MULTI-REGIONAL CLINICAL TRIALS
BIOETHICS
COLLABORATIVE

The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard Bioethics Collaborative

Therapeutic Misconception Revisited

Wednesday, June 4, 2025

Introduction:

According to the Belmont Report and other canonical research ethics texts, there is a fundamental distinction between clinical care and research. Clinical care is aimed solely at the well-being of the individual patient, while research primarily aims to produce generalizable knowledge. When this distinction is blurred or misunderstood, it can give rise to a "therapeutic misconception (TM)," the belief that research is designed primarily to benefit the participant. TM was first identified in the 1980s, when interviews with research participants suggested that participants persistently misinterpret the risk-benefit ratio of participating in research because they fail to understand the underlying scientific methodology and aspects of research, such as blinding, randomization, and placebo controls, that do not exist for the benefit of the participant.

There is debate in the bioethics literature over how exactly to define TM, with proposals including inaccurate beliefs about the aim of research, the likelihood of personal benefit, risk-benefit, and key study design elements. Further, while empirical studies using validated measures have documented TM in over 50% of study participants, the prevalence and implications of TM remain open to discussion. Some writers have noted that what is categorized as TM may instead be closely related phenomena such as therapeutic optimism, understood as expressions of hope or statements of one's personal motivations for participating in research, rather than an objective assessment of the likelihood of benefit. These distinctions are crucial from an ethical perspective. While many acknowledge that TM is or can be ethically concerning by interfering with effective informed consent, merely hoping that one might benefit from research, or participating out of such a hope, does not, on its own, raise ethical concerns. This general suggestion has been taken up in a body of empirical work indebted to linguistic pragmatics, which hypothesizes that, in empirical work on TM, participants may be answering different questions than the ones intended by researchers and that the prevalence of the TM may be less than is commonly supposed.

Closely related to how exactly we should understand TM is the question of its ethical significance. Perhaps the most salient ethical concern regarding TM is whether it undermines informed consent. If participants are enrolled in studies without a clear and accurate understanding of the research, the validity of their consent and the ethics of the research could be questioned. Based partly on the apparent prevalence of TM, some have argued that comprehension and understanding are not the cornerstone of or even necessary for valid informed consent, emphasizing instead the importance of individuals voluntarily choosing to enroll, even when understanding is lacking. This is just one example of how reflection on TM has led to more general debates on foundational issues in research ethics.

Presentations and Discussion:

After the introductory presentation, members debated whether TM necessarily makes research unethical, noting that all research must be approved by an IRB, ensuring that the research is ethical and protective of the rights of human subjects. One member clarified that one potential limitation of IRB review, in light of the standard idea that valid informed consent requires comprehension, is that the current IRB regulations ensure that all needed information is disclosed, but they do not explicitly require participant comprehension of the material. Others argued that ethical enrollment requires confirming patient understanding, comprehension, and voluntariness to be in line with the Belmont Principles.

Members noted concerns about language in participant-facing materials and how it may lead potential participants to confuse research with clinical care, particularly when studies are conducted in non-traditional settings, like retail pharmacies, and among target populations with limited access to healthcare. This can heighten the risk of TM and raises ethical concerns about the potential exploitation of underserved communities and the disproportional enrollment of individuals who do not understand the nature or intent of the research.

Other members mentioned how comparative effectiveness research or embedded pragmatic trials may complicate TM, given that these studies often aim to test accepted medical interventions in real-world situations. The relationship between research and care aspects in these studies remains a matter of controversy, raising challenges for how to apply TM to these types of research. While susceptibility to TM may be higher in embedded pragmatic trials, given their resemblance to usual care, the specific research risks of these studies (as opposed to the clinical risks), and thus the importance of TM, are less obvious, turning largely on how research risk is understood and measured. One member noted that many comparative effectiveness and pragmatic trials reverse the traditional research-care dynamic, with care being the primary focus and research secondary, challenging the straightforward

application of TM in these cases. Members acknowledged that researchers often also demonstrate TM, thereby rendering participant understanding almost impossible.

The first speaker addressed four common misconceptions about TM. The first misconception states that any belief that a study may have therapeutic benefit is a TM. In reality, TM cannot be assessed without knowing specific study methods; these assessments are highly context-specific. For instance, high estimations of personal benefit may be accurate in a comparative effectiveness trial (as both arms have benefit), but in a phase 1 or 2 trial evaluating a previously unstudied therapy, that belief could be considered an instance of TM. The second misconception is that judgments about the presence of TM are subjective and do not rest on a shared definition of TM or related concepts. Contrary to this, TM can be assessed using a validated scale developed in 2012, which quantifies three dimensions of TM—individualization, benefit, and purpose—across different levels of application. The tool demonstrated significant discriminant validity in distinguishing participants with and without TM. The third misconception is that TM is unavoidable. A 2017 study showed that a scientific reframing video explaining research design and intent significantly reduced the prevalence and degree of TM without affecting participants' willingness to enroll, and confirmed that higher educational attainment correlates with lower TM.[1] Finally, the speaker challenged the idea that TM is not serious enough to try to ameliorate, arguing that TM can significantly distort participants' understanding of risks and benefits, leading to serious negative consequences for both patients and research integrity.

One member questioned whether TM invalidates consent altogether, or merely detracts from its quality without vitiating it. The speaker replied, first, that TM exists on a spectrum, with different thresholds for different studies based on their methods and risks. Certain beliefs or forms of misunderstanding may count as instances of TM in one context, but not in others. More importantly, researchers should specify what is essential for participants to understand before recruitment begins, then test comprehension after consent, and provide additional education if needed. Whether the TM invalidates consent is, therefore, context-sensitive.

Another member noted the wide variation in TM scores across educational levels and questioned whether certain populations might be excluded from research based on concern for this vulnerability. The speaker advocated for better educational processes rather than exclusion, while also acknowledging that individuals with less education may need more help

[1] Christopher, P. P., Appelbaum, P. S., Truong, D., Albert, K., Maranda, L., & Lidz, C. (2017). Reducing therapeutic misconception: A randomized intervention trial in hypothetical clinical trials. PloS one, 12(9), e0184224. https://doi.org/10.1371/journal.pone.0184224

understanding scientific methods. Others noted that individuals often don't read consent forms and rather trust the consent conversation (which then is itself influenced by the investigator's communication skills and bias) and/or the process of ethical research.

The second speaker addressed the conflicts between research and individual patient care, arguing that they are unavoidable and must be acknowledged, and that the ethical approach is to minimize conflict and ensure participants understand key aspects of research as clearly as possible. The speaker emphasized that informed consent is not a perfect process, but rather a ritual that expresses commitment to values such as autonomous action, free choice, and rationality, with the core ethical obligation of protecting participants through appropriate safeguards. For example, enrolling a patient with a life-threatening condition in a placebo-controlled trial when an effective treatment exists would be unethical regardless of the presence of consent or absence of TM. The speaker concluded with a story of a surgical resident trying to obtain consent from an unconscious patient by putting a pen in their hand and signing, illustrating how consent can be meaningless if not done properly.

One member agreed that the ritual aspect of informed consent is valuable, emphasizing that it also requires clearly defined roles and proper execution. The group also explored whether participants meaningfully engage with consent forms, or whether having already decided on enrollment renders the process a formality. This raises the question of whether the consent stage is the optimal stage to address TM. Another member noted that lengthy consent forms can overwhelm participants, limiting their bandwidth to engage and process the information. Additionally, blurred boundaries between care and research were highlighted as confusing and complicated to patients, especially in settings where patients interact with multiple providers across specialties, or within decentralized clinical trials involving additional experts. This complexity can make it difficult for participants to understand who is responsible for their care and distinguish clinical and research roles.

The third speaker focused on comparative effectiveness and embedded pragmatic trials, suggesting that TM may be less relevant in these newer research frameworks. Traditionally, research participants received interventions that were primarily for research purposes but mistakenly interpreted as clinically driven. However, in comparative effectiveness trials, participants are randomized between treatments already used in routine clinical practice, making randomization the distinguishing feature of research. The speaker questioned whether the primary goal of such trials is truly research versus clinical care. Using the example of randomizing patients between two well-established drugs with similar profiles, the primary purpose would be patient care, and the research question would be answered through

clinical care using traditional research methods. In this context, the significance of TM might vary depending on how the risks of the research (and the experience of randomization) are understood. Lastly, the speaker spoke to mitigating TM not only to ensure individual informed consent, but to foster community trust, noting that ongoing communication post-enrollment is recommended as a way to help understand participation and prevent future misconceptions.

The discussion that followed included the question of whether patients must always provide formal consent for embedded comparative effectiveness studies, or rather whether they just need to know they are in a learning health system. Some presenters expressed the idea that consent will still be important due to the presence of randomization, which is not part of standard care. One member shared an example where a patient joined a study in hopes of receiving a higher dose of medication. When the patient learned about randomization, they felt deceived, showing that misunderstanding can damage trust. The group then discussed whether randomization creates risks or otherwise shapes TM and related assessments.

The closing discussion emphasized that while research is beneficial and serves a good purpose, it also requires greater public education. It was noted that consent forms are extensive and filled with procedural information, much of which is unrelated to the research question, identifying a need for clearer distinctions between research activities and clinical care. Members emphasized the importance of strategies such as teach-back and ongoing communication throughout a study to support participant understanding. Lastly, there was a consensus that efforts to address TM should be prioritized in contexts where participant comprehension is essential to exercising autonomy and making informed decisions.

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