FAIR PAY: LEGALIZING COMPREHENSIVE COMPENSATION IN CLINICAL TRIALS

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Summary

There are simple legislative remedies that remove two major barriers to competitive payment of clinical trial participants, which slow recruitment, and by extension, the pace of critical medical research. First, federal regulations on human research subjects should be changed to discourage institutional review boards (IRBs) from rejecting proposed compensation for clinical trials as "too high" barring extremely unusual circumstances. Second, as is the case with other forms of socially desirable economic activity, the tax code can be changed to incentivize participation — most notably, by exempting clinical trial income from income tax, participants (especially those with rare diseases or disabilities) will not jeopardize welfare benefits by partaking in the research that needs them.

Change and Opportunity

Recruitment is a consistent problem in American clinical trials. Clinical trials can be extremely onerous and time-consuming, which is why compensation is frequently offered for participation. Ideally, a clinical trial that is failing to recruit adequate numbers of participants could raise compensation rates to increase enrollment. IRBs may prohibit this, however, because of vague regulatory mandates to avoid "undue influence," which IRBs often interpret as paying so much as to alter the rational ability for participants to provide informed consent.

Given the vagueness of what actually constitutes "undue influence," IRBs default to a risk-averse approach, often barring clinical trials with the budget and need to pay more from doing so. The Office for Human Research Protections (OHRP) in particular has sought to advertise that cases of monetary undue influence are vanishingly rare, and that IRBs are far too concerned with the issue — at the expense of participants who otherwise could be paid more when budgets permit.[1] Academics have likewise decried IRBs' obsessive focus on monetary undue influence.[2]

Despite nudging from regulators, IRBs — which approve or reject compensation levels proposed by trial investigators, but do not set compensation themselves — are slow to change. This is bad for participants and for clinical trials in America at large.

Allowing for greater payment is not a universal solution to the problems of clinical trial recruitment. Some clinical trials have extremely narrow recruitment criteria, or study very rare diseases, all of which make recruitment especially challenging. Still, financial incentives are important for many participants,[3] are a critical tool available to researchers, and that tool should not be burdened by artificial, paternalistic notions that "paying too much" is unethical. Blood plasma donation offers a useful parallel: paid donation is viewed as unethical in some countries, but payment in the United States creates a large surplus, which is then exported abroad, much to the benefit of both the donors who are paid and recipients whose lives are saved.[4]

Some clinical trial participants who stand to gain from potential early stage therapies may be willing to join a clinical trial for free, but if they happen to be on welfare, the compensation may cause them to lose benefits.[5] In the status quo, then, someone disabled by a rare disease may not be able to afford to join a clinical trial to study their condition, because even modest compensation to make participation affordable may disqualify them from welfare.

Plan of Action

Recommendation One: Amend the Food and Drug Administration (FDA) and OHRP regulations that command IRBs to avoid undue influence (21 CFR 50.20 and 45 CFR 46.116(a), respectively).[6] Both require clinical trial investigators to recruit subjects under circumstances "that minimize the possibility of coercion or undue influence," but neither actually mention compensation. Revising 21 CFR 50.20 and 45 CFR 46.116(a) to specify that the prospect of undue influence alone cannot be used as a reason to reject compensation proposed by clinical trial investigators would force

1 OHRP's 2022 workshop on compensation represented a very strong message to IRBs that they tend to overweight concerns of undue influence. The FDA Office of Good Clinical Practice has not updated its guidance or otherwise signaled a more liberal approach towards compensation as clearly as OHRP has. *(https://www.hhs.gov/ohrp/education-and-outreach/exploratory-workshop/2022-workshop/index.html) (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/payment-and-reimbursement-research-subjects)*

2 For an academic overview, see Largent & Fernandez Lynch, Paying Research Participants: Regulatory Uncertainty, Conceptual Confusion, and a Path Forward, Yale J Health Policy Law Ethics, 2017. *(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5728432/)*

3 Treweek, Pitkethy, Cook & Fraser et al., Strategies to improve recruitment to randomised trials, Cochrane Database Syst Rev, 2018; Tishler & Bartholomae, The Recruitment of Normal Healthy Volunteers: A Review of The Literature on the Use of Financial Incentives, J Clin Pharmacol, 2002. *(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7078793/)(https://pubmed.ncbi.nlm.nih.gov/11936560/)*

4 The plasma trade is becoming ever-more hypocritical, The Economist, August 2024. *(https://www.economist.com/finance-and-economics/2024/08/29/the-plasma-trade-is-becoming-ever-more-hypocritical)*

5 Rand & Kesselheim, Payments for research participation: Don't tax the Guinea pig, Clin Trials, 2022. (https://pubmed.ncbi.nlm.nih.gov/35786008/)

6 21 CFR 50.20: "An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence." 45 CFR 46.116(a)(1) is nearly identical, with minor wording adjustments. *(https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-50/subpart-B/section-50.20) (https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46/subpart-A/section-46.116)*

the long-overdue acknowledgement that payment is due to participants among IRBs. In doing so, a major barrier to compensating participants fairly, and recruiting participants quickly, could be removed.

Revising this directly, instead of relying on agency action, is preferable in part because previous executive branch attempts at revising the guidelines that IRBs operate under has been very slow and marginal — a revision of the Common Rule took nine years (2009-2018) and resulted in minimal change.[7]

Recommendation Two: Removing the corresponding tax barrier by excluding clinical trial compensation from gross income calculations would also reduce barriers to recruitment. One such method is the proposed Harley Jacobsen Clinical Trial Participant Income Exemption Act[8]. Doing so would also ensure that low-income participants are not excluded from research because they may lose access to the Supplemental Nutrition Assistance Program or disability benefits.

Conclusion

Removing barriers to fairly compensating participants in clinical trials is crucial for accelerating medical research and ensuring diverse participation. We can remove significant barriers to recruitment by amending the regulations that encourage IRBs to arbitrarily limit compensation and exempting trial income from tax calculations. These changes would benefit all participants, especially those in rare disease trials and with low incomes.

7 Schrag, Vexed Again: Social Scientists and the Revision of the Common Rule, 2011-2018, J Law Med Ethics, 2019. *(https://pubmed.ncbi.nlm.nih.gov/31298093/)*

8 https://kelly.house.gov/media/press-releases/kelly-houlahan-introduce-harley-jacobsen-clinical-trial-participant-income

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