

To Pay or Not to Pay: How Do We Determine Participant Payment for a Clinical Study?

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Prior to initiating a human subject study protocol, issues such as methods, recruitment and retention, budget and logistics must be evaluated and determined. One essential area is deciding whether reimbursement or payment will be made to the research participant. The mechanism for determining participant payment is not established and guidelines and clinical practice are vague at best. The investigators must determine the payment and then the Institutional Review Board (IRB) must approve of the payment. Ripley has previously reviewed the practices and guidelines for paying participants.¹ The guidelines and regulations agree that the payment must not be coercive or provide undue influence, but how can this be determined?

A 2006 survey of IRB members at Virginia Commonwealth University (VCU) showed various opinions about why research participants should be paid as well as marked variations in the quantity and type of payment appropriate for different types of studies.¹ Although several studies have looked at the impact of payment on the participant,^{2,3,4,5,6,7,8,9,10,11} no prior study has evaluated why and how investigators determine what payment should be offered for research participation. The study discussed in this article surveyed investigator and non-investigator faculty members at Virginia Commonwealth University to explore the attitudes, practices and purposes of compensating research participants. A comparison group of non-investigator faculty members was used to evaluate differences between faculty members actively involved in clinical research and a peer group that was not involved.

Methods

Following IRB approval of this study at VCU, a web-based survey was distributed to faculty members of the University. An email invitation to participate was sent to each faculty member. Two follow-up emails were sent to non-responders at weekly intervals again requesting participation. All responses were recorded anonymously.

Respondents were classified as investigator (someone who had conducted or helped conduct clinical research in the past 5 years) or non-investigator. Descriptive statistics were used to evaluate the responses and, where appropriate, mean \pm SD results are given. Participants responded to the importance of various reasons for payment on a five-point scale from not important to extremely important. Responses were dichotomized to important (extremely important, very important, or important) or not important (somewhat important or not important). The dichotomized data was then compared using Pearson's Chi Square for significant responses. A probability of $p < 0.05$ was considered significant as to whether respondents rated the reason for payment as either 'important' or 'not important.' A $p > 0.05$ was considered discordant, indicating that a similar number of respondents considered it an 'important' reason and a 'non important' reason. The results of questions regarding factors in determining payment were similarly analyzed. A $p < 0.05$ was considered significant. Investigator responses vs. non-investigator responses were compared for key questions. Significant differences are reported with Pearson's Chi Square X^2 and p value.

Results

A total of 378 individuals responded to the survey. Of these, 210 respondents were classified as investigators and 168 respondents were classified as non-investigators. Table 1 shows respondent demographics.

Significantly more investigators ($n = 96, 46\%$), compared to non-investigators ($n = 46, 27\%$), responded that they had personally participated as a subject in a research study (Pearson's Chi Square $X^2_1 13.375 p=0.003$). For the investigators, 53 of the 96 (55%) had received payment and 36 of the 53 (68%) thought that the payment was an important determinant of their participation.

VCU has a policy document that discusses compensation of human subjects for participation in research, available at http://www.research.vcu.edu/irb/wpp/flash/wpp_guide.htm#XVII-2.htm. However, 135 (64%) investigators were not sure if VCU had written policies regarding payment and another 20 (10%) said there were no policies. Not surprisingly, 119 (71%) of non-investigators were not sure if VCU had written policies.

Respondents rated the importance of payment for each of the four primary indications for payment: reimbursement for study-related expenses; inconvenience; appreciation for their participation; and as an incentive to encourage the participation. Tables 2 and 3 showing the investigator and non-investigator responses are summarized in Table 6. Investigators and non-investigators agreed on indications for payment. Both responded that payment for reimbursement, compensation for inconvenience, and payment as an incentive were important. Both groups were discordant on the importance of appreciation.

Table 1. Respondent Demographics

	Investigators	Non-Investigators
Number (N)	210	168
Gender	49.4% Male	49.5% Male
Age in Years	46.3±9.4	48.2±10.7
Academic Rank	4% Clinical instructors 35% Assistant professors 34% Associate professors 26% Professor	7% Clinical instructors 38% Assistant professors 30% Associate professors 21% Professor
Types of Research	Survey, social behavioral, drug therapy, IND, placebo, medical testing	n.a.

Table 2. Reasons for Payment: Investigators

Pearson's Chi Square Comparison of Important vs. Not Important for each factor

Reason for Payment		N	Proportion	95% CI	Pearson's Chi Square X^2_{DF1}	p-value
Reimbursement	Important	181	.86	.81-.90	110.02	<0.0001
	Not	27	.12	.09-.18		

	Important					
Inconvenience	Important	169	.80	.75-.85	78.02	< 0.0001
	Not Important	37	.18	.13-.22		
Appreciation	Important	115	.55	.48-.61	1.90	0.1675
	Not Important	94	.45	.38-.52		
Incentive	Important	134	.64	.57-.70	16.02	< 0.0001
	Not Important	73	.35	.29-.41		

Table 3. Reasons for Payment: Non-investigators

Pearson's Chi Square Comparison of Important vs. Not Important for each factor

Reason for Payment		n	Proportion	95% CI	Pearson's Chi Square X^2_{DF1}	p-value
Reimbursement	Important	148	.88	.82-.92	97.52	< 0.0001
	Not Important	17	.10	.06-.16		
Inconvenience	Important	138	.82	.76-.87	69.43	< 0.0001
	Not Important	28	.17	.11-.23		
Appreciation	Important	97	.57	.49-.64	2.88	0.0896
	Not Important	71	.42	.35-.50		
Incentive	Important	118	.70	.62-.77	27.52	< 0.0001
	Not Important	48	.29	.22-.36		

Respondents were then asked to rate the importance of nine factors in determining the amount for the payment: risk, time required, inconvenience, demographics of the study population, income of the participants, funding source, budget, number needed to recruit; and anticipated difficulty in recruiting. Both groups agreed on the importance of the majority of factors in determining payment. When asked to rank the reasons for paying participants, both groups ranked risk as the most important, followed by time and inconvenience. Interestingly, 46.7% of investigators ranked risk most important, while 71.4% of non-investigators ranked this factor first (Pearson's Chi Square X^2_{14} 36.026 $p=0.001$).

Investigators rated factors of direct interest to the study participant – risk, time requirements, and inconvenience – as important in determining payment. In contrast, they

rated income of the population as not important and demographics of the population as neutral. Investigators also rated factors related to the study budget and anticipated difficulty recruiting as important. They rated the funding source as not important and the number needed to recruit as neutral.

Non-investigators rated risk, time required, inconvenience, and demographics of the study population as important, but the income of the population as not important. They rated factors related to the study budget, number needed to recruit, and anticipated difficulty recruiting as important. They rated funding source as neutral. Tables 4 and 5 show these findings, which are summarized in Table 7.

Table 4. Factors in Determining Payment: Investigators

Pearson's Chi Square Analysis for each factor

Factor in determining payment		n	Proportion	95% CI	Pearson's Chi Square X_1^2	p-value
Risk	Important	178	.85	.79-.89	101.50	< 0.0001
	Not Important	23	.11	.07-.16		
Time Required	Important	192	.91	.87-.95	144.17	< 0.0001
	Not Important	10	.05	.03-.09		
Inconvenience	Important	186	.89	.84-.92	124.97	< 0.0001
	Not Important	15	.07	.04-.11		
Demographics of study population	Important	101	.48	.41-.55	.30	0.5809
	Not Important	101	.48	.41-.55		
Income of population	Important	70	.33	.27-.40	23.33	< 0.0001
	Not Important	132	.63	.56-.69		
Funding Source	Important	89	.42	.36-.49	4.88	0.0272
	Not Important	113	.54	.47-.60		
Budget	Important	127	.60	.54-.67	9.22	0.0024
	Not Important	72	.34	.28-.41		
N needed to	Important	114	.54	.48-.61	1.54	0.2142

recruit	Not Important	88	.42	.35-.49		
Anticipated Difficulty Recruiting	Important	148	.70	.64-.76	35.22	< 0.0001
	Not Important	54	.26	.20-.32		

Table 5. Factors in Determining Payment: Non-investigators

Pearson's Chi Square Analysis for each factor

Factor in determining payment		n	Proportion	95% CI	Pearson's Chi Square X_1^2	p-value
Risk	Important	155	.92	.87-.95	120.02	< 0.0001
	Not Important	11	.07	.04-.11		
Time required	Important	160	.95	.91-.98	137.52	< 0.0001
	Not Important	6	.04	.02-.08		
Inconvenience	Important	156	.93	.88-.96	123.43	< 0.0001
	Not Important	10	.06	.03-.11		
Demographics of study population	Important	103	.61	.54-.68	8.60	0.0034
	Not Important	62	.37	.30-.44		
Income of population	Important	57	.40	.27-.41	17.36	< 0.0001
	Not Important	108	.64	.57-.71		
Funding Source	Important	85	.51	.43-.58	0.024	0.8774
	Not Important	81	.48	.41-.56		
Budget	Important	101	.60	.53-.67	6.88	0.008

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	Not Important	64	.38	.31-.46		
N needed to recruit	Important	104	.62	.54-.69	9.52	0.0020
	Not Important	62	.37	.30-.44		
Anticipated Difficulty Recruiting	Important	134	.80	.73-.85	59.52	< 0.0001
	Not Important	29	.17	.24-.54		

Using a bonus for study completion was always or sometimes acceptable to 71 (34%) of investigators, compared to 89 (53%) of the non-investigators (Pearson's Chi Square X^2_5 21.856 $p=0.0006$). Non-investigators also held that larger payments to populations with rare conditions or diseases was more acceptable [always-24 (14%), frequently-30 (18%), sometimes-84 (50%), rarely-14 (8%), never-11 (7%)] than investigators [always-6 (3%), frequently-26 (12%), sometimes-82 (39%), rarely-46 (22%), never-45 (21%)] (Pearson's Chi Square X^2_5 44.705 $p<0.0001$).

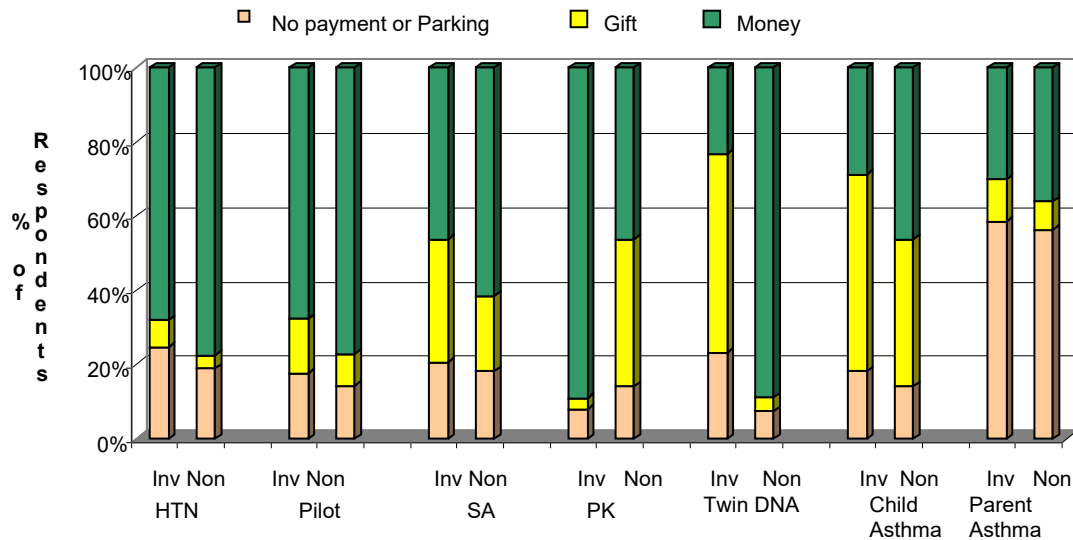
The survey contained five short case studies. Each case included the type of study (8-week placebo-controlled hypertension trial, a pilot exercise study, a survey of substance abusers, a healthy volunteer pharmacokinetic study, or pediatric asthma medication study), duration, target population, and a brief description of the study. The cases varied by type of study, population being studied, risk of study and duration. After reading the case scenario, the respondent was asked to decide what payment was appropriate. The payment options were: no payment or only payment for parking, a gift certificate, or money. (Respondents were given the option of money either at completion or prorated. Because many respondents would give money that was both prorated and at completion, it was not possible to determine with certainty which was intended and therefore these responses were counted simply as money payment.) Figure 1 shows the recommended types of payments for the five cases for both parents and children. (For the pediatric asthma trial, recommendations for both the parent and the child are shown.)

Type of payment varied by case study and by respondent-type. For the pharmacokinetic healthy volunteer study, 89% of investigators and 85% of non-investigators stated that money was an appropriate form of payment. For the hypertension trial, 68% of investigators and 77% of non-investigators would provide money as payment. On the other hand, for the substance abuse survey, only 46% of investigators would pay money, 33% would give a gift certificate, and 21% chose no payment or payment for parking only, whereas 62% of non-investigators would pay money, 20% would give a gift certificate, and 18% chose no payment or payment for parking only. For the normal volunteer exercise study, 67% of investigators and 77% of non-investigators stated that money was the best form of payment.

For the pediatric asthma study, investigators most-commonly recommended a gift certificate or movie tickets for the child (53%). Non-investigators most-commonly recommended money (46%), with a gift certificate as the second choice (39%) (Pearson's Chi Square X^2_4 , $p=0.0023$). For the parents, both investigators (59%) and non-investigators (56%) most-commonly recommended no payment or payment for parking

only. The amount of payment for both the child and the parents varied from no payment to several hundred dollars.

Figure 1. Types of Payment Recommended*



* Inv - Investigator, Non - Non Investigator, HTN - hypertension placebo controlled trial, Pilot - exercise pilot study, SA Survey - one hour survey of substance abuse, PK - normal volunteer pharmacokinetic study, Asthma - pediatric asthma medication study (payments for both child and parent).

Discussion

The ethics of paying research participants is greatly debated. Federal regulations offer little detail regarding payment, only the vague rule that it should not be coercive or unduly influential. The interpretation of this rule varies. Dickert and Grady¹² showed institutional differences by surveying 32 research organizations (9 academic medical centers, 7 pharmaceutical companies, 8 contract research organizations, and 9 independent ethical review committees). They found that standards of payment varied widely. 58% of organizations described payment as an incentive. Most organizations reported that subjects were paid for their time (87%), inconvenience (84%), or travel (68%). Thirty-two percent reported that subjects were paid for risk. Independent ethical review committees were more likely than affiliated committees to report that risk level affected payment decisions. Only three organizations had explicit restrictions on paying patient participants. Most of the organizations required the informed consent form to include the amount of payment participants can expect and 84% required the terms of the compensation.

Differences in actual payment were shown by Grady, Dickert, Jawetz, Gensler and Emanuel.¹³ They reviewed 467 protocols and consent forms offering payment to research subjects that had been approved by one of 11 ethical review committees across the United States. Money was offered in a wide variety of study types. Dollar amounts varied widely with unexplained variation in amounts across similar studies or across different sites participating in the same multisite study, and for similar procedures across studies, sometimes even within one site.

By regulation, IRB panels consist of members with a variety of backgrounds, including scientists from multiple fields and nonscientists. This diversity is intended to offer a spectrum of viewpoints and the ability to analyze a variety of protocols. Similar to the ethical debate in the literature, prior work at VCU has shown that IRB members agreed in some areas and disagreed in others about paying study participants.² IRB members tended to agree about the importance of certain reasons or factors for payment. There was agreement that research participants should be reimbursed for study-related expenses and inconvenience, and for factors that affect the participants, such as risk, inconvenience and time requirements. There was no agreement regarding the importance of study-related factors that may affect the success of the study, such as number of participants needed to recruit or anticipated difficulty recruiting. Funding source was considered "not important," but there were differing opinions about the importance of the budget. Interestingly, there was agreement that the income of the subject population was not important.

IRB member recommendations for payment for different types of studies varied from no payment to several hundred dollars. Not only was there variation in payment between studies but for the same study the recommendation for payment varied from no payment to several hundred dollars.²

Given this variability in IRB member opinions, the researchers questioned how investigators determine appropriate payment. This article is the result of that survey. The non-investigator group was determined by their response that in the past 5 years they had not conducted or helped to conduct clinical research projects (medical or behavioral research studies involving human participants). As individuals not conducting clinical research, their views on research payment served as a convenient comparison to the views of self-identified investigators. However, neither group can be generalized to the general public.

This is the first study to evaluate investigator and non-investigator attitudes about paying research participants at an academic medical center. Investigators and non-investigators generally agreed on the reasons for payment. In particular, they agreed that reimbursement of expenses was the most important reason.

Interestingly, there was disagreement between the groups about the importance of some factors that can be used to determine payment. For example, non-investigators stated that participant demographics were important and investigators stated they were not important.

Comparing the reasons for payment by IRB members obtained in our previous study with the opinions of investigators and non-investigators in this current study shows that there is agreement that reimbursement for expenses and compensation for inconvenience are important reasons for payment among all groups. IRB members were evenly divided as to whether providing an incentive for participation is an adequate reason to provide payment, while investigators and non-investigators responded that this was an important reason for payment. Likewise, there was agreement that payment for risk, time and inconvenience is important. Only the IRB members collectively responded that income of the participant should be considered when determining payment. IRB members also were divided on the importance of study-related factors such as budget and anticipated difficulty in recruiting. Tables 6 and 7 summarize the opinions of the investigators and non-investigators from this study and also show the VCU IRB member opinions obtained in a similar but separate study.

Table 6. Reasons for Paying Participants

Reason	Investigators	Non-Investigators	IRB Members²
Reimbursement for expenses	Important	Important	Important
Compensation for Inconvenience	Important	Important	Important
Incentive for enrollment	Important	Important	Discordant*
Appreciation for participation	Discordant*	Discordant*	Discordant*

* "Discordant" means that a similar number of respondents considered it an 'important' reason and a 'non important' reason.

Table 7. Factors for Determining Payment

	Investigator	Non-Investigator	IRB Members²
Participant Factors			
Risk	Important	Important	Important
Time	Important	Important	Important
Inconvenience	Important	Important	Important
Income	Discordant*	Discordant*	Important
Demographics	Not Important	Important	Discordant*
Study Related Factors			
Budget	Important	Important	Discordant*
Anticipated difficulty recruiting	Important	Important	Discordant*
Funding Source	Discordant*	Not Important	Not Important
N needed to recruit	Not Important	Important	Discordant*

* "Discordant" means that a similar number of respondents considered it an 'important' factor and a 'non-important' factor.

Limitations

Neither the current study nor the previous study of IRB members investigated the reasoning behind these choices. Potential reasons for differences may include concern about pressuring individuals to participate and unfair levels of payment (e.g., if reimbursing time do you vary payment depending on the participant's usual hourly wage? Or, do you consider geographic differences in cost of living when determining payment for a multicenter trial?)

The cases show that different studies call for different amounts of participant payment. However, even within the same study, there was variation among respondent recommendations in both the kind and quantity of payment. For example, some respondents from both the investigator and non-investigator groups would not pay participants in any of the cases considered. Although this study did not allow an analysis of the rationale behind the choices in payment type, a nationwide study by the authors is exploring IRB members' and investigators' reasoning about risks, inconveniences, difficulty recruiting, and other factors involved in determining research payment.

Conclusion

As in the previous study of IRB members, this study demonstrates that views about subject payment vary among individual faculty members. However, as of yet, there is no evidence that either high or low payments have compromised the welfare of human research participants. OHRP and FDA guidelines requiring that payment not be coercive or unduly influential are clearly too vague to create any consistency. Further research is needed to help understand why we pay participants and the impact of these payments on both the participants and the study.

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