In the last decade, biomedical research conducted by researchers from developed countries in developing countries has been a topic of significant controversy. One serious concern is that research participants in the developing world are unable to give valid informed consent and thus are highly susceptible to exploitation. Some critics voice concerns about understanding—perhaps no matter how extensively researchers explain the details and essence of a particular study, uneducated participants will never be able to grasp what is being presented to them. Others claim that it is virtually impossible for participants in such settings to freely and voluntarily join a clinical trial. These worries about voluntariness appeal to the argument that most subjects have no other option but to enter research studies and are therefore not able to make fully autonomous, uncoerced decisions. Together, these critics believe that valid informed consent is not obtained nearly enough in clinical research in the developing world.

Undoubtedly, conditions of poverty and poor education make it more difficult to uphold this ethical requirement of clinical research, as the critics suggest. However, I argue that there is no reason to believe that valid informed consent is impossible to obtain in such settings. Beyond this, I offer some considerations for how we might improve the quality of informed consent, in both developing and developed settings. Here, I emphasize the need to employ a more serious interdisciplinary approach to research ethics. Only by considering multiple perspectives—using empirical and qualitative work in philosophy and anthropology—can we improve the quality of informed consent and minimize the possibility of exploitation in the increasingly globalized efforts of biomedical research.

**WHAT IS INFORMED CONSENT?**

Informed consent represents the need to respect people’s autonomy. Although it is never entirely sufficient for ethical clinical research, informed consent is widely
recognized as a requirement for ethical research on human subjects. Three requirements are necessary in order to obtain valid informed consent from either the participant or his or her surrogate. First, participants must be accurately informed of the purpose, methods, risks, benefits, and alternatives of research. Second, they must understand this information and how it is related to their personal clinical situation. Third, individuals must make a voluntary and uncoerced decision whether to participate (Emanuel et al. 2000, 2706). Each of these elements is necessary to ensure that individuals freely and rationally determine that the research is consonant with their interests.

For the purpose of this paper, I will assume that the first requirement is generally upheld. Certainly it is always possible for researchers to disclose to participants the relevant information involved in a study. The real concern is with the latter two requirements, namely participant understanding and voluntariness. Let’s look first at the possibility of obtaining participant understanding in clinical research in developing countries.

OBTAINING ADEQUATE UNDERSTANDING

Is the validity of informed consent severely jeopardized in research conducted in areas with poor education or little familiarity with biomedical research? Many critics who believe this to be true site anecdotes like the following from a 1997 New York Times article:

They gave me a bunch of pills to take, and told me how to take them. Some were for malaria, some were for fevers, and some were supposed to be for the virus. I knew that there were different kinds, but I figured that if one of them didn’t work against AIDS, then one of the other ones would (French).

This account, taken from a participant in one of the controversial AZT trials in Cote d’Ivoire, raises serious concerns about participant understanding, the second requirement of valid informed consent mentioned above. This example cannot be generalized to all trial participants in the developing world. However, the case is understandably disconcerting for those who prioritize participant understanding in biomedical research.
Undoubtedly, there are many barriers to ensuring participant understanding in research. Language and cross-cultural differences are among the more daunting hurdles. Some languages lack certain words and many cultures cannot readily conceptualize important biomedical and scientific ideas (LaFraniere 2000). For example, it is oftentimes very challenging for researchers to explain to participants the concepts of a placebo and randomization (Hawkins, Emanuel 2008, 24). Some argue that poor and uneducated participants cannot fathom these ideas regardless of a researcher’s efforts to explain them.

However, it is not evident that research participants in the developing world even have these characteristics. For example, a recent survey conducted in Thailand found that as many as 72 percent of participants in an HIV trial had completed high school (Pace et al. 2003). Not only are assumptions about participant characteristics unwarranted; there is also no substantial evidence that understanding differs between participants in the developing world and those in developed countries. When it comes to the concept of randomization, for example, empirical data show that there is no significant difference in understanding between the settings (Campbell et al., in press).

Rather than assuming the inability of some people to grasp western biomedical concepts, researchers need to realize that understanding suffers in both developed and developing settings and that the real focus should be on adapting the universal paradigms of research to local cultural norms, ideas, and literacy levels. This is echoed by Emanuel et al., who say that the ethical requirements of biomedical research “must be adapted to the health, economic, cultural, and technological conditions in which clinical research is conducted” (2000, 2708). The demanding nature of this task, particularly with informed consent protocols, was revealed by a 2007 study in Tibet. Results from this two-year study show that the presentation of informed consent protocols will be more effective if it is more flexible and focuses on the intent rather than the specific information of the informed consent process (Adams et al. 2007, 448). By maintaining an adaptable protocol throughout a research study, they conclude, researchers can adequately bridge cross-cultural and language differences and significantly improve participant understanding. The success of this study underscores the need to view international biomedical ethics through a multidisciplinary lens—one sensitive not only to universal
requirements but also to local paradigms of understanding. This type of multidisciplinary approach should be incorporated into researcher training in order to improve cultural competence (Beach et al. 2006).

To conclude, while it may be a daunting task, achieving adequate participant understanding is possible, even in settings unfamiliar to clinical research. But what exactly is adequate understanding? An interesting, currently unanswered question regarding understanding and informed consent is: how much understanding must be achieved in order for clinical research to proceed? At one extreme, no understanding would be necessary for informed consent to be valid. At the other end of the spectrum, participants must understand every detail of the study. If the latter requirement were true, then theoretically no research—in either developed or developing world—could be considered ethical. While most theorists hold a view somewhere in the middle of these two extremes, there is no consensus on where exactly to draw this line (Hawkins, Emanuel 2008, 24). At this blurry border, researchers need to use sound discretion to ensure that participants are adequately informed throughout the process of research.

**Voluntariness**

Another commonly voiced concern regarding the validity of informed consent relates to participant voluntariness, the third requirement mentioned above. A quote from George Annas, law professor and bioethicist, captures the spirit of this concern:

I’d argue you can’t do studies ethically in a country where there is no basic health care. You can tell a person there that this is research, but they hear they have a chance to get care or else refuse their only good chance at care. How can you put them in that position and then say they are giving informed consent (from LaFraniere et al. 2000).

Annas’ language—using phrases like “have a chance” and “or else refuse”—implies that he is referring to participant voluntariness. There are two possible infringements on voluntariness: coercion and undue inducement. Therefore, if Annas claims that giving voluntary informed consent is impossible in these settings, he must mean that either every circumstance is coercive or that there is no way of avoiding undue inducement (Hawkins,
Emanuel 2008, 25). While Annas correctly recognizes the harsh situations in which research can take place, his conclusions cannot be logically substantiated.

For one, there needs to be a distinction between harsh choice circumstances and coercion. It is oftentimes assumed that no matter what someone chooses from a harsh set of alternatives (even if the choice is in one’s best interest), that choice must have been coerced. However, a more precise understanding of coercion shows that this view is incorrect. Coercion constitutes two elements (Hawkins, Emanuel 2008, 25): the set of choices of the agent (B), and the actions of external parties (A) that have unfairly affected that set of choices. It is the second element—the actions of others—that distinguishes mere harsh circumstances (poor choice set) from coercion. There is no evidence to suggest that researchers threaten subjects or in any way try to limit participant rights or choices. They simply make them offers that are, in the unfortunate context where subjects have few options for good health care, very attractive (Hawkins, Emanuel 2008, 25).

Such a situation is not unlike that faced by many people in developed countries who participate in trials testing for cures to currently untreatable diseases. One certainly would not say that a man approached about joining a trial for an experimental drug for rapidly progressive Glioblastoma Multiforme, a fatal brain tumor, could not act voluntarily. The choice to join the trial would simply be the best decision given his current, unfortunate circumstances. While some incorrectly say that these circumstances compromise one’s ability to exercise autonomy (Fisher 2007, 889), the real problem here, as echoed by Andrew Siegel, rests not with the validity of consent but with the tragic circumstances that make the choice to enter clinical trials compelling (Hawkins, Emanuel 2008, 184).

The second concern related to voluntariness and consent is undue inducement. Some express the worry that in impoverished settings virtually all transactions constitute undue inducement, which is the idea that some offers are excessive and therefore irresistible in a way that is morally problematic. But how do you determine what is ‘excessive’ and ‘irresistible’? Some say that an offer is excessive when it makes you pursue something you normally would not pursue. However, this is a highly implausible account of why undue inducement is morally problematic. If this were true, it would
suggest that taking a job with a high salary would count as undue inducement (Emanuel 2004, 100). A more accurate account of what is morally problematic with undue inducement is that some excessive offers may cause participants to make choices that are not in their best long-term interests (Hawkins, Emanuel 2008, 26). But, as pointed out by Emanuel, this is a misplaced worry if all the other ethical requirements in research are upheld (2004). In developing settings, people joining ethically reviewed clinical trials really are making decisions that will benefit them in the long term.

Because neither coercion nor undue inducement are necessary elements of offers made to research participants in developing countries, there is no reason to believe that voluntary informed consent is impossible to obtain in these settings.

**SUBJECT RECRUITMENT: DOES IT AFFECT INFORMED CONSENT?**

Do infringements to subject voluntariness extend beyond coercion and undue inducement? In the past, according to Pace and Emanuel, researchers have incorrectly included unfair subject recruitment in the equation for calculating voluntariness (2005). Unfair selection occurs when researchers choose their study cohort for reasons other than scientific appropriateness or participants’ potential of benefit. Unfair selection can happen *even if participants give fully informed consent* (Pace, Emanuel 2005).

While this distinction is important, it should not imply that subject selection mechanisms cannot influence the informed consent process. To view the ethical requirements of clinical research individually, each in a vacuum, may prohibit the realization of interventions that could potentially improve the quality of informed consent.

Ethnographic work on clinical trials in developed settings suggests that selection techniques can significantly impact the informed consent process. In Fisher’s 2007 article, “Ready-to-Recruit” or “Ready-to-Consent” Populations?, the focus is on a particular television ad advertising a trial for new asthma medication. The commercial mentions only possible benefits and says virtually nothing about potential risks. In short, it is very misleading because it implies a set of results (the benefits) that are the very purpose of the study itself. Because many people participate in trials based on this type
of information, it can be deduced that structural variables, such as race and socioeconomic class, are oftentimes much stronger determinants of participation in clinical trials than are the details of specific studies. In other words, people likely give ‘consent’ to a study with a significantly skewed sense of what is at stake. Fisher concludes by saying that informed consent—both as a concept and as a practice—is impotent in light of recruitment strategies and the structural reasons motivating individuals to participate in clinical trials (Fisher 2007, 890). This analysis raises two important points.

First, the analysis correctly highlights the need to avoid misleading recruitment strategies in order to improve the quality of informed consent. Researchers trying to obtain informed consent from participants should be mindful of not only the information presented on the informed consent form but also the information that the participant may have been exposed to before the meeting. Therefore, as suggested by Fisher, bioethicists need to shift the focus from how subjects participate to why they do (Fisher 2007, 890). This could help researchers address any misconceptions that participants may have about the informed consent process and improve its quality, particularly with understanding.

Second, the claim that the informed consent process is impotent against the backdrop of recruitment strategies and structural reasons raises two problems. As discussed above in the discussion about voluntariness, individuals can make perfectly voluntary and autonomous decisions despite having a few harsh alternatives (or, according to Fisher, difficult “structural” circumstances). In addition, this view of informed consent as ‘impotent’ assumes that the process is merely a vehicle for allowing people to exercise decision-making power.

However, the informed consent process is important for other reasons. Many empirical studies show that people in developed countries are not as interested in making decisions for themselves as theorists assume (Degner 1992, Ende 1989). These participants, however, are still commonly interested in being informed about what is going on, even when they are letting someone else decide for them. Therefore, the process of informed consent can still serve an ethical function even when participants allow others to make decisions for them. Additionally, the practice of obtaining informed consent serves the function of transparency—a function that is oftentimes overlooked.
The process of informed consent can benefit subjects indirectly because of the ways it influences the behavior of researchers. If researchers know that participants are aware of what is going on, it makes them more accountable and more likely to uphold ethical behavior throughout the research process (Hawkins, Emanuel 2008, 28). Fisher’s conclusion regarding the impotence of informed consent, therefore, cannot be substantiated because it overlooks these important aspects of the consent process.

Whereas Fisher points to the significance of advertisements in the subject recruitment process, others question whether payment for trial participation could also influence the quality of informed consent. Could payment for participation in research reduce therapeutic misconception? How could payment influence voluntariness? Could it influence whether or not participants are willing to remain in a study? How may the answers to these questions vary across cultures? These and many other interesting questions could have significant bearing on how we improve the quality of informed consent in both developed and developing worlds. One thing is certain: future research must consider not only the components particular to informed consent. It must also heed to the other biomedical research processes, such as subject recruitment, in order to shed light on how we can more readily meet the critical need to obtain voluntary informed consent and protect human subjects in research.

CONCLUSION

The concerns about obtaining valid informed consent in developing countries are understandable. Poor education, little access to health care, and participants’ unfamiliarity with biomedical research make upholding this ethical requirement a daunting task for researchers. However, people living in these settings are neither incapable of understanding the nature of research nor unable to voluntarily participate. The possibility of obtaining truly informed consent from participants in research conducted in developing countries is therefore not a myth, but a reality.

Current efforts to improve the quality of informed consent—including simplifying and adapting consent protocols—are necessary, especially when dealing with cultures and languages previously unexposed to biomedical concepts and terminology. However,
future research must also look beyond the dyadic interaction of researcher and participant. To improve both understanding and voluntariness, we must also consider the perceptions of potential participants—the reasons why people enter research—both before and throughout the process. Therefore, in future efforts to more thoroughly understand informed consent and how to improve it in both developed and developing settings, we need to take seriously the intersection of quantitative data and qualitative inquiries from both philosophy—justifying universal biomedical standards—and anthropology, which highlights the need to understand structural realities and their influence on local cultural perspectives. Only when we fully embrace multidisciplinary exploration can we more fully uphold this ethical requirement of biomedical research.
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