Paying Hypertension Research Subjects

Fair Compensation or Undue Inducement?

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CONTEXT: Cash payments are often used to compensate subjects who participate in research. However, ethicists have argued that these payments might constitute an undue inducement.

OBJECTIVES: To determine whether potential subjects agree with theoretical arguments that a payment could be an undue inducement.

DESIGN/SETTING/PARTICIPANTS: Survey of 350 prospective jurors.

MAIN OUTCOME MEASURES: Belief that a \$500 payment for research participation would impair their own, and others' ability to think carefully about the risks and benefits of a clinical trial.

RESULTS: Two hundred sixty-one jurors (74.6%) believed that a \$500 payment would impair subjects' ability to think carefully about the risks and benefits of research. Ninety-six of 120 (80%) expressed this concern about subjects with a low income (<\$20,000) compared to 92/117 (79%) of those with a middle income (\$20,000 to \$50,000), and 73/113 (65%) with a high income (>\$50,000). In contrast, only 69 (19.7%) of jurors believed that a \$500 payment would influence them. Jurors who believed that this payment would influence them reported lower incomes and less education.

CONCLUSION: Members of the general public share ethical concerns about the influence of payments for research, although they believe that these concerns are more applicable to others than to themselves.

KEY WORDS: research ethics; informed consent; inducement; hypertension.

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Recent scrutiny of the ethics of research has brought concerns about the appropriateness of paying research subjects.¹⁻³ Although paying research subjects may appear to be a fair way to compensate them for their participation, ethicists have argued that some payments might constitute an undue inducement: "an excessive, unwarranted, inappropriate, or improper reward or other overture in order to obtain compliance."⁴ Undue inducements

decrease voluntariness, an essential component of valid consent.^{4,5} Payments may have an even stronger effect among poor subjects, raising the additional concern that paying subjects effectively targets low-income individuals for participation in research.

However, it is not known whether potential subjects agree with theoretical arguments that a payment could be an undue inducement for others, or whether they recognize the effect that inducements may have on themselves. These questions are important because ethical concerns about subject payments are largely theoretical debates over potential problems. Missing from these debates are data describing the views of those people who might receive payments. Therefore, we surveyed public opinion about payments for research participation.

METHODS

Survey respondents were Philadelphia residents who were called for jury duty. In this county, jurors are selected from among those residents who either pay taxes, are registered to vote, or have a current driver's license, which ensures a subject population that is ethnically and economically diverse. This population was chosen because it offers a diverse subject population whose views would not be influenced by a specific institutional setting (e.g., experience with a clinic or providers). Jurors were compensated for their time with a candy bar.

Jurors were given a questionnaire that described a hypothetical 8-week placebo-controlled clinical trial to evaluate the effectiveness of an antihypertensive medication. They were told that patients enrolled in the trial would receive either the study medication or a placebo. Risks of participating included the side effects of the medication, such as dizziness, lightheadedness, fatigue, fainting spells, slow heart rate, swelling in the feet, heart palpitations, and headache. The surveys also described the risks of a myocardial infarction ("heart attack") and "stroke" for those patients who received a placebo. Jurors were told that clinical trial subjects would be paid \$500 for their participation.

Jurors were asked in two dichotomous questions: 1) whether \$500 "would prevent people from thinking carefully about the risks and benefits of this study" and 2) whether this payment would prevent them (the jurors) from thinking carefully about these risks and benefits. The concept of an undue inducement was phrased in this way because extensive pilot testing demonstrated that this language was the most understandable to jurors. Pilot testing included iterative testing of descriptions of an inducement in blocks of 40. Descriptions were modified based on jurors' responses to open-ended questions to

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produce a description that was meaningful to almost all jurors.

Three versions of the questionnaire were randomly distributed, and differed only in the annual income ranges of the clinical trial's potential subjects: <\$20,000, \$20,000 to \$50,000, and >\$50,000. These categories were chosen to correspond to terciles of the juror pool's self-reported income that were defined in pilot testing. Jurors were asked to provide information about their age, sex, ethnicity, education, and whether they had ever participated in research. Income was collected as a 9-category ordinal variable, which could be collapsed into the 3 income categories described in the 3 survey versions.

Nonparametric and χ^2 tests were used to compare the characteristics of jurors receiving the 3 versions, jurors' answers across versions, and to identify juror characteristics that influenced their beliefs about the effect of payment on themselves and on others. Pairwise deletion of missing data was used, and a Bonferroni correction was applied to multiple comparisons. Juror characteristics that were significant in bivariate analysis were evaluated simultaneously in a logistic regression model. Paired comparisons of jurors' assessments of the influence of payment on others and on themselves were performed using the sign test. This analysis was limited to those jurors who reported the same income as the subjects in their survey were described as having.

Three hundred fifty jurors were surveyed to ensure adequate power to analyze those jurors who received a survey version that corresponded to their own self-reported income. We estimated that these incomes would match for approximately 100 jurors, which would provide 90% power to detect a 15% (75% vs 60%) difference in the proportion who thought that a payment would influence others versus themselves (paired comparison, 2-tailed; $\alpha = 0.05$).

This survey was approved by the University of Pennsylvania's Institutional Review Board.

RESULTS

The characteristics of the 350 jurors, and the distribution of the 3 survey versions, are described in Table 1. There were no significant differences among jurors assigned to each of the 3 versions with respect to age, sex, education, income, or ethnicity.

Across all 3 versions, 261 jurors (74.6%) believed that a \$500 payment would prevent potential subjects from thinking carefully about the risks and benefits of the clinical trial. Ninety-six of 120 (80%) expressed this concern in the version that described potential subjects with a low income (<\$20,000) compared to 92/117 (79%) in the middle-income version (\$20,000 to \$50,000), and 73/113 (65%) in the high-income version (>\$50,000). Using a Bonferroni correction, the high versus low ($P = .008$) comparison was significant but the high versus middle was not ($\chi^2 P = .018$). Jurors' opinions about a payment's

Table 1. Juror Characteristics (N = 350)

Characteristic	Value*
Mean age (range) [†]	43 (20 to 77)
Sex, n (%)	
Male	121 (35)
Missing	8 (2)
Income, n (%)	
Low (<\$20,000)	67 (19)
Middle (\$20,000 to \$50,000)	149 (43)
High (>\$50,000)	110 (31)
Missing	24 (7)
Ethnicity, n (%)	
White	150 (43)
All other	194 (55)
Missing	6 (2)
Education, n (%)	
0 to 8 years	5 (1)
Less than high school	25 (7)
Completed high school or GED	103 (30)
Business or trade school	34 (10)
1 to 3 years of college	96 (28)
Completed college	35 (10)
Post-college education	45 (13)
Missing	7 (2)
Previous participation in research, n (%)	80 (23)
Survey version, n (%)	
Low income	120 (34)
Middle income	117 (33)
High income	113 (32)

* Percents may not add to 100 due to rounding.

[†] 8 Surveys had missing values for age.

influence on others were not related to their own income (Rank sum test $P = .34$), education (Rank sum test $P = .38$), sex (χ^2 test $P = .25$), or prior participation in research (χ^2 test $P = .69$).

In contrast, only 69 (19.7%) of jurors believed that a \$500 payment would influence them. Those who believed that this payment would influence them reported lower incomes (median income: \$20,000 to \$29,999 versus \$40,000 to \$49,999; Rank sum test $P < .001$) and less education (median education: high school versus 1 to 3 years of college; Rank sum test $P < .001$). In a logistic regression model in which education and income were treated as continuous variables, both income (odds ratio [OR], 0.58; 95% confidence interval [95% CI], 0.38 to 0.89; $P = .012$) and education (OR, 0.74; 95% CI, 0.59 to 0.90; $P = .004$) remained significant.

Eighty-nine jurors (25.4%) received a survey version that described subjects who had an income that was the same as theirs. They were less likely to believe a \$500 payment would influence them than they were to think that it would influence others with the same income (17 [19%] vs 62 [70%]; sign test $P < .001$). This difference was significant in all 3 juror income categories (sign test: low $P = .012$; middle $P < .001$; high $P = .001$) (Fig. 1). These discordant answers were not related to age, sex, ethnicity, income, or previous participation in research.

FIGURE 1. Jurors' assessments of the influence of payment on others versus on themselves, by the jurors' incomes.

DISCUSSION

Although concern about the ethics of paying subjects to participate in research has produced considerable debate, little is known about how potential research subjects view these issues. This study sheds light on public perceptions of these payments in 3 ways. First, we found that only a small proportion of potential research subjects believe that a payment of \$500 would prevent them from thinking carefully about the risks and benefits of a clinical trial. Potential subjects with high income or high education were even less likely to think that they might be influenced in this way.

Second, we found that members of the public are sensitive to differences in subject income in deciding whether a payment would influence others. This finding is consistent with the opinions of ethicists that a given payment may be an improper inducement on one population but not in others.^{1,2} Third, we found that people believe a payment would influence others more than it would influence them. This difference persists even when the others described have similar incomes, suggesting that potential subjects may underestimate the influence of payments on themselves, or that they overestimate the influence of payments on others.

It is important to note that this juror population may not be representative of the general public. Therefore, the opinions described here should be interpreted cautiously as a measure of the opinions potential subjects are likely to have about research. Nevertheless, these opinions do

represent a novel description of the way that the lay public views issues of payments for research.

More generally, this study suggests that potential subjects have measurable opinions about whether a payment would affect their own and others' ability to think carefully about the risks and benefits of a study. In the absence of a clear standard that can be applied to determine whether a given payment is really an undue inducement, it is reasonable to seek the views of the potential subjects. Therefore, investigators, clinicians, and Institutional Review Boards may wish to consider the opinions of potential subjects in determining whether a level of compensation for a study is an undue inducement.

How these assessments should be interpreted is less clear, as these results demonstrate. On one hand, a direct assessment by potential subjects has intuitive appeal. However, the possibility that these potential subjects underestimate the influence of payments on themselves, compared to others, suggests that potential subjects' opinions about themselves are inappropriately sanguine. Therefore, these results suggest that investigators can gain a more conservative estimate of the likely effects of a payment by asking prospective subjects about its effect on others. Ultimately, though, research is needed to define the effects of payments on decision making about research enrollment, and to define empirically the point at which reasonable compensation becomes an undue inducement.

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