



Removing Barriers: Reimbursement and Compensation for Participation in Oncology Clinical Trials

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It is an often-repeated statistic that only 3% -5% of patients with cancer participate in clinical trials for cancer therapies. The reasons for this are myriad. One survey found that only 16% of patients were aware of relevant clinical trials when discussing treatment options with their providers,¹ although more than 50% of patients will agree to enroll in a trial when approached. About 20% of cancer clinical trials will never be completed, because they fail to enroll enough participants to be able to answer the research question.² To better understand the reasons for low clinical trial participation, the American Cancer Society's Cancer Action Network (ACSCAN) commissioned a committee to investigate this question and to develop a report on the barriers to research participation, and consensus recommendations for overcoming these barriers.² One of the findings in the report was that concern about the potential costs of research participation prevented patients from finding out more about trials, or from participating in trials. In this paper, we look at the issue of the costs of research participation, and best practices for the reimbursement and compensation of research participants.

How Payment Impacts Participation

Financial considerations related to participation in clinical trials can include both medical and non-medical costs. Medicare and most private insurance plans are now required to cover the costs of routine medical care that occurs during cancer clinical trials, with trial sponsors usually covering the expenses for procedures or medications that are necessary only for the research study. However, participants may be asked to cover out-of-pocket non-medical costs, such as for travel, lodging, parking and meals. This is often due to the need to travel greater distances to take part in a clinical trial, or the need to visit the clinic more frequently for additional trial-related treatment or monitoring. Even if these ancillary costs are comparable to expenses experienced during normal medical care, participants often perceive that they may be spending more money, and frequently cite this as a reason for not considering trial participation.^{3, 4, 5, 6}

This sensitivity to costs manifests itself in disparate trial participation rates between high and low-income cancer patients, resulting in underrepresentation of low-income populations in clinical trials. Researchers have also found that individuals from poor neighborhoods travel over three times as far as individuals from non-poor neighborhoods for clinical trial participation (58.3 vs 17.8 miles), so there may be a true difference in the expenses of participation, in addition to sensitivity to extra costs.⁷ Researchers have found that individuals with an income under \$50,000 per year are more than 30% less likely to participate in

a cancer clinical trial compared to those with incomes over \$50,000.⁸ Providing funding to cover the non-medical expenses has been shown to boost overall enrollment, especially among those experiencing greater financial stress.⁹

The significance of the issue of financial compensation has been considered to have such a considerable impact on cancer clinical trials that the American Society of Clinical Oncology (ASCO) convened a roundtable meeting to discuss the foundations of this problem, and to develop recommendations for policies and actions both at individual institutions and for the overall clinical research system. The discussion and outcomes of this roundtable was published in the fall of 2018.¹⁰

The Ethical Perspective on Payment for Research Participation

The underlying concern about the financial payments to research participants is related to the concept of undue influence. In general, the worry is that potential research participants may be willing to accept study risks or discomforts that they would ordinarily find unacceptable, but that they are willing to allow only because they want or need the financial compensation that comes with study participation.

Research sponsors and investigators have often been wary about offering payment of any kind to research participants, out of concern that they will be seen as



trying to act inappropriately in persuading patients to participate in clinical trials. For that reason, they will sometimes offer no reimbursement of expenses or other compensation, or only very low amounts of compensation that don't cover actual expenses, to research participants. One pharma company, for example, has an internal policy that they will not allow token gifts (small toys, low-value gift cards or other treats, etc) as a thank you to children who participate in their pediatric clinical studies, out of concern that any form of payment could be interpreted as "bribing" children to participate in research. Unfortunately, this discomfort has resulted in the cost burden of participation being shifted to the participant.

Recently, however, this attitude has been shifting. While the concern about undue influence has always been a hypothetical one, newer research with potential research participants has shown that, in fact, they do not accept increasing levels of risk even when potential payments continue to increase. No research (that is subject to current regulations) can be conducted without approval by an Institutional Review Board

(IRB); one of the criteria that the IRB assesses in the approval of research protocols is whether the risks of the research are reasonable in relation to the potential benefits (direct benefits to the participant and/or the benefit to society of having the knowledge to be gained from the study). Therefore, as Largent and Fernandez Lynch have argued, no potential participant could be unduly influenced, because the research would not be proceeding at all unless the risks had already been determined to be reasonable—payment, by itself, could not make those same risks be unreasonable, whether the payment offered was \$5 or \$5000.¹¹

There are a number of ethical arguments in favor of participant compensation. The financial burden of research also becomes an issue of distributive justice. If participating in a clinical trial costs a participant \$40 each time they have to come in for a study visit to pay for their gas, parking in the hospital garage for 3 hours, and a meal from the hospital cafeteria, then only people who can afford those extra expenses will be able to participate in the clinical trial, as evidenced by lower participation by those making under \$50,000/year.⁷ Therefore, both the risks and the potential direct benefits of research participation accrue only to people who have financial means, and people who can't afford these expenses are effectively prohibited from participating. Importantly, the requirement of the Common Rule to avoid undue influence through the use of financial payments was meant to avoid unduly shifting research onto low-income patients, but excessive caution in financial support has created the opposite effect.



In addition, ethicists often point out that a clinical trial which cannot answer the research question it is designed to address puts participants at risk but does not achieve the expected benefit of the scientific knowledge that was expected to result when the study was designed and was approved by an IRB. A study cannot answer a research question with sufficient confidence (or statistical significance) if it cannot accrue the necessary number of evaluable participants from whom to collect outcomes data. Therefore, there is an ethical imperative to ensuring that clinical trials are able to enroll enough participants and compensation, and sometimes payments above fair compensation, are not just appropriate but necessary if they are needed to achieve this goal.

Best Practices

It is often easiest to consider payment for research in three separate categories; reimbursement for expenses, compensation for time and inconvenience, and incentive payments.



Essentially all parties involved in clinical research agree that reimbursement for study-related expenses is ethical and appropriate,¹² and many feel that it is ethically necessary for participants to not have financial costs for research. In research studies sponsored by biopharma companies, research costs are almost always covered. This includes study-related doctor visits, tests, and procedures that would otherwise be out-of-pocket costs for participants. It also usually includes incidental expenses such as transportation to study visits, parking, and meals during long study days. In studies that are funded by other sources, or that do not have specific funding sources, such as investigator-initiated trials, there may be no financial resources to draw from to cover the reimbursement of expenses. There are some organizations, including non-profit groups, who are trying to change this and who may be able to assist in covering these costs.¹³

Sponsors are now using new methods to provide things like study visit transportation by, for example, setting up accounts with ride-sharing companies that are direct-billed to the sponsor. When study transportation

is more extensive and may involve flights and hotels, there are study concierge services who can make all those arrangements on behalf of the participants. While some IRBs were initially wary of these new arrangements, most are comfortable with them as they become more familiar with the arrangements, particularly since there have been no apparent ethical concerns or issues raised by participants.

In most cases, compensation for the time and inconvenience of research participation is also considered ethical and appropriate.¹⁰ There are many opinions on what constitutes “fair” compensation; some authors suggest that compensation should be based on local minimum wages. Others point out that only people with high-paying jobs are unlikely to accept that payment rate if it means losing time from (higher-paid) work, and low compensation rates disproportionately shift the burden and benefits of research onto less well-paid members of society. The payment rates that can be offered are also likely to be dependent on the available funding. While there is no “right” amount of payment, the general message should be that compensation for research participation is ethical, acceptable, should not be prohibited, should not be avoided or reduced out of concern for undue influence, and should be determined out of respect for the time and inconvenience of the participants and the available research funding. IRBs which are in line with the current ethical thinking on compensation issues should not restrict or limit these payments.

Finally, in some studies, incentive payments that go above and beyond what might be considered to compensate for time may be appropriate in some studies. As discussed above, a study that fails to fully enroll and cannot answer the study question asks participants to accept risks, but there is no benefit to society. If incentive payments are a feasible way of ensuring full enrollment, and as discussed above, the risks of the study have been determined to be reasonable through IRB review, there is no regulatory or ethical prohibition on higher payments to participants. In fact, incentive payments are routinely used to recruit healthy volunteers into early phase drug testing, where the participants are exposed to risk, but have no prospect of direct medical benefit.

Conclusion

The issues around reimbursement and compensation in cancer clinical trials are complex, and solutions to address these issues will need to be multi-factorial and integrated into multiple parts of the clinical research ecosystem. But in order to increase participation in research studies to allow us to move new and promising therapies forward, we need to address these barriers in comprehensive and thoughtful ways. Solutions for policies and procedures should involve the participation of patient voices, as well as those of the professional research community.

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