all aspects of the study. However, just reading the consent document and asking the potential subject; “do you understand?” is not adequate to ensure understanding and avoid the therapeutic misconception.

Patients may confuse invitations to participate in research with individualized recommendations for treatment. This is especially true when the investigator is also the patient’s treating physician. It may be difficult for patients to understand why their physician would offer participation in a clinical trial unless it were the best option for them or would involve the promise of direct benefit.

Therapeutic misconception can be hard to recognize and evaluate because it is affected by factors such as an individual’s motivation for participation, their understanding of science, general attitudes toward risk taking, and emotions. For example, patients may falsely believe that new treatments, although still experimental and unproven, are better than standard available treatments. Perhaps the most vulnerable to therapeutic misconception are those patients with very serious or terminal diseases that lack known, effective treatments. For these patients, emotions such as desperation frequently motivate them to participate in a clinical trial based on unrealistic hope for an effective treatment.

Understanding the factors that can lead to therapeutic misconception can help investigators assess an individual’s motivations and understanding of the potential risks and benefits of participation in a research study. There are other measures investigators can employ to avoid therapeutic misconception. For example, the language used in the informed consent document and during the informed consent process should be neutral. Meaning, care should be taken to avoid overstating the benefits and/or underestimating the risks. Sometimes language can, in a very subtle way, influence an individual’s perception. Note the names of the hypothetical drugs used in this case. Would you rather take a drug named “Super” or one named “Plain?” Words like “new” should be avoided to describe an experimental drug, device or therapy, as something new can easily be perceived by potential research subjects as “new and improved.”

Perhaps the most effective way to assess understanding is the use of an interview or “teach back” technique during the informed consent process. This involves the investigator asking the potential research subject a series of questions after explaining the study. For example, questions like; “what do you think was the main purpose of the research?” or “what do you think are your chances to benefit?” are good ways to assess understanding and provide an opportunity to correct any misconceptions. Investigators can better understand an individual’s motivation by asking them to explain, in their own words, why they would like to participate in the study.

Such a teach back method would also help to decrease the type of misunderstanding that occurred in this case study. By asking the potential subjects questions such as; “what do you think your chances are to receive the study drug?” or “will you be able to continue on the study drug at the end of the study?” might have avoided these problems.

The study in this case was well designed to reduce bias and produce scientifically valid results. However, as many of you pointed out, the sample size may be too small to find statistically significant differences between the two groups. Because the study results were valid, it would be considered

unethical to throw out the study results (or to not publish negative results) because to do so, would have put subjects at risk without the benefit of gaining scientific knowledge.

### **Student Responses:**

01.11.10

1. No, I don't think they had a therapeutic misconception because they had someone explain to them that it wasn't, they had signed a paper, and told the researcher that they understood what was happening.
2. I would say that they should get it because it works, but ONLY if it has already been approved for medical use to make sure that there aren't any harmful side-effects.
3. I think that they were valid because even though there was a "double-blind" and the test subjects didn't know which cream they were using, there must have been someone who knew which was being given but just didn't interfere so that the results wouldn't be bias.
4. No, it's due to the fact that the subjects had the procedure explained to them and knew what was happening. Also, they had said that they understood what was happening, so the results shouldn't be thrown out because the subjects lied and that could affect the discovery of a new cream that could treat psoriasis effectively.

A.R. - South Texas High School for Health Professions

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01.11.10

1. Yes, 14 students were therapeutic misconception because they thought they were on Super X while there were actually in Plain P.
2. I would tell them that Super X seemed to work real good against the disease. Once the government approves it everyone can use it.
3. No, because many people Super X had better results and is not still approved by the government.
4. Yes, because if they weren't sure what they were doing and if someone gets hurt using the cream because of their studies they can get in a lot of trouble.

J.S.

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01.11.10

1. No, because a therapeutic misconception is when the subjects think they are getting standard treatment. The subjects in this case thought they were getting the research treatment.
2. Super-X seems to work well against psoriasis. After it is approved they should consider continuing to use Super-X.
3. I think the studies were valid because a crossover, double-blind research design was used, leaving little room for invalid results.
4. I think it should be thrown out because if the subjects thought they were using the research medicine it may have affected the results because of "mind over matter."

A.J.- Med High

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01.11.10

1. I believe that the fourteen subjects did become part of therapeutic misconception because they could not tell what medication they were on. This is what the whole idea of therapeutic misconception is.
2. I would recommend it since it helped a good amount of subjects.
3. No, a study is supposed to be conducted this way. Procedures were followed and results were reached, so in this case the results should be valid.
4. Once again, subjects shouldn't exactly understand what is going to happen to them, or how they are affected. If they didn't understand, the consent form given to them shouldn't have been signed.

M.E.- Med High

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01.11.10

1. No because they understand that they were being tested by a new drug and they saw the improvements but they believed they were taking the drug the whole time they were under research.
2. I say that "Super X" is very good when treating psoriasis and once it is approved by the government then it should work and help many people.

3. I think it is valid because the tests show that the cream did take effect and work but they should have tested more people to get a better more accurate conclusion.

4. No because they wanted to see an improvement in the subjects and they did. The researchers did explain but it was not their fault that the subjects did not comprehend the whole procedure.

V.A.

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01.10.10

1. Yes, I think that most of the 14 were.
2. That once all the procedures are done, they should try it
3. Yes, because they don't know which one did a better job.
4. Yes, because they should only keep the stuff they need.

S.R. – Med High School

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01.10.10

1. No, because they spent over an hour going over the study procedure, and all the subjects sign a consent form that tells all the details of the study.
2. Super X can be able to clear your skin, but it is not yet fully proven.
3. Yes possibly, because they might have used the cream incorrectly.
4. I think they should not be thrown out, because they might be good information later for the researchers.

S.S. - South Texas High School for Health Professions

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01.10.10

1. Due to their response to the study, I believe the fourteen did have “therapeutic misconception”. This is due to their response to the outcome. The fourteen could not tell when they were actually receiving the “Super X” cream, the test cream.
2. Since the new skin cream, Super X, has not been approved for doctors to prescribe, I would ask the subjects to constantly check on the internet and track the progress of this product.

3. The results of this study are valid. The use of both crossover and double blind techniques emphasize the importance of the study coordinators for an unbiased outcome.
4. The research results are valid. The research coordinator took the time to spend one hour with each.

J.V. - Med High School

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01.10.10

1. I think that some of the subjects had a "therapeutic misconception" but not all of them because the scientists told the subjects what they were doing and explained this for a hour meaning that at least one must have known what was going on.

2. I would tell them that they would need to wait to use it until it is approved by the government in case there are side effects or anything of the sort.

3. I think the results of the study are valid because they used both the "double-blind" & "crossover" methods and although the experiment isn't precise it's valid because nobody was bias. 4

. I don't think the experiment should completely be thrown out since the scientist can use the information they learned from the experiment and make another one with more details explaining to the subject more carefully the procedures of the experiment.

L.E.G. - South Texas High School for Health Professions

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01.10.10

1. It is possible to have had a misunderstanding in research, because some subjects failed to understand the procedures and it was most unlikely that these patients had a "therapeutic misconception" in which they had to sign a form of consent stating all major details of the certain procedure and that they understood what it was about.

2. I would tell the patients this new skin cream called "Super X" has not yet even been approved by the government yet alone prescribed by a doctor to test on their skin! If they were to go ahead and test the skin cream making sure it had no negative side effects, then maybe they should keep using the cream until the government says otherwise.

3. I do believe this experiment is valid and not invalid just for curiosity and due to the fact that all patients used this product correctly even though they didn't even know which cream they were given. It is valid, but not precise and accurate.

4. I think the results should be kept because they did sign a consent form saying what they were getting themselves into. Results should never be thrown out because you can always use it again to improve the experiment and see what mistakes you made in the past.

K.B.- Med High

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01.10.10

1. I do believe the 14 students had a "therapeutic misconception" because they asked why they were taken off of it. If it weren't the misconception they would've known that it was just research and even if they were sick... it wasn't standard medicine.

2. I would say Super X is very effective for many reasons. Primarily because there was improvement. Secondly because 14 students, which is more than 50%, asked why they were being taken off of it. Which means it was good medicine showing improvement.

3. I don't think the study results are invalid. They used their variables and compared equally. Even though the students weren't specifically "treated" the results and improvements speak for themselves.

4. I don't think the results should be thrown out. Our brain is very powerful and it can manipulate your way of thinking and seeing things. I think it's actually an advantage that it happened so they wouldn't manipulate their results according to their desires of improvement.

A.C - South Texas High School for the Health Professions

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01.10.10

1. Yes, because they did not fully understand the procedure. They thought they were on the Super X the whole time instead of only half the time. The other half the time they were on Plain P.

2. I would not agree unless it was the only way they had a chance on being treated. I would not prescribe something that has yet not been approved.

3. No, I think they are valid because both the doctors and the patients did not know what treatment they were on at a certain time. So that doctors and/or patients try to prove that one medication works better than the other.

4. No because the results are still accurate just that next time make sure the patient is completely aware of the procedures.

I.A. - Med High

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1.10.10



1. No, I do not think the fourteen subjects has a "therapeutic misconception", all the subjects signed a consent form telling them of the details of the study, meaning they already knew they were not doing this for treatment simply for study. Although they asked why they were taken off Super X, they just believed they were on it the entire time. They understood correctly.

2. I would tell the patients that Super X is not yet approved by the Government and that they should not expect it to be approved, so it would not be available in markets, but for time being to use other products such as Plain P.

3. No, I do not think the results of the study were invalid; this was a double-blind study. Meaning both subjects and doctors do not know which drug is being given, and they performed the cross-over so neither subject nor doctor knew what drug was given first.

4. I do not think the results should be thrown out, just because the subjects thought they would be on Super X the whole time doesn't mean that its bad results, the study was done correctly, the doctors followed what they were suppose to do and the results are correct.

A.M-South Texas High School for Health Professions

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01.08.10

1.NO, they did not have therapeutic misconception because they were aware of the Super X they were using.

2. NO, not to use it because the fact that it did not show a lot of difference comparing to Plain P.

3. NO, results aren't invalid because they were tested, the only thing is that it did not show that much of a difference than Plain P. 4. NO, because it doesn't matter if the subjects understand the research it doesn't affect the testing of the product.

E.R.

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01.08.10

1. Yea, because each group thought they had a substance when they had a substance yet they had another different than the other, and that made them think it was different from the first substance.

2. I would say that Super X is not yet approved by the government so be careful and that we are just making some tests and be careful. Also they will sign a contract saying that they tested this substance and that they are okay with it.

3. I don't think the results were invalid because the test could of being the same thing like they could of both have Super X.

4. Yes, they could throw it away and start all over, but this time for one group to get Plain P, and the other group Super X to see the results each group gets.

C.P.H. - South Texas High School for Health Professions