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Paying Research Participants: The Outsized Influence of “Undue Influence”

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Offers of payment to research participants, though quite common, persist as a source of ethical controversy. U.S. regulations governing human subjects research do not specifically address offers of payment; yet, in practice, many institutional review boards (IRBs) seem to fear that approving offers of payment that are “too high” runs counter to their regulatory obligation to minimize the possibility of coercion and undue influence.¹ As a result, there is a tendency toward payment conservatism: offers of payment to research participants are kept low as a precautionary measure.² This better-safe-than-sorry approach, however, fails to appreciate that coercion is not a payment problem, that IRB review itself serves as protection against undue influence, and that whether an offer of payment is too high should not be the only — or even the most prominent — consideration. Real ethical and practical concerns associated with payments that are “too low” should command IRBs’ attention.

In this article, our argument proceeds in three parts. First, we argue that, properly understood, coercion is not a legitimate payment-related concern, and undue influence may be a legitimate concern, but only in very limited instances. In practical terms: IRBs should *never* worry that offers of payment are coercive and ought to be much less concerned than they currently appear to be that offers of payment are unduly influential. Second, we argue that payment conservatism is not only *not* as protective of research participants as seems to be widely assumed — it can actually have perverse consequences. On our view, the fundamental problem with payment conservatism is that it fails to give adequate weight to the impact of low payment on the majority of participants for whom undue influence is not a legitimate concern. Finally, we argue that the default approach to payment should be flipped — rather than assuming payments are too high, IRBs should start asking whether payments are high enough.

Concerns Regarding High Payment

The Federal Policy for the Protection of Human Subjects (known as the “Common Rule”)* and the equivalent FDA regulations do not directly address offers of payment made to research participants. Instead, they require IRBs to ensure that investigators “seek informed consent only under circumstances ... that minimize the possibility of coercion or undue influence.”³ Thus, an offer of payment that fails to minimize the possibility of either coercion or undue influence is impermissible. But when is this the case?

Unfortunately, neither coercion nor undue influence is clearly defined in U.S. regulations or guidance—nor are the terms well-understood by IRBs or investigators.⁴ Thus, IRBs and investigators have been left without adequate support to distinguish between ethically problematic and unproblematic offers of payment and without a sense of what counts as sufficient with regard to minimizing the risk of problematic offers. Nonetheless, they are warned to be “sensitive” to the possibility a proposed payment will be an undue influence and “cautious” about high payments.⁵ Against this background, IRBs and investigators clearly need additional guidance on how to assess offers of payment against the regulatory terms.

Coercion

Coercion is best defined as a *threat* to violate someone else’s rights, or to fail to satisfy an obligation to them, in order to obtain compliance in situations where that person has no reasonable alternative but to comply.⁶ This definition has the greatest explanatory power, comports with understandings of coercion outside the research context, and allows for necessary differentiation between the concepts of coercion and undue influence.⁷

On this definition, a genuine offer to pay a research participant is not a threat and, therefore, cannot coerce. Thus, while it is possible that someone could be coerced to participate in research by other means, *coercion is simply not a relevant concern when assessing offers of payment* made to prospective research participants. Eliminating coercion from our payment lexicon will increase accuracy within IRB deliberations and elevate the quality of conversation about payment by shifting discussion away from emotionally laden allegations toward actual problems.

Undue Influence

Over some disagreement in the regulated community, we endorse Emanuel’s view that undue influence is best understood as an *offer* to provide an excessive reward that results in bad judgment, meaning that it results in a choice that is *unreasonably* against the offeree’s self-defined values and interests.⁸ According to this view, undue inducements are problematic because they result in excessive exposure of the offeree to risk.

*Revisions to the Common Rule published in January 2017 made no amendments relevant to payment. The definition of vulnerability now focuses exclusively on susceptibility to coercion and undue influence, but there has been no refinement of those terms themselves. U.S. Department of Health and Human Services et al. Final rule: Federal policy for the protection of human subjects; 82(12) FED. REG. 7149, 7204 (Jan. 19, 2017).

Note that an excessive reward may cause prospective “subjects to lie, deceive, or conceal information that, if known, would disqualify them as participants in a research project.”⁹ In some instances, this lying will expose research participants to risks from which exclusion criteria were designed to shield them—such that the act of evading them is per se unreasonably against the offeree’s interests. This is consistent with Emanuel’s definition of undue inducement.

Emanuel’s account may be incomplete, however. This is because, in other cases, lies might not expose participants *themselves* to unreasonable risks, but could instead jeopardize the scientific integrity of the research. Emanuel’s definition, which is focused on risk of harm to the offeree, cannot account for cases in which the undue inducement has an effect *other than* to expose the offeree to unreasonable risks. For example, an exclusion criterion might be in place to facilitate statistical analysis or allow for a clean causal inference rather than to protect research participants. If that is the case, an individual may make a wholly reasonable decision (from her perspective) to evade such an exclusion criteria in order to be paid. Nonetheless, we include this type of lying under the heading of undue influence for reasons explained below.

Examples illustrate how the two types of lies are distinct. First, take Ashley. Ashley is considering participation in a trial that excludes those with a history of malignancy. Such individuals are excluded because the experimental intervention can greatly increase their risk of cancer going forward. Ashley, inexorably drawn in by an offer of high payment, lies to conceal her disqualifying medical history, putting herself at risk in a way the IRB intended to exclude as unreasonable. Now, consider Brian, a prospective participant in a behavioral weight loss study. In order to isolate the effects of the particular weight loss intervention under investigation, simultaneous participation in another weight loss study is an exclusion criterion. Brian lies to conceal that he is participating in multiple studies simultaneously. Given Brian’s overwhelming desire to make money and the (stipulated) fact that the lie doesn’t increase any risk to him from study participation, the lie is reasonable from his viewpoint. The investigators, however, will be understandably frustrated if Brian’s weight loss (or lack thereof) contaminates their data. Under Emanuel’s definition, only Ashley has been unduly influenced, whereas Brian is acting rationally. Under our view, however, the offer of payment has unduly influenced both Ashley and Brian.

In practice, participants themselves will often be unable to parse which inclusion/exclusion criteria are for their personal well being and which are rooted solely in a desire to protect scientific validity or social value. (And, to be sure, some criteria will have both aims.) In other words, it will be difficult for participants to know precisely when or whether their lying unreasonably risks harm to self. Could Brian actually know, for example, that excluding simultaneous participants was not a mechanism of protecting participants from excessive and unhealthy weight loss? Since lying *could* create unreasonable risk, lies of either type induced by an offer of payment properly count as instances of undue influence.

Even if, however, one resists the idea that lies endangering scientific integrity are actually a species of undue influence, it is possible to concede that these two types of lies exist in research. Because both stem from offers of payment, they can often be addressed in the same

manner. Thus, our following analysis about payment conservatism holds regardless of how lies are classified.

Before moving on, it is important to highlight the differences between a mere influence — that is, an offer that encourages the offeree to do something that is reasonable but that he or she *might* otherwise choose not to do — from an undue influence — an offer that encourages the offeree to do something that is unreasonable and that he or she *would* otherwise choose not to do. Simply put, while mere inducements color our judgment as we weigh reasonable choices, undue inducements cloud our judgment as we confront unreasonable ones. Thus, unlike undue influence, mere inducement is neither an ethical nor a regulatory concern.

To illustrate, imagine there has been a blizzard and that your neighbor, Cate, prefers to stay inside. It would be mere inducement for you to offer to pay Cate to go outside and shovel your sidewalk. By contrast, if Cate has a heart condition that makes shoveling a lethal undertaking, an excessive offer of payment could unduly influence Cate to unreasonably risk her health by shoveling.

Ultimately, when an offer of payment causes an individual to participate in research that is unreasonably against his or her interests and/or the interests of the community more generally, undue influence is indeed a valid ethical and regulatory concern. It is important to recognize, however, that IRB review and approval will offer key protections against undue influence in many circumstances (short of participants flouting inclusion/exclusion criteria). We turn now to this role of IRBs.

IRB Review as Protection against Undue Influence

IRB approval is, by regulation, conditioned on a threshold determination that a study has a favorable risk-benefit ratio.¹⁰ IRBs must determine both that physical, social, and other risks to participants have been minimized, and that the residuum of risks is outweighed by the social value of the knowledge to be gained and/or the prospect of direct benefit to the research participants. Critically, IRBs are directed to make this assessment without weighing any proposed offer of payment to research participants as a benefit.¹¹

To emphasize, 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. Instead, avoiding undue influence requires only that acceptance of an offer to participate not be *unreasonably* against one's interests. Of course, we accept risk all the time without it being unreasonably against our interests to do so; for example, no one would say it is unreasonable to drive to work each day despite the risks of motor vehicle transit.

Note, however, that IRBs approve protocols for a general study population, and short of adopting a dramatically different system than the one we have now, IRBs cannot possibly evaluate a protocol's propriety for every individual research participant.¹² As a result, Emanuel's prominent claim that undue influence is "nonsense on stilts," i.e., that IRB review

completely eliminates the possibility of undue influence in research,¹³ is too expansive. We agree that in many circumstances, the IRB's determination that a study is not unreasonably against the interests of the target study population is sufficient to avoid concern about undue influence. It is possible, however, that, in some limited cases, an individual's participation in an IRB-approved study may be unreasonable for him or her, even if it is reasonable for the broader target population.¹⁴

Importantly, for the majority of participants who do not fall into one of the two groups susceptible to undue influence discussed below — certain idiosyncratic individuals and deceptive participants — once the IRB's original determination of reasonableness is made (independent of payment), no amount of payment, regardless of how high, can legitimately raise the concern of undue influence. This is because no offer of payment can render an inherently reasonable offer unreasonable. Returning to the snow-shoveling example, if it is reasonable for Cate to agree to shovel your driveway for free, it certainly does not become unreasonable for her to shovel it if she is offered \$10, or even \$100 or \$1000 or more to do so. Although these offers would doubtlessly influence her decision-making, they cannot accurately be deemed *unduly* influential.

To the extent that an IRB finds itself worrying about undue influence as a matter of course, rather than in the circumscribed contexts described below, we suggest that this may be a signal that the IRB is not satisfied by its own analysis of risks and benefits and should reassess. Perhaps the IRB in these cases has indeed permitted unreasonable risks to slip through.

Research Participants Still Susceptible to Undue Influence

There are two groups of potential research participants who may be susceptible to undue influence despite the fact of IRB approval, a point that has not yet been sufficiently appreciated in the literature on payment. The first group consists of idiosyncratic research participants, those with particular characteristics that even a well-functioning IRB will not be able to account for, and the second group consists of people who may lie about disqualifying information.

Group 1: Idiosyncratic Individuals

Participation in approved research may be unreasonable for individuals with characteristics that fall outside of the IRB's purview or ability to consider if those characteristics create idiosyncratic risks to physical or personal integrity.

Physical Risks—Many physical risks to research participants that might render their participation unreasonable will be captured via the elaboration of appropriate inclusion/exclusion criteria and refinement of the target study population. The possibility of undue influence for idiosyncratic participants within that target population based on susceptibility to unique physical risks arises when (i) the characteristics relevant to risk are known to the potential research participant, but (ii) fall outside an IRB's generalized risk assessment, and so are not embedded in inclusion/exclusion criteria. *Both* elements must be present for

undue influence to occur in this context. Note, however, that while these are necessary factors, they are not sufficient to guarantee *actual* undue influence, as described below.

Individual characteristics relevant to risk include: (A) known characteristics that would unreasonably increase either the probability or magnitude of harm (direct risks); (B) known characteristics that would, conditional on the harm occurring, render the effects of the harm particularly damaging such that it would be unreasonable to participate (indirect risks); and (C) unknown characteristics that would unreasonably increase either the direct or indirect risks. Let us now consider how each of these affects susceptibility to undue influence in IRB-approved research.

In Group 1(A), a potential participant may have some physical trait or condition, say an allergy to a preservative in the investigational product, that he knows would make research participation unreasonable for him because it elevates the direct risks of participation. If the participant is aware that this particular physical trait or condition unreasonably increases the direct risks of participating in this study, then it is the sort of thing that the investigator and IRB can be expected to be aware of as well — not necessarily that the trait or condition afflicts this particular individual, but rather that it elevates direct risks of participation in those who have it. As the IRB is responsible for considering and minimizing the direct risks of research participation, IRB review should ensure that the allergy is an exclusion criterion and that individuals with the allergy are excluded from the target study population. Since the offer to participate and to be paid will not be made at all to individuals from Group 1(A) because they do not qualify for the study, undue influence is not a concern (unless the individual engages in deception, as discussed below in Group 2).

In Group 1(B), an individual may have a unique trait that does not change the probability or magnitude of research-related harms; however, should the harm occur, the consequences will—for some unique reason—be amplified in a way that makes participation unreasonable. Imagine an investigational procedure that poses the risk of numbness in the extremities. There may be nothing about individual participants that renders them more or less susceptible to numbness (such that they ought to be excluded from participating), but the materialization of that risk might be more damaging to some individuals than others. A concert pianist, for instance, might recognize that he could lose his livelihood if such numbness occurred, although exclusion criteria would not, of course, be based on occupation. More generally, such indirect or conditional harms are not something the IRB could be expected to identify or address for each individual participant. Thus, it may be that for these individuals, participation would be unreasonably against their interests but they are not explicitly excluded by protocol criteria and may nonetheless decide to enroll due to a generous offer of payment. Thus, undue influence is a possible concern in this context.

Finally, potential research participants in Group 1(C) have some physical condition that places them at higher risk of direct or indirect harm as a result of participation, but in a way that neither the participant nor the investigator or IRB could be aware of. For example, the investigational product may include a wholly novel preservative. While an individual may be allergic to it, he cannot know that before being exposed. Of course, there are many uncharacterized risks in clinical research, which is partly why it is done. If there is no way to

know *ex ante* that an individual should be excluded from the target study population (or that the risk would be particularly damaging if it materialized), there is no risk of undue influence. This is because the participant rests wholly unaware that participation may be particularly risky for him, and as a result, there is no concern that payment would cloud his judgment and lead him to do something he would, in the absence of the offer of payment, know to be unreasonable.

Personal Integrity Risks—In addition to narrow, idiosyncratic physical risks, IRBs are also unsuited to consider risks to personal integrity that may arise from participating in a study that one knows is discordant with one's settled values and interests, whether secular or sectarian in origin. As examples, consider a devout Jehovah's Witness contemplating participation in a study that requires receiving a blood transfusion or a woman who is philosophically opposed to contraception considering a study of a new birth control pill, in both cases solely because the studies offer large payments. In these two examples, there is something unique about the individuals that would not (or could not) be contemplated by the IRB's review, such that a decision to participate in an IRB-approved study might nonetheless be unreasonable for the particular individuals in question. As with the relevant physical risks, for the possibility of undue influence to arise, the risks to personal integrity must be known to the potential participant but not fall within the purview of the IRB. Personal integrity risks, therefore, also fall into Group 1(B). This is summarized in Table 1.

What we have described so far are circumstances in which the possibility of undue influence may arise in IRB-approved research due to idiosyncratic features of research participants that are known to the individual participant but which are beyond the reach of the IRB. The Common Rule emphasizes the need to minimize the possibility of undue influence.

Yet, we caution that *possibility* is distinct from *actuality*. Some idiosyncratic participants may simply refuse to participate in research that would be unreasonably risky for them, despite the offer of money. This conceptual claim is consistent with empirical findings suggesting that offers of money do not in practice distort research participants' judgment regarding study participation.¹⁵ Such empirical evidence should be given significant weight when IRBs are considering the ethical trade-off between lower and higher levels of payment.

Moreover, for those idiosyncratic individuals who do choose to participate, undue influence is not the only explanation. It is possible that although participation runs contrary to *certain* interests of these individuals (whether physical or related to personal integrity), they will rationally determine that, in the present circumstances, their financial interest trumps. The result is a clear-headed decision that the money renders participation not unreasonably against their interests at all. Obviously, people make decisions between competing interests — including between assumption of various kinds of risks and monetary interests — on a regular basis; for example, people enlist in the military or work as firefighters and police officers. If we are open to the possibility that no undue influence exists in those employment contexts, there is no reason why research should be any different.¹⁶

This is a foundational challenge in identifying *actual* instances of undue influence for those in Group 1(B): has the offer of payment simply tipped the balance in favor of an otherwise

undesirable but not unreasonable choice (mere inducement), or has the offer of payment spurred an unreasonable/irrational choice (undue inducement)? Because we cannot know precisely how any given individual is weighing his or her competing interests, this question will often not have a clear answer. However, if we grant that apparently incongruous decisions can nonetheless be rational/reasonable, the mere possibility of undue influence should not lead us to conclude that undue influence has occurred.

Group 2: Deceptive Individuals

Apart from the subset of idiosyncratic individuals described above in Group 1(B), there is also another group that IRBs may find it challenging to protect from undue influence: namely, research participants who might, if an offer of payment is sufficiently attractive, lie, deceive, or otherwise conceal information that would exclude them from participation.¹⁷ Deceptive participants deliberately lie in order to appear to fall within the target study population and receive payment.

Above, we drew the distinction between (A) lies that create unreasonable risks for the study participant and (B) lies that create threats to a study's scientific validity, and therefore its value to the broader community. Extending that analysis, Group 2(A) includes people who would otherwise fall outside the target study population approved by the IRB because their participation would be unreasonably risky for them (i.e., liars from within Group 1(A)). Revisiting our earlier example, an individual who has a known allergy to a preservative in the investigational agent might lie about the allergy in order to avoid being excluded and thereby receive payment.

Group 2(B) consists of individuals who fall outside the target study population for reasons other than participant protection. Participation is not unreasonably risky for these individuals, and it may even be in their best interest to obtain the payment,[†] but their participation is nevertheless problematic because it threatens the scientific validity of the study and, in turn, causes a problem that the research community would generally seek to avoid.

As described above, deceptive individuals may not themselves know whether they fall into Group 2(A) or Group 2(B), despite the fact that they know they are lying. While the problems caused by lying are clear, it is unclear whether lying is a general problem in practice — and if so, for which types of studies or populations it may be most prevalent.¹⁸ More empirical work is needed.

We have now identified two overarching groups of prospective research participants who may be susceptible to undue influence, despite IRB approval of a given study, as summarized in Table 1: certain idiosyncratic individuals and deceptive participants.

[†]While it is beyond the scope of this article, we note an individual might also be unduly influenced to lie in order to receive an experimental intervention, rather than just payment; depending on an individual's alternatives, participation in research may be in their best interests, making the lie reasonable from their perspective, although still unreasonable vis-à-vis the community more generally. Typically, IRBs do not worry about undue influence in such contexts, which is an important inconsistency compared to how offers of payment are handled.

However, as we explore in the next section, the mere existence of such individuals is insufficient justification for keeping participant payment low.

Concerns Regarding Low Payment

One consequence of myopically focusing on minimizing the possibility of undue influence—a concern that we demonstrated above to be possible but overblown in IRB-approved research—is that the real ethical and practical concerns associated with payments that are too low can too easily be overlooked. Here, we present the most salient concerns related to low payment.

Exploitation

To exploit someone is to take *unfair* advantage of him or her.¹⁹ Exploitation occurs when one party to a transaction insufficiently benefits or assumes an unfair share of burdens relative to other parties to a transaction. Exploitation is an ethical concern, even if it is not an explicit regulatory consideration as outlined in the Common Rule. In the clinical research context, participants may be exploited when they are not offered adequate compensation or other benefits as compared to the value of their contribution, including the burdens of participation, their time, effort, inconvenience, and opportunity costs (in terms of other options forgone in order to participate in research).

Importantly, exploitation can be either harmful or mutually beneficial, non-consensual or consensual.²⁰ In instances of mutually beneficial exploitation, both parties are better off than they were at their baseline; in consensual exploitation, the exploited party gives valid consent to the transaction. So, if we return again to the snow shoveling example in which Cate simply prefers to stay inside, imagine you offer her \$10—take it or leave it—to shovel your driveway, and she agrees. Assume a fair rate is \$50 and that Cate knows this (or at least she knows that \$10 is not fair given the amount of work involved), but she decides that she would be better off shoveling your driveway and getting \$10 than not shoveling it and getting no money at all. This is an instance of mutually beneficial, consensual exploitation.

The wrongfulness of harmful and/or non-consensual exploitation is self-evident, but mutually beneficial consensual exploitation is ethically more challenging. As just explained, a competent individual may voluntarily agree to accept lower benefits than would actually be fair on the grounds that *some* benefit is better than none at all. Thus, we do not necessarily take the position that mutually beneficial consensual exploitation must always be avoided in research, as this would be over-protectionist; the opportunity to obtain *some* benefit should not be withheld solely because *more* benefit is not forthcoming. However, we do argue that IRBs seeking to fulfill their responsibility to potential research participants have a responsibility to promote fair compensation.²¹ Thus, it is appropriate for IRBs to encourage higher payment as a mechanism to avoid exploitation, even if they might not reject a study that had the potential to exploit consenting participants due to low payment.

Exposure to Unjustifiable Risks due to Recruitment Shortfalls

Paying participants too little might also hinder trial recruitment,²² thereby delaying scientific and medical progress, contributing to research waste, and/or unethically exposing

participants to risks and burdens that cannot be justified by their scientific value if studies fail to complete or achieve appropriate statistical power.²³ A shortfall of research participants is an obvious and demonstrated barrier to completion of clinical trials.²⁴ While there is a need for more empirical research to show whether and how increasing offers of payment might affect recruitment for clinical trials specifically, it certainly makes intuitive sense that it would, and there is evidence that larger offers of payment improve recruitment in survey research.²⁵ Of course, offers of payment should not be construed as a panacea for recruitment problems, as there are other known barriers to participation beyond inadequate compensation, and study budgets impose an upper bound on what it is possible to pay. Nevertheless, higher payment for participation seems likely to improve study enrollment in at least some contexts.

Overburdening Certain Populations

Finally, higher offers of payment may draw in a more diverse pool of research participants because a greater range of individuals is likely to find participation attractive as offers of payment increase. This could help ensure that the burdens of socially valuable research are spread more evenly over the population, rather than primarily among lower income groups, though more research is needed on this possibility.²⁶ Not only is it desirable for all people who benefit from clinical research to contribute to its progress, clinical research may also have greater value when a more diverse (and therefore representative) population agrees to participate. Additionally, it has been speculated that higher offers of payment may make it possible for more people to access the potential benefits of research participation.²⁷ Again, more research is needed.

How Should IRBs Proceed? Balancing Concerns Regarding High and Low Payment

The status quo approach to payment is problematic. Payment conservatism overestimates the scope of undue influence — fearing it in every instance, rather than only for certain idiosyncratic individuals and lying liars — and goes well beyond the regulatory requirement to simply minimize the possibility of undue influence. Moreover, payment conservatism is not merely less protective than it may initially seem, it also has the perverse consequence of introducing exploitation as a widespread concern, among other problems.

From our perspective, rigorous review to determine that study participation is a reasonable offer for the target study population will satisfy an IRB's regulatory responsibilities, even though some undue influence remains possible. Note that this is exactly the result that the system of human subjects protections we have in place under the Common Rule — one aimed at population-level evaluation of studies — is designed to reach. It is not possible to fully protect everyone because IRBs do not analyze the circumstances of each individual research participant. By telling IRBs to “minimize”—rather than to “eliminate”—the possibility of undue influence, the regulations acknowledge that some instances of undue influence may be unavoidable.

That said, although it will not be possible for IRBs prospectively to identify and exclude the idiosyncratic individuals subject to undue influence (Group 1(B)), they may have some capacity to address the problem of deceptive participants (Groups 2(A) and 2(B)) short of demanding that offers of payment be kept low. For example, IRBs could push investigators to use objective metrics (rather than self-report) when evaluating prospective research participants against a study's inclusion/exclusion criteria, to utilize more extensive screening before enrollment, and to rely on registries (when available) to provide information about enrollment in other trials.²⁸ Steps such as these may reduce the possibility of deception by simply minimizing opportunities to lie. IRBs cannot guard research participants against all risks that result from the participants' own wrongdoing and should not be expected to. Nevertheless, we acknowledge that in extreme circumstances it may still be necessary to limit payment to avoid the threat to study integrity posed by deceitful research participants.

IRBs do not have a responsibility to "level down" to make sure that no participant is subject to undue influence when higher payment would be preferable for the vast majority of prospective participants. Therefore, IRBs must choose between protecting some participants against undue influence, while exposing others to exploitation and difficulties related to recruitment and diversity, or vice versa. On our view, the balance falls in favor of being substantially less concerned about high payment, given not only the likely ratio of participants on either side of the problem. The problems generated by low payment ought to be of much greater concern to IRBs and investigators than they are at present, and indeed, are generally worthy of greater attention than concerns about high payment. To summarize: how should IRBs proceed? First, they should work with investigators to make sure that studies have been designed in a way that maximally reduces the possibility of deception in the first instance. Then, they should acknowledge that their careful review of research will protect the vast majority of potential research participants from undue influence and recognize that they are not required to eliminate the possibility of undue influence completely. Finally, they should account for their ethical responsibility to avoid exploitation, not by completely eliminating the opportunity to participate in low-paying (or non-paying) studies, but by promoting offers of payment that are fair.

What Counts as *Fair* Payment?

It is essential to point out the seismic shift of what we are recommending compared to the status quo of simply playing it safe by avoiding high payment. While a full accounting of what renders an offer of payment for research participation "fair" is beyond the scope of this article, we suggest some preliminary contours here in preparation for future work on this topic.

At a minimum, participants should be reimbursed for any expenses they incur; no one should have to pay out of pocket to contribute to socially valuable research. Additionally, participants should be compensated in the manner that would generally be expected in their locale for assuming similar burdens and time commitments in non-research contexts. This benchmarking principle stands even if particular participants may themselves lack opportunities to undertake such similar burdens and time commitments; the *actual* options available to each individual outside of the research setting are not relevant to determining the

fairness of research compensation. This is because it would be inappropriate to penalize individuals who lack alternatives to generate income by insisting on low payment. Instead, they should be compensated for the burdens they voluntarily undertake by participating in socially valuable research. For example, when homeless people participate in research, there is often concern that they lack alternatives to make money outside the research setting. However, IRBs cannot be responsible for addressing such unfair background conditions, and instead should assess the fairness of payment in light of the burdens undertaken.

Further fairness considerations include assumption of risk and availability of other benefits within the study. Although IRBs cannot consider payment as a benefit to countervail risk, once a study is approved, they can legitimately assess what is fair with respect to the risks participants are assuming. Indeed, risk is often a factor deemed relevant when considering compensation outside the research setting. Additionally, we note that fair compensation could be lower if there is a prospect of direct medical benefit to the individual participant or if collateral, non-financial benefits are made available to participants.²⁹

Conclusion

Many IRBs are understandably concerned — due to uncertainty and one-sided regulatory guidance — about offers of payment to research participants being too high. Once undue influence is properly understood, however, it becomes clear that offers of payment, even those that are quite high, should not generally be cause for ethical concern so long as IRBs are functioning as intended when evaluating a study's risks and benefits. We concede that the risk of undue influence cannot be completely eliminated by the simple fact of IRB-approval, but the regulatory text of the Common Rule calls only for *minimization* of the possibility of undue influence.

Payment conservatism suggests that IRBs may be keeping offers of payment low in an effort to avoid the possibility of undue influence altogether. Although a zero tolerance approach may be superficially laudable, on further examination, keeping payments so low as to fully eliminate the possibility of undue influence is not cost-free. To the contrary, it may result in exploitation of participants, exposure of participants to unjustifiable risk, and unfair distribution of research-related burdens and benefits over the population.

Ultimately, there is a choice: keep offers of payment low to eliminate even the possibility of undue influence and, as a result, risk potentially undercompensating the vast majority of research participants for whom undue influence is not at all a concern, or offer fair payments (which in many instances are likely to be higher than the status quo), which are ethically preferable for the vast majority of research participants, while allowing for the possibility that a few individuals may be unduly influenced. Both approaches entail some ethical risk, but we argue that the risk-benefit ratio of allowing higher payment to participants is the more favorable of the two — particularly should higher payment enable improved recruitment to and completion of socially valuable trials.

IRBs must come to recognize the inverse relationship between undue influence and exploitation and the fact that it may not be possible to completely avoid both in all contexts.

Given the rarity of possible undue influence in IRB-approved studies and the real risk of exploitation when payment is too low, we argue that the default rule for IRBs should be altered: rather than asking whether proposed offers of payment are too high, as IRBs are currently wont to do, they should instead start by asking whether payment is high enough to be *fair*.

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TABLE 1

Research Participants' Susceptibility to Undue Influence

Group	Participation Poses Unreasonable Risk to Individual	Risk Known to Individual	Risk within Purview of IRB	Participation Poses Threat to Scientific Validity/Community Benefit	Prone to Undue Influence
Idiosyncratic Individuals					
1(A)	Yes	Yes	Yes	--	No, because excluded from study population
1(B)	Yes	Yes	No	--	Yes, because might make unreasonable decision to participate
1(C)	Yes	No	No	--	No, because risk not known <i>ex ante</i>
Deceptive Individuals					
2(A)	Yes	Maybe	Yes	No	Yes
2(B)	No	Maybe	Yes	Yes	Yes