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Are Payments to Human Research Subjects Ethically Suspect?

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Abstract

Bioethicists and institutional review boards often worry that paying human subjects too much money for research participation might compromise informed consent by coercing or unduly influencing individuals to enroll in studies against their better judgment. However, empirical research does not support the hypothesis that payments adversely impact judgment and decision-making concerning research participation, and the opposite problem — underpayment — also raises significant ethical concerns, such as exploitation, and under-enrollment. In this article, I argue that our ethical qualms about the negative impact of money on decisions concerning research participation are largely unfounded and reflect more general concerns about the need to avoid repeating abuses of human subjects that occurred in the past. I will also argue that the best way to promote the rights and welfare of human research subjects is to treat them as competent adults who have the capacity to make wise choices involving money. What this argument means in practice is that offering human subjects money for their participation should not be regarded as ethically suspect, absent substantial evidence to the contrary.

Introduction

Bioethicists and institutional review boards (IRBs) often worry that paying human subjects too much money for research participation might compromise informed consent by coercing or unduly influencing individuals to enroll in studies against their better judgment (Grady 2001, 2005; Klitzman 2013, 2015; Largent et al. 2012, Largent and Fernandez Lynch 2017a, 2017b, Lee 2019). The lure of money might cause some people, especially those who are socioeconomically disadvantaged, to take unreasonable risks for financial gain (Macklin 1981; McNeill 1997) or to lie to investigators about important health information to qualify for enrollment (Dresser 2013). However, empirical research does not support the hypothesis that payments adversely impact judgment and decision-making concerning research participation (Gelinas et al. 2019). The opposite problem — underpayment — also raises significant ethical concerns, such as exploitation and under-enrollment, but have received relatively little attention in the bioethics literature or IRB meetings (Shamoo and Resnik 2006; Resnik 2015a; Klitzman 2013, 2015; Largent and Fernandez Lynch 2017a, 2017b).

To the layperson, concerns about overpayment might seem puzzling or nonsensical, since, outside the human research protection milieu, most of the discussion concerning the relationship between labor and financial compensation revolves around problems with paying people too little money rather than too much. The main purpose of minimum wage laws, for example, is to protect workers from exploitation and to ensure that they can earn a living wage (Levin-Waldman 2001). Although people often complain that top corporate executives or professional athletes make too much money, these moral qualms about overpayment have to do with unfairness rather than coercion or undue influence. We do not worry that sports team owners coerce or unduly influence professional athletes into signing contracts by offering them exorbitant amounts of money, although we might think it is unfair that athletes earn much more money than school teachers or nurses.

Why does paying people money for research participation seem ethically suspect to so many commentators and IRB members? In this article, I will argue that our ethical qualms about

the negative impact of money on decisions concerning research participation are largely unfounded and reflect more general concerns about the need to avoid repeating abuses of human subjects that occurred in the past. The legacy of historical abuses casts a long shadow over our thinking about research with human subjects and often leads to policies that are paternalistic and overprotective (Miller and Wertheimer 2007; Resnik 2015b, 2018). I will further argue that the best way to promote the rights and welfare of human research subjects is to treat them as competent adults who have the capacity to make wise choices involving money. What this argument means in practice is that offering human subjects money for their participation should not be regarded as ethically suspect, absent substantial evidence to the contrary.

Payments to Research Participants

Research subjects often receive various types and amounts of financial compensation for their participation. Types of compensation might include reimbursement for expenses (such as travel, hotels, parking, lost wages, and medical bills); payment for time, effort and inconvenience; and bonuses for completing studies (Grady 2005). Subjects might receive money for participating in clinical studies (such as Phase I, II, III or IV clinical trials), epidemiological research (such as long-term cohort or case-control studies), basic biomedical research (such as investigations of physiological mechanisms), and social and behavioral research (such as surveys, interviews or behavioral experiments). Payments range from $25 or less for completing an interview or providing a blood or urine sample to several thousand dollars for participating in a Phase I trial on healthy volunteers (Grady et al. 2005; Largent et al. 2017a). Reasons for offering compensation include reimbursing subjects for their time or expenses; offering subjects incentives for enrolling in studies; providing subjects with a fair wage for their labor; and showing appreciation for subjects' participation (Grady 2005; Largent and Fernandez Lynch 2017a).

While some ethicists (e.g. Chambers 2001) argue that any form of payment for research participation is ethically suspect because people should enroll in studies for altruistic motives, most ethicists agree that some form of remuneration is acceptable (Largent and Fernandez Lynch 2017a). Most of the ethical debate has focused on issues related to paying people too much money rather than paying people at all (Largent and Fernandez Lynch 2017b). Many commentators argue that IRBs should carefully review payments to avoid the potential for coercion or undue influence (Dickert and Grady 2005, Grady 2005, Gelinas et al. 2019). For example, Dickert and Grady (1999) argue that studies that recruit healthy volunteers should pay research subjects roughly the amount of money that is typically earned for unskilled labor involving some risks.

Coercion and Undue Influence

The main concern about offering human subjects too much money is that it might compromise their judgment or decision-making concerning research participation (Gelinas et al. 2019). Regulations and ethical guidelines require that individuals participate in research only if they have freely consented to it (Resnik 2018). Consent is important for respecting the individual's autonomy and promoting his or her welfare (Resnik 2018). To ensure that individuals can make free choices concerning research participation, consent should take place under conditions that minimize the potential for coercion or undue influence (Grady 2001; Department of Homeland Security et al. 2017; Food and Drug Administration 2019).

Some bioethicists and IRB members are concerned that offering money to individuals for research participation could constitute coercion (Macklin 1981; Largent et al. 2012), but this way of thinking about the issue rests on a conceptual mistake. Although research

regulations do not define "coercion," we can view coercion as the use of force, intimidation or threats to compel someone to do something (Wertheimer 1999; Wertheimer and Miller 2008, Gelinas et al. 2019). Monetary offers do not involve the use of force, intimidation or threats. Indeed, since most people regard money as beneficial, proposing to pay someone to do something constitutes an offer to benefit that person, not to harm them (Wertheimer and Miller 2008; Resnik 2015a). If we want to claim that paying individuals for research participation can sometimes compromise their free choice, we should express this idea in terms of concerns about undue influence rather than coercion (Grady 2005; Wertheimer and Miller 2008; Largent et al. 2017a, Gelinas et al. 2019).

Research regulations also do not define "undue influence" (Largent and Fernandez Lynch 2017a). One way of understanding this concept is to view undue influence as a type of influence that compromises or distorts a person's judgment or decision-making so that he or she makes a choice contrary to his or her best interests or values (Resnik 2015a; Largent and Fernandez Lynch 2017b). An offer of money could constitute an undue influence if it compromises someone's judgment or decision-making. For example, in the movie Indecent Proposal, a financially struggling married couple encounter a billionaire at a casino in Las Vegas, Nevada, who offers them one million dollars if the woman will spend a night with him and have sex. If we set aside the issue of whether offering someone money for sex is immoral, we could still say that this proposal was unethical (i.e., "indecent') because the offer of money was so high and the couple's circumstance so dire that they could not resist accepting an offer that was against their best interests or values (Resnik 2015a). The proposal was against their best interests or values because it would undermine marital fidelity.

Some ethicists have argued that monetary offers for research participation might operate like the billionaire's indecent proposal by causing some individuals, especially those who are financially distressed, to make decisions contrary to their best interests or values. McNeill (1999), for example, argues that offers to pay individuals money to participate in research might interfere with their ability to assess risks and benefits. People who are unduly swayed by lure of money are likely to underestimate the risks of research and overestimate their personal benefits. As a result, they are likely to take unreasonable risks to gain financial rewards. Other writers (e.g. Macklin 1981) have adopted a similar view of the potential impact of money on informed consent for research participation. For the sake of brevity, we can refer to this as the unreasonable risks view.

Emanuel (2004, 2005) argues that monetary offers for research participation cannot cause individuals to take unreasonable risks because IRBs are charged with protecting human subjects from these risks. Research regulations and ethical guidelines require that IRBs (or similar oversight committees) determine that risks are reasonable in relation to benefits to the subjects or to the value of the knowledge that might be gained, prior to approving a research proposal (Department of Homeland Security et al. 2017, Resnik 2018). Since ethical guidelines instruct oversight committees to not treat money as a benefit (Largent and Fernandez Lynch 2017a), they should not approve studies that expose subjects to unreasonable risks without any significant benefits other than personal, financial gain. Thus, even if an offer of money might impact an individual's decision to enroll in a study, it cannot constitute undue influence because participating in the research would not expose the individual to unreasonable risks (Emanuel 2004).

There are two problems with Emanuel's critique of the unreasonable risk view. First, oversight committees are not perfect, and they sometimes make mistakes concerning risk/benefit assessments due to lack of information about risks, insufficient time to review proposals, or a failure to appreciate the seriousness of risks (Klitzman 2015, Resnik 2018). When this happens, study participants might be exposed to unreasonable risks. Since individuals still play a key role in safeguarding their own welfare, it is important to ensure

that their decision-making regarding research participation is not unduly influenced by money.

Second, undue influence involves more than making a decision that leads to objectively unreasonable risk exposure (Resnik 2015a). Undue influence can occur when a person is induced to take risks that he or she would otherwise consider to be unreasonable. For example, suppose that a financially distressed college student is normally very risk-averse but that he sees an advertisement for a research study posted on campus that he finds difficult to resist. The study will pay healthy subjects $1,000 to spend an hour in a breathing chamber in which they are exposed to diesel exhaust, followed by a bronchoscopy to take a sample of cells from their bronchial tubes. Subjects will also undergo a clinical examination and provide blood and urine samples. The college student decides to enroll in the study because he needs the money. Even if we assume that an IRB has carefully reviewed the study and determined that the risks are reasonable in relation to the benefits, we could still say that this monetary offer could constitute undue influence if it causes subjects to naturally consider money to be a benefit and therefore take risks that they would otherwise not consider to be reasonable. Since research participants make their own judgments concerning the reasonableness of risks, which may or may not coincide with judgments made by oversight committees, it is possible that offering individuals money to participate in research might induce them to make decisions that are inconsistent with their values (Largent and Fernandez Lynch 2017a).

If we reject Emanuel's argument that monetary offers for research participation cannot cause people to take unreasonable risks, we should turn our focus to empirical questions related to the impact of financial incentives on judgment and decision-making. Does money cause people to underestimate or fail to appreciate the risks of research? Several studies have shown that money influences the decision to enroll in research, but none have found that it distorts risk assessment. For example, Bentley and Thacker (2004) surveyed 317 pharmacy students concerning their willingness to participate in three different types of studies, stratified by risk (low, medium, high) and payments for participation ($350, $800, $1800). They found that payment influenced willingness to participate but not assessment of risk. Likewise, Mantzari et al. (2014) surveyed 275 university faculty and students and found that the amount of money offered influenced the decision to participate in a hypothetical study involving ingestion of an experimental medication but did not affect information processing concerning risks. Cryder et al. (2010) surveyed 1,857 participants who lived in Pittsburgh, PA, or were readers of the New York Times. Participants were randomized to receive information about a hypothetical study. The groups were offered $25, $100 or $1,000 for participation. The study found that the amount of payment affected willingness to participate but did not have a negative impact on risk assessment (Cryder et al. 2010).

While these and other studies (e.g. Chen et al. 2017) indicate that financial incentives affect willingness to participate but do not unduly influence the risk assessment, they have some limitations. First, these studies all involve choices concerning hypothetical scenarios, and it may be the case that the choices people make when faced with real participation options differ from the choices they make when faced with hypothetical ones. Second, the studies did not test for the effect of socioeconomic status (SES) on decision-making, although they did include participants from diverse educational and income levels. It might be the case that SES affects willingness to participate or risk assessment, but further research is needed to ascertain whether this occurs (Klitzman 2005; Largent and Fernandez Lynch 2017a, 2017b).

Deception by Research Subjects

A second way that offering too much money for research participation could constitute an undue influence would be if it encourages some people to deceive investigators about their health history or other important information to qualify for enrollment. Those who choose the path of deception might have a sound grasp of the risks of research yet still act against their values by doing something (e.g., lying or withholding important information) that they would not otherwise do. Money would be a corrupting influence when it affects people this way.

Deception by human subjects is a serious problem, especially in clinical research, because it can place participants at risk and undermine the integrity of the data (Dresser 2013, Resnik and McCaan 2015). Investigators have implemented a variety of measures to deter or detect deception, including using laboratory tests or medical records to verify participant-reported information, and requiring volunteers in Phase I studies to enroll in a registry to allow investigators to check for concurrent or recent enrollment in other studies (Resnik and Koski 2011, Resnik and McCaan 2015).

Anecdotal evidence indicates that deception is highly prevalent among research subjects who participate in studies as a primary source of income, otherwise known as "professional research subjects" (Elliott and Abadie 2008, Abadie 2010). To estimate the prevalence of deception among professional research subjects, Devine et al. (2013) surveyed 99 people who had participated in at least two studies in the past year. The average number of studies among this group was 12, with a range from 2 to 100. Devine et al. (2013) found that a significant percentage of respondents admitted that they had lied to investigators or withheld information to qualify for enrollment in a study. Devine et al. (2013) found that 43% of subjects failed to disclose concurrent enrollment in another study, 28% did not disclose prescription drug use, 25% admitted to exaggerating symptoms, and 14% said they had pretended to have a health problem they did not have. Other studies have found rates of deception by research subjects ranging from 3% to 25% (Lee at al. 2018). Actual rates of deception might be even higher than these estimated rates because these surveys ask respondents to self-report their own misbehavior, and some people might not be willing to admit, even in a confidential survey, that they have engaged in unethical conduct.

While the evidence concerning deception by research subjects is cause for concern, only one study has examined the relationship between deception and financial compensation for study participation. Fernandez Lynch et al. (2018) conducted a survey experiment involving 2,275 participants to determine whether the amount of money offered for study participation encourages individuals to deceive investigators about their eligibility for a study. Participants were randomly assigned to one of seven groups: a control group that received $5 for taking the survey, and six experimental groups that received $5, $10 or $20. Half of the members of the experimental groups were told that receiving an influenza vaccine within the last six months was required for eligibility, and half were told that not receiving the vaccination was required. All participants were asked if they had received an influenza vaccine in the last six months. Since members of the control group had no reason to lie about their vaccination status, their responses to this question were used as a baseline estimate of the vaccination rate for this population (Fernandez Lynch et al. 2018). The reported rate of influenza vaccination for participants who were told that vaccination was required for eligibility (63%) was significantly higher than the control group rate (52%), and the reported rate of vaccination (45%) was significantly lower for those who were told that not being vaccinated was a required for eligibility. Using the control group as a baseline, the investigators estimated that the proportion of participants who lied about their vaccination status ranged from 11% to 23% (Fernandez Lynch et al. 2018). However, there was no significant association between the amount of money offered and divergence the from baseline vaccination rate. This study thus suggests that a high percentage of people are

willing to lie to participate in studies for money but that the amount offered does not increase the risk of deception.

While the study by Fernandez Lynch et al. (2018) provides data that has some relevance to the issue of undue inducement in research, it does not show that paying people too much money for participation increases the risk of deception. While money might be a risk factor for deception, it is far from clear that increasing the amount of money offered will lead to more deception or that decreasing it will lead to less, since a high percentage of people may be willing lie to researchers (or other people) to earn money. For these people, money does not corrupt their judgment or decision-making by causing them to act against their values, because they are already prone to engage in deceptive acts to earn money. In contrast, some people might have such a firm commitment to honesty that they will not lie to earn money, regardless of the level of payment. To determine whether money is a corrupting influence, it might be necessary to conduct additional research that queries people about their values and controls for commitment to honesty.

Underpayment of Research Subjects

Having examined ethical issues related to paying human subjects too much money, we shall now consider issues related to underpayment.

Exploitation

Several writers have argued that paying research subjects too little money could lead to exploitation (Shamoo and Resnik 2006; Resnik 2015; Largent and Fernandez Lynch 2017a, 2017b). According to Wertheimer (1999), an exploitative relationship involves at least one of three conditions: harm, compromised consent (including lack of consent), and unfair distribution of benefits. Some forms of exploitation, such as slavery, involve all three elements, but exploitation can occur even when no harm occurs and the parties' consent, when the *distribution* of benefits is unfair. For example, one might argue that some companies that operate clothing factories in developing nations exploit workers by paying them extremely low wages because the owners of these companies and their stockholders derive far more benefits from these relationships than the laborers. Although research regulations and guidelines do not address exploitation, most ethicists would agree that exploitation is morally wrong and ought to be avoided (Wertheimer 1999).

Underpayment of human subjects could lead to exploitation if research sponsors, institutions and investigators reap most of the financial benefits from a study and the human participants receive very little economic or other benefits in return (Resnik 2003). The risk for exploitation is highest when the study population is socioeconomically disadvantaged and the research is financially lucrative. For example, clinical trials conducted in developing nations and Phase I trials on healthy volunteers have a significant risk of exploiting human subjects (Hawkins and Emanuel 2008). One way to avoid exploitation is to ensure that subjects are adequately compensated for their contributions to the research. In clinical research, access to treatment will usually be sufficient to achieve this goal, except when the subjects are healthy volunteers, in which case ensuring that payment is adequate would be important for avoiding exploitation (Shamoo and Resnik 2006).

Failure to Meet Enrollment Goals

Another risk of underpaying human subjects is that it might prevent a study from meeting its enrollment goals (Largent and Fernandez Lynch 2017b, 2018). Most studies are designed to enroll a specified, minimum number of subjects to ensure that the results will be statistically significant. A study that fails to meet its enrollment goals might yield data and results that are not significant and therefore potentially useless. Research regulations and

guidelines require that the risks to human subjects must be justified in terms of expected benefits to the subjects or society, i.e., the value of knowledge gained (Department of Homeland Security et al. 2017; Resnik 2018). When a study is not likely to meet its enrollment goals, the risks to human subjects will not be justified because the value of the knowledge gained is minimal or nonexistent (Largent and Fernandez Lynch 2017a, 2017b). In addition, the study might waste time, effort, money and other resources that could have been put to better use elsewhere. Most IRBs require investigators to provide them with enrollment data during continuing review of research, so they can ascertain whether studies are meeting their goals. If a study is not meeting its enrollment goals, an IRB might require an investigator to develop a plan for boosting enrollment. As noted earlier, one of the main reasons for providing financial compensation to human subjects is to meet enrollment goals. Investigators sometimes increase the amount of compensation offered to subjects when they are having difficulty meeting their enrollment targets (Resnik 2008).

Access to Beneficial Research

As noted above, some studies compensate research subjects for travel, time off work, and other costs. If these payments are insufficient, low-SES subjects might be unable to afford to participate in studies, such as Phase II or III clinical trials, that offer them medical or other benefits (Largent and Fernandez Lynch 2018). When this happens, the study population might consist mostly of people who can afford to participate without a great deal of compensation, i.e., people with higher SES. One might argue that justice requires researchers to help people of low SES gain access to studies that offer potential benefits. Providing participants with enough compensation helps investigators do this (Largent and Fernandez Lynch 2018). Additionally, underrepresentation of certain demographic groups might limit the generalizability of the findings, which can impact the social benefits of the research.

Justifications for Special Protections from the Influence of Money

Thus far, we have seen that, while empirical evidence suggests that money is often a motivating factor for enrolling in research, it does not support the widely held belief that money frequently unduly influences judgment and decision-making related to participation. We have also seen that underpayment raises some significant ethical concerns, including exploitation and failure to meet enrollment goals. Largent and Fernandez Lynch (2017a, 2017b) have written extensively about issues related to paying people to participate in research. After carefully considering both sides of the debate, they argue that concerns about undue influence have had a disproportionate impact on bioethical thinking about paying research subjects and that we should pay greater attention to the problems related to underpayment (Largent and Fernandez Lynch 2017b).

I agree with Largent and Fernandez Lynch's perspective on issues related to payment, but I would like to probe the topic a bit deeper. Why is it the case that concerns about undue influence have had a disproportionate impact on bioethical thinking about paying research subjects? Why do commentators and IRB members fret about paying healthy volunteers too much money for participating in Phase I trials but have no ethical qualms about increasing the wages for other occupations that carry some risk, such as firefighting, coal mining, or logging? More to the point, why do so many people think that subjects require special protections from the influence of money on judgment and decision-making that we do not usually apply to competent adults outside the research context? I shall now consider three justifications one might offer for special concern about the impact of money on research participation. These justifications emphasize differences between paying money for research participation and paying people money for other types of labor or activity.

Research Participation is Riskier

The first justification is that human subjects require special protections from the influence of money on judgment and decision-making because participating in research is generally riskier than other types of labor or human activity. Research often involves significant risks to subjects, ranging from minor adverse events, such as pain, discomfort, bleeding and minor infections, to serious adverse events, such as hospitalization, disability and death.

There are several problems with this justification. First, the risks of research vary considerably, depending on the nature of the research, the study design, the population, the interventions, and so on (Resnik 2018). Some types of research, such as studies involving only the collection of blood or urine or survey data, pose only minimal risks to participants, while others, such as oncology clinical trials, pose more than minimal risks, while offering research subjects potential benefits, such as treatment for their disease. If risk is the main reason for worrying about the influence of money on research subjects, we should be concerned about paying people to participate in high-risk, non-beneficial studies and have few qualms about paying people to participate in low-risk studies. However, the ethical concerns expressed by commentators and IRB members about the influence of money on research participation seem to apply to both high-risk and low-risk research alike.

Second, even if bioethical qualms about the influence of money pertain only to high-risk research, these qualms would not be good reasons for applying special financial protections to human subjects, since there are many other high-risk occupations that people perform for money, such as firefighting, policing, coal mining, logging, roofing, steel working, race car driving, and boxing, which set no upper limits on payment (Resnik 2018).

Third, most countries have extensive regulations that protect human subjects from risks, including oversight by government agencies and IRBs or similar committees (Emanuel 2004, Resnik 2018). Therefore, there is no need for additional protections that focus specifically on the risks of remuneration. Thus, the idea that research subjects require special protections from the influence of money because of the risks they face does not stand up to scrutiny.

Research Participation has a Greater Potential for Exploitation

A second justification is that human subjects require special protections from the influence of money because participating in research involves a greater potential for exploitation than other types of labor or human activity. Study sponsors, investigators and institutions have financial or professional interests that often run contrary to the interests of subjects. There are also significant disparities in power, knowledge and expertise between sponsors, investigators, institutions and research subjects. Sponsors, investigators and institutions might therefore be prone to use their power, knowledge or expertise to take advantage of subjects in various ways, and they might also use money to entice subjects to participate in studies that are exploitative. History provides ample evidence of the potential for exploitation in research with human subjects. Infamous abuses of human research subjects, such as the Nazi experiments on concentration camp prisoners, the Tuskegee syphilis study, and the US government's secret radiation experiments, have involved exploitation.

There are also problems with this justification. The potential for exploitation also varies considerably in research. While the potential for exploitation is high in clinical trials sponsored by pharmaceutical companies in developing nations (Hawkins and Emanuel 2008), it is very low in survey research sponsored by government agencies. If the potential for exploitation is the main reason for worrying about the influence of money on human subjects, we should be concerned about paying people to participate studies with a high potential for exploitation and have few qualms about paying people to participate in studies with a low potential for exploitation. However, the ethical concerns expressed by

commentators and IRB members about the influence of money on research participation seem to apply to studies with both high and low potential for exploitation.

Second, even if bioethical qualms about the influence of money pertain only to research with a high potential for exploitation, these qualms would not be good reasons for applying special financial protections to research subjects, since there are many other occupations with a high potential of exploitation, such as agricultural work and factory work, which set no upper limits on payment (Resnik 2018).

Third, most countries have extensive regulations that protect human subjects from exploitation (Emanuel 2004, Resnik 2018), and there is no need for additional protections that focus specifically on remuneration. Thus, the idea that subjects require special protections from the influence of money because of the potential for exploitation does not stand up to scrutiny.

Human Subjects Research Must Overcome the Legacy of Past Abuses

A third justification is that human subjects require special protections from the influence of money so the research enterprise can overcome the legacy of past abuses that has eroded the public's trust in the research enterprise. To restore and safeguard the public's trust, researchers should follow rules and norms for protecting the rights and welfare of human subjects that provide more protection than people ordinarily have outside the research context (Miller and Wertheimer 2007; Resnik 2015b, 2018). Miller and Wertheimer (2007) describe these additional protections as paternalistic because they restrict autonomy to safeguard human subjects from harm. For example, the requirement that consent documents contain no language in which subjects waive legal rights is paternalistic because outside the research context we can waive many different types of legal rights (Resnik 2018). IRB oversight of research is paternalistic in that it protects people from taking risks deemed by the IRB to be unreasonable. Outside the research context, people are free to take many kinds of risks without external oversight (Edwards et al. 2004; Resnik 2018). Likewise, one might view policies that give IRBs authority over payments to research subjects as paternalistic insofar as they limit the economic freedom of the subjects to obtain higher amounts.

While this third justification is more convincing that the first two, it also has some problems. First, payments to participants have had little to do with most of the infamous abuses of human subjects, such as the Nazi experiments, the Tuskegee syphilis study, and the secret human radiation experiments (Resnik 2018). Most of these cases involved blatant violations of informed consent, egregious harms to human subjects, exploitation, or all three. While there have been some recent, highly publicized cases of serious harms to participants in Phase I trials (Resnik 201), it is not clear whether excessive payments were the main factor contributing to these harms. Jesse Gelsinger, who died in a Phase I gene therapy experiment at the University of Pennsylvania in 1999, received free treatment but no significant financial compensation for his participation (Resnik 2018). Six healthy volunteers in a Phase I trial of the monoclonal antibody TGN1412 at St. Mark's Hospital on London, UK in 2006 were hospitalized after developing a severe immune response to the drug. Most of the criticism of the trial has focused on the unsafe dosing procedures, not on the payments to the participants (Resnik 2018).

Second, it is not clear that avoiding excessive payments to participants is an essential — or even effective — means of promoting public trust. It might be the case that the public would be more distrustful of the research enterprise if payments to participants are too low, rather than too high, given the contemporary debates about raising the minimum wage and concerns about underpayment of teachers and other occupations. Members of the public might be more concerned about the potential for exploitation arising from underpayment of

human subjects instead of the possibility of undue influence associated with overpayment. However, since, remarkably, there are no published studies pertaining to this issue, research is needed to better understand what impact, if any, payments to human subjects have on the public's trust in the research enterprise.

Conclusion

Many bioethicists and IRB members are concerned that paying human subjects too much money for their participation could unduly influence them to enroll in research against their better judgment or values. However, empirical evidence does not support the widely held view that money often unduly influences research participation decisions, and there are significant ethical problems related to underpayment, such as exploitation and failure to meet study enrollment goals. Nevertheless, worries about undue influence continue to have a disproportionate impact on debates about payments to research subjects. Many bioethicists and IRB members believe that human subjects need special protections from the influence of money that we do not apply to other types of human labor activity. The most plausible justification for this viewpoint is that human subjects need these special protections to overcome the legacy of past abuses and promote the public's trust in the research enterprise. However, I have argued that this justification does not withstand scrutiny because most of the infamous abuses of human subjects have not involved ethically questionable payments to participants, and the public might be more distrustful of the research enterprise if subjects are paid too little money, rather than too much.

None of the foregoing discussion suggests that bioethicists and IRB members should not be concerned about the potential for effects of financial compensation on research subjects' decision-making and behavior. In some situations, remuneration merits special scrutiny because the recipients might not have the capacity to make wise choices involving money, due to their age, mental disability, or socioeconomic circumstances. However, the arguments and evidence explored in this paper imply that bioethicists and IRB members should be skeptical of the idea that competent, adult human subjects need special protections from the influence of money. We live in a society in which competent adults routinely exchange money for goods and services. Most adults have a good understanding of the value of money and what they are willing to do for it. The best way to promote the rights and welfare of adult human research subjects is to treat them as autonomous agents who have the capacity to make wise choices involving money, and not like children or mentally disabled individuals who need to be protected from its influence. What this means, in practice, is that offering human subjects money for their participation should not be regarded as ethically suspect, absent substantial evidence to the contrary.

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