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EDITORIAL

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Undue worry about paying research participants?

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"It is time to stop worrying and move forward on developing guidance for determining reasonable amounts of money to offer research participants in different studies and settings."

"Money often costs too much"
Ralph Waldo Emerson

Why do we keep worrying about paying research subjects? Offering payment to research participants is a longstanding and widespread practice, similar to paying people in other kinds of transactions, yet disagreement persists about the appropriateness and practice of paying participants [1]. At the same time, money has a pervasive presence in the conduct of clinical research. The estimated total spending on health-related research and development by the drug industry and the Federal government has tripled since 1990 [101]. Conducting clinical research is expensive; estimated per patient costs for a clinical trial can exceed US$47,000 [102]. Pharmaceutical and biotech sponsors, although they spend millions conducting research, are among the most profitable companies globally. Private and public research sponsors pay large amounts of money to clinical researchers, contract research organizations, data managers, recruiters and others to help conduct efficient and quality trials. Significant recent attention has focused on potential conflicts raised by investigator and institutional financial interests [2]. In spite of this large and growing research enterprise, available estimates suggest that the average payment per participant for a research study – when they receive any payment – is usually quite modest, although there is a range of dollar amounts and details about payment are limited [3].

Timely and adequate recruitment, vital for successful clinical research, can be difficult and cause delays in study completion. Offering money to research participants may be critical for recruitment, and could save money overall. Evidence suggests that payment is an important recruitment incentive for healthy volunteers [4], improves response rates in social science research [5], and increases willingness to participate in hypothetical studies [6]. There are more limited data on the effectiveness of payment in recruiting patients into clinical research studies [7]. Patients often enroll in research because they are seeking treatment for their condition, want access to treatment otherwise unavailable, or are following the recommendations of their physician. More research is needed to evaluate the effect and acceptability of monetary incentives for recruitment into clinical research. Accumulating data from the use of monetary incentives for adherence and behavioral change may offer some insights [8]. Even more limited data exist on the effectiveness of payment for retention in clinical studies, also critical to successful trial completion.

Although money may motivate people to participate in research, participants are offered payment for reasons beyond recruitment. Commonly, money is offered as reimbursement for travel and other expenses in order to simply make participation

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in research possible or revenue neutral. Participants may also be compensated for their time and contribution or be offered money as gratitude for their participation. Different models of payment have been proposed based on these various reasons for offering payment to subjects [9]. Some have argued that payment to participants should be acceptable because it increases available money-making options for people, especially low-income individuals, and also could augment not only the number but the variety of participants [10].

Nonetheless, concerns remain about the ethical appropriateness of paying research participants. A persistent worry seems to be that money could be an undue inducement or even coerce people to participate in research. A recent study found that research ethics professionals in the USA have broad ethical concerns about paying research subjects, especially when substantial payment is involved. The majority of respondents found it more acceptable to offer payment as reimbursement or compensation for time and inconvenience than as an incentive or as compensation for risk, and most expressed concerns – along with some inconsistency in their views – about payment being coercive or unduly influential [11]. Although some assume that paying healthy subjects is less problematic than paying patient subjects, respondents in this study did not distinguish the two groups and in practice patient subjects are often offered payment.

The US Federal Regulations for the protection of human research subjects do not explicitly mention payment, but they do emphasize the importance of the voluntary consent of research participants and require that informed consent be obtained *"…under circumstances … that minimize the possibility of coercion or undue influence"* [12] . Although neither coercion nor undue influence are defined in the US regulations, they are described as distinct concepts in the Belmont Report as follows: *"Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance"* and, undue influence *"occurs through an offer of excessive, unwanted, inappropriate or improper reward or other overture in order to obtain compliance"* [103]. By these definitions, the 'distinct concept view', an offer of payment, no matter how large, is not coercive as it is not an overt threat of harm [13]. By contrast, it is possible, although not necessarily the case, that money – as an excessive, unwanted or inappropriate reward – could unduly influence a prospective participant by distorting her reasoning and invalidating her consent. Importantly, the mere fact that inducements influence individuals' behaviors does not make them undue. We are commonly induced by financial incentives, and money often influences our decisions and behaviors. This is ordinary and unproblematic. Working for a salary, shopping for a discount, motivating our children to rake the leaves, and countless other daily decisions and behaviors, are clearly influenced by the associated financial incentives. Incentives in theory become undue when they are excessive or unwanted, distort our reasoning and, thus, lead us to do something contrary to our interests. In research, an individual unduly influenced by money might enroll in an objectionable or excessively risky study, misrepresent medical history or side effects, or do something else that could jeopardize her safety and the integrity of the study. Some argue that since ethics review committees do not (or should not) approve studies that are unjustifiably risky, concerns that money will unduly influence participants to enroll are overstated [14]. Furthermore, other motivations besides money could distort judgment, so concern about the possibility of distortion or misunderstanding on the part of research participants should be addressed more directly. Attention should also be aimed at verifying previous medical history and reports of symptoms to mitigate any potential misrepresentation.

Might there still be legitimate concerns about money as an *"…excessive, unwanted, inappropriate or improper reward,"* as undue influence was described in the Belmont Report? Concerns about payment being excessive are largely unsupported by available data regarding payment to research subjects, and run counter to arguments that payment should not be too low in order to reduce the possibility of exploitation [15]. If money were to be unwanted, potential participants can choose not to accept it, or choose not to enroll in a study. Worries about money for research participation being inappropriate or improper because of possible commodification of the body, a desire for all research participants to be altruistic gift-givers, or a view that we should not pay people to assume risks have all been articulated but not adequately developed. Further, these concerns imply a 'research exceptionalism', an unjustified and largely improbable view that research is substantively different than other human endeavors and transactions in which money is exchanged [13].

So if offering payment to research subjects benefits research and the individuals who receive it, why do we keep worrying about it? It is time to stop worrying and move forward on developing guidance for determining reasonable amounts of money to offer research participants in different studies and settings [16], gathering further evidence about positive and negative effects that money may have on recruitment and retention, and developing and improving methods for ensuring that participants understand what they are agreeing to when they enroll in research.

Disclaimer

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