Compensating Participants in Clinical Research: Current thinking

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In clinical research studies, it is not uncommon for monetary compensation to be provided to research participants; as reimbursement for study-related expenses, as compensation for time and effort, and even as incentive payments to encourage enrollment. Sponsors, researchers and Institutional Review Boards (IRBs) are often wary about payments in research participation, citing concerns about coercion and undue influence, whether real or perceived, and have avoided payments that are "too high." But new research on how people make decisions about research participation, and new approaches to this question, bring a new perspective; are payments to participants actually too low? This paper explores this question, and whether we should, in fact, worry much less about restricting compensation for research participants.

Undue influence and Coercion

At the foundation of the concerns about research participant payment are the issues of *undue influence* and *coercion*. These words are not clearly defined in research regulations or guidance, and are often used interchangeably when talking about participant payment, but they actually have very different meanings.

To coerce means to achieve something by using force or threat. Situations of true coercion are rare in clinical study recruitment situations. An example of coercion might be a physician who is seeing a patient at a free clinic who says, "If you don't agree to be in my research study, you can't come here for care anymore." Payment offers, though, are not force, nor are they threats. Therefore, offers of payment for participation in research can never be coercive.

Influence is a different concept. Influence, in itself, is not a bad thing. Everyone makes decisions about what they do based on factors that influence them, and sometimes those factors are financial. While many of us really enjoy our jobs, if our employer told us that we wouldn't get paid anymore, we'd probably stop showing up for work. The issue, then, is not influence, but *undue* influence. In legal terms, undue influence means that someone makes someone else behave in a way that is contrary to their interests. In research, we often describe undue influence in study recruitment as someone agreeing to take risks that were not reasonable, because they were influenced by other considerations (in this situation, by the offer of money).

But as discussed in the excellent recent paper, *Paying Research Participants: The Outsized Influence of "Undue Influence"* by Emily Largent and Holly Fernandez Lynch[1], the possibility of unreasonable risks requires more consideration as well. In order for an IRB to approve a research study, the Board must ensure that the risks of the research are reasonable in relation to the anticipated benefits, for the target study population. If this is the case, for a research protocol that has been IRB-approved and a potential participant who is in the target study population, how can the offer of payment influence them to take risks that are unreasonable, when the risks have already been determined to be reasonable? With this argument, Largent and Lynch explain that the potential problem of undue influence in IRB-approved research is significantly overestimated, although possible in some very specific situations (for example, when potential participants are likely to deceive the researchers about their eligibility or when they have some unique characteristics outside the IRB's purview). In an effort to reduce the occurrence of these situations—although they are already rare—we as a research community have erred on the side of caution in preventing payment or encouraging payment to be kept relatively low. However, underpaying for participation results in the possible exploitation of research participants, the overburdening of certain populations who are willing to accept low payments, and the scientific risks of failed studies due to under-enrollment.[1] For minimal risk research, any concern at all about compensation is likely unnecessary, as the risks are so low that it would be very unlikely that any participant could be making a decision to take a risk that is unreasonable.

> "…the IRB must conclude that participation in any protocol it approves is reasonable (i.e., not unreasonable) for individuals in the target study population. This is not to say that no risk remains or that participation in research would be in the best interest of potential participants. Neither is required in order to avoid undue influence."[1]

Types of Payment to Participants

Reimbursement of Study-Related Expenses

Reimbursement of expenses related to participation in research studies, whether provided by the sponsor or by the institution, should never be of ethical concern. While there are rare instances in which ethically-acceptable studies involve requiring participants to pay for study-required procedures or medications—most often in situations where diagnostic testing is being used for both clinical and research purposes—for the most part, research participation should be cost-neutral. Making research cost-neutral helps to ensure the principle of distributive justice, and that the risks and benefits of research participation are fairly distributed. If each research visit involves out-of-pocket expenses for gas, food during a long wait between scheduled blood draws, parking fees, and child care, then only those who can afford those expenses would be able to participate in the research.

Coverage of expenses for airfare, overnight hotel stays, and other long-distance travel for research participation used to prompt additional ethical concerns based on the higher amounts of money involved. Comfort for these practices has grown over the last several years, in part based on studies in rare diseases and more specific patient populations, where the research is conducted at centers of excellence but potential subjects may be coming from other states or even other countries.

A number of different models for covering out-of-pocket expenses are acceptable including collection of receipts and reimbursement in cash or check; vouchers for taxis, parking or meals; pre-funded debit cards; or providing a per-diem amount based on average and expected expenses. Comfort has also grown with using third party vendors such as Uber and Lyft to bring participants to study visits, with direct billing to the sponsor.

Compensation for Time and Effort

Studies which include compensation for the time and effort of research participants should make an effort to consider the actual time spent on the study, including study visits, tasks outside study visits (completing surveys or diaries), and even travel time to clinical sites, keeping in mind that participants may be missing work in order to complete the study requirements. Payment amounts should be high enough so that they do not take advantage of populations with lower income; proposed payment amounts are sometimes based on local minimum wages, which provides a handy benchmark, but basing study payment on a low wage does have the effect that anyone who makes more than that wage will be losing money if they miss work for study commitments.

There are a number of models that have been proposed for the compensation of research participants, including a wage-payment model, and payment based on market forces and supply and demand.[2]

Incentive Payments

Some study plans include, either explicitly or implicitly, the payment to potential participants in a manner or at a rate that is intended to persuade them to participate in the research study, above what might be considered compensation for time or effort. For example, one study offered to pay the costs of elective plastic surgery for which the patients were already scheduled—several thousand dollars—if the patients agreed to participate in a 24-hour-long post-operative study comparing a new pain medication to the standard medication. Another study offered access to services (consultation with personal coaches) and gifts up to a value of approximately $6000 for participation in a study that required the completion of a survey every three months for a year. While the initial reaction to the

amounts of money involved is usually caution, if we go back to the discussion of undue influence earlier in the paper, is there truly a valid concern? In both cases, an IRB had determined that the risks of the research were reasonable in relation to the potential benefits; in the second example, the risks were minimal. If the sponsor is willing to pay a certain amount of money to ensure that they were able to enroll the study with the necessary number of participants and in a reasonable amount of time, these types of payments should be acceptable.

Conclusion

Efforts to protect research participants from undue influence, and researchers and sponsors from perceptions of trying to use undue influence, have long been a major concern for IRBs. However, the true risk of undue influence is significantly lower than has often been assumed, when considering research that has been IRB-approved and for which the risks are considered to be reasonable. Instead, parties involved in research should consider whether payments to research participants are sometimes too low.

About the Author

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References

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