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EDITORIAL

Therapeutic misconception in clinical trials: fighting against it and living with it

Los malentendidos terapéuticos en los ensayos clínicos: luchando contra ellos y viviendo con ellos

Dal-Ré et al.[1] have helpfully highlighted some of the issues related to therapeutic misconception (TM) and its threat to the validity of informed consent to participation in clinical trials. We agree with many of their suggestions, including the potential value of paying participants in trials a nominal amount to make clear that participation in a trial is different than receiving ordinary medical care – although we note that this testable proposition has not yet been subject to empirical validation. Nonetheless, we have 4 specific concerns with their portrayal of TM and its impact.

1. By focusing primarily on placebo use and randomization as contexts in which TM is problematic, they understate the differences between routine clinical care and clinical trials.
2. We would shift some of the authors' emphasis on what is written on consent forms in favor of a focus on the dialogue between investigator and potential subject.
3. They seem excessively – and we would suggest prematurely – pessimistic about substantially reducing TM.
4. We understand the uses of TM measures differently.

We discuss these issues in order.

Placebo use and randomization are, of course, critical parts of clinical trial design but they are not the only design elements that affect participants. Imagine the response of a patient if he or she walked into the doctor's office and was told: ''*I am going to give you one of two medicines but I won't know which one of them you are going to get and I won't be able to monitor your tests or make decisions about your care. Those decisions will be made by someone else whom you don't know and you won't meet. Neither that person nor I can adjust the dosage based on how you are doing on the medication and we can't give you some other medications that might help you, only one of these two.*'' Most patients would find that a very strange process of providing medical care. This is not to say that there are no compensations for participating in clinical trials including better monitoring, more contact with the clinicians, etc., but there is more involved for the patient/subject than just being randomized among interventions or running the risk of receiving placebo. It is important to understand just how many differences there are between what subjects would receive in ordinary care and what happens when they participate in a trial. TM is a major problem in consent to trial participation broadly, not just when placebos are used or interventions are assigned on a randomized basis.

A second point of concern is the emphasis on written consent forms. The authors emphasize the importance of well-written information, although they do note in the conclusion that conversation is a principle element of obtaining informed consent. Clear writing is always to be preferred, of course, but it is important to remember that the consent form should be only a documentation of what was discussed. The dialogue between the individual presenting the trial and the potential subject is what matters. It is this discussion that needs improvement, and represents the best hope for avoiding TM.

Third, the authors seem excessively pessimistic about the possibility of significantly reducing TM. We have recently suggested that TM does not merely reflect a lack of understanding of the specific facts but the different primary cognitive frame with which potential subjects approach research, compared with clinical investigators.[2] The researcher understands a trial as an experiment requiring a certain number of subjects and specific procedures to obtain a scientifically valid result. The potential subject comes to the interaction expecting care for a disorder. As we have described in detail elsewhere, these different cognitive frames, and some secondary frames, are ideally

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arranged to produce the systematic misunderstanding that is referred to as TM. To reduce that, clinical researchers must do both more and less than provide additional information: they must transform the subjects' cognitive frame about ''What is going on here?'' We are beginning a new study to test the effectiveness of such an approach. In any event, given the paucity of experimental efforts to reduce TM, pessimism is decidedly premature.

Finally, we are concerned that the authors suggest that there is no adequate measure of TM, including the one in our recently published paper.[3] Adequacy depends on the purpose to which a tool is put. We intend our measure to be used for two purposes, as a research tool and as a screen to assist the clinical researcher gaining consent. Although the measure has moderate predictive power with regard to distinguishing subjects with and without TM as dichotomous categories, it is not at all clear that this is the right way to think about its use. As Dal-Ré et al. note,[1] TM exists along a spectrum of more or less, rather than in categories of present or absent. Hence, insofar as the TM scale reflects a highly reliable quantitative measure of TM, it is likely to be useful to TM researchers seeking to determine whether particular interventions ameliorate the problem. Similarly, as a screening tool the measure should help clinical researchers assess the adequacy of the dialogue that lies at the heart of the informed consent process. We would very much oppose a requirement by Research Ethics Committees that all subjects need to ''pass a test'' for TM based on this instrument.

In spite of these modest differences with the authors, we believe that, by highlighting the issues involved in TM, they have performed a valuable service for us all.

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