Author's response to reviews

Title: When is it rational to participate in a clinical trial? A game theory approach incorporating trust, regret and guilt

Authors:

Benjamin Djulbegovic (bdjulbeg@health.usf.edu)
Iztok Hozo (ihozo@iun.edu)

Version: 2 Date: 11 November 2011

Author's response to reviews: see over
Response to the critiques

When is it rational to participate in a clinical trial? A game theory approach incorporating trust, regret and guilt” (MS: 1491207956551098)

Reviewer #1

Reviewer #1 states “this paper begins from a totally unacceptable premise. It is widely recognized that 'equipoise' is the basis of all trial recruitment. If this does not exist then randomisation is unethical - full stop. Game theoretic issues have no role in this decision.”

Response:

While we are sympathetic to Dr. Cuzick’s normative argument, we believe that several lines of reasoning justify the approach we have taken in our paper:

1) The requirement for equipoise as the entry criterion in RCTs is not uniformly held. In fact, as recently as 2011, some very influential ethicists forcefully argued that “equipoise is neither necessary nor sufficient” criterion for enrollment into RCTs.[1, 2] In the same vein, unlike the so-called “similarity position” espoused by the equipoise concept, these ethicists argue that there exists a fundamental difference between research and practice (“difference position”). This “difference position” implies that the interests of patients and researchers are inherently different (even if these interests may often coincide).[1, 2] Importantly, while the “similarity position” assumes no difference in interests between patients and researchers, the “difference position” does, which makes interactions between researchers and patients suitable to game modeling.

2) Equipoise applies at the point of randomization, which in fact is modeled in our tree (see inset in Fig 1). However, the patient’s most important decision is whether to accept or decline enrollment into a trial, and not which arm he/she should be randomized to. This decision is what we have modeled. Other authors also noted that the “positive expected value of participation” relates to the types of decisions we modeled in our paper and not to the question of assignment to a particular study arm.[3] Nevertheless, as stated, we did model equipoise as traditionally understood in the current literature, which is, in fact, in line of Dr. Cuzick’s position (see Fig 1 as well as Results).

3) We, therefore, believe that writing in the current literature provides ample rationale for approaching participation in RCT from the game theory perspective.

References:

Reviewer #2

“This is a well done study on an important subject. The findings are disturbing and cynical but believable. The paper is understandable and quite readable but many prepositions are missing and it will take a native English speaker only a few minutes to add those. I suggest that be done. Algebraic variables in the text should be in italics for ease in readership. The prisoner’s dilemma is an important concept in this paper but not described at all. It should be given a paragraph early in the paper just to aid the general readership. Recommendations are proper based on results presented. This paper might be read by patients considering joining a clinical trial. They won’t be able to follow the math but they will surely understand the results. My compliments to the authors.”

Response:

We thank Dr. Retsky for complimentary comments. As per his recommendations we have made the following changes in the paper:

1) We included discussion of the prisoner’s dilemma (as a separate Box to enable readers quick familiarity with this important game theoretical construct/game)

2) We have asked our colleague Dr. Jane Carver to thoroughly edit the manuscript (we have acknowledged her help)

3) Equations are presented in italics