Published in final edited form as:
J Law Med Ethics. 2008 ; 36(2): 413–418. doi:10.1111/j.1748-720X.2008.00285.x.

Currents in Contemporary Ethics:

Ethical and Practical Concerns in Developing Payment Policies for Research Involving Children and Adolescents

Ana S. Iltis, **Hisako Matsuo**, and **Shannon R. DeVader**

An Institute of Medicine (IOM) panel charged with reviewing the system for overseeing research involving children concluded in 2004 that Institutional Review Boards (IRBs), institutions engaged in research, and study sponsors should "adopt explicit written policies on acceptable and unacceptable types and amounts of payments related to [children's] research participation."[1] We previously reported data on practices and policies in the U.S. regarding payments to children who participate in research and their parents.[2] Here, we report additional results from our study and identify some of the decisions that must be made in developing payment plans and on which payment policies will be expected to offer guidance. We conclude that further conceptual analysis and empirical research are necessary before IRBs, institutions, and sponsors can develop specific rules on numerous aspects of payment. Nevertheless, payment policies that promote the ethical treatment of children in research and their parents can be developed. We propose a structure for such policies.

At the time the 2004 IOM report on pediatric research was issued, very little was known about practices and policies related to payments to either children who participate in research or to their parents. We conducted a study to document such policies and practices in research that enrolled children from birth through adolescence.[3] We developed a four-page survey that included open- and closed-ended questions and contacted the first or corresponding author of studies that met the following criteria:

1. results were published in 2003 in *Pediatrics, Archives of Pediatrics and Adolescent Medicine, Journal of the American Medical Association*, or *New England Journal of Medicine*; (2) studies were conducted solely in the United States; (3) the first author was listed at an institution in the United States; (4) the study involved some prospective data collection…and (5) some research was conducted with children.[4]

Of the 175 eligible participants who received surveys, 81 completed the survey, for a response rate of 46.3 percent. Approximately one-half (51.9 percent, n=42) paid subjects, and the others (48.1 percent, n=39) did not. Cash (42.9 percent, n=18) and gift certificates (39.1 percent, n=16) were the most common forms of payment. For all 81 returned surveys, we used institutional Web sites and made direct contact with IRB offices when necessary to determine whether the institution had a policy that addressed payments to either children who participate in research or to their parents and whether those policies were in place at the time the studies that led to the publications in question were conducted. In the fall of 2005, 43 institutions (53.1 percent) had such policies. Some policies were more specific than others, and some included requirements that conflicted with guidelines in other policies. For example, three policies said that it was acceptable to correlate payments with risk, six said this was unacceptable, and the others did not address the issue.[5] Of those 43 institutions that had policies in fall of 2005, only six (14 percent) had a policy in place when the published study was conducted.

Our survey asked a number of questions about why investigators paid particular amounts of money for study participation or why they did not pay subjects, as well as their beliefs about the relationship between payment, recruitment, and retention. Only 4.8 percent (n=2) of

investigators who reported paying subjects stated that study risks played a role in determining the amount of payment offered while 61.5 percent (n=24) of those who did not pay stated that the fact that a study involved only minimal risk influenced the decision not to pay subjects. We have further investigated the relationship between risks and payment amount. We used the Kruskal-Wallis test, a non-parametric approach, to compare differences in the amount of payment offered among different risk factors, namely the following: the amount of physical risk, the amount of psychological/emotional risk, the amount of social risk, the amount of physical discomfort, the amount of psychological/emotional discomfort, and the funding source. The non-parametric test is used when the value of the dependent variable does not have a normal distribution, when the dependent variable is highly skewed, or when the sample size is small. Results are reported in Table 1. There were significant differences among the categories in the amount of physical risk (x^2=10.444, df=3, p<0.05), the amount of social risk (x^2=7.173, df=2, p<0.05), the amount of physical discomfort (x^2=7.811, df=2, p<0.05), and the amount of psychological/emotional discomfort (x^2=6.561, df=2, p<0.05). There were no statistically significant findings in the amount of psychological risk or the funding type. No physical risk received the highest mean of ranking (35.33), followed by more than a minor increase over minimal risk (28), minor increase over minimal risk (24.29), and minimal risk (16.19). The pattern for other variables appeared to be the same. In other words, if investigators offered any payment, they offered a relatively large sum for studies that they stated posed no risk. (All research that involves human subjects carries some risk, though perhaps that risk is minimal and some think negligible.) When a study involved a risk and the study paid, then, as the risk level increased, the payment also increased. This does not show that investigators paid more because of the increased risk, but it does raise questions about whether risk may have influenced the amount of payment directly or indirectly and about what level and types of payments are acceptable in higher risk research. Although there was no statistically significant difference in payment amount among studies with different funding sources, when investigators received funding from industry, federal government, or private foundations, they appeared to have paid more than when they were funded by local/state government or by their own institutions.

Because our previous study found that investigators reported that the length of study and time required for study were the two major factors influencing the amount of payment offered,[6] we investigated further the relationship between time and payment. As reported in Table 2, the Pearson product moment correlational analysis found a statistically significant positive correlation between the total amount of payment and the number of visits required (r=0.546, p<0.001). Although the correlation between the total amount of payment and the average length of visit was positive (r=0.165), it was not statistically significant.

Payment Plans

These results together with our previous publication and other work on pediatric research highlight a number of decisions that must be made when developing and evaluating payment plans. These are matters on which payment policies will be expected to offer guidance. We discuss issues pertinent to the development and evaluation of payment plans and identify gaps in our current knowledge that render development of specific rules on many of these matters premature.

1. Will subjects and/or parents be paid? If so, who will be paid, for what will they be paid, and how will payment be calculated?

A number of factors might be considered as bases for paying and for increasing or decreasing payments, including risks, pain, discomfort, time, and inconvenience. To provide specific guidance on which factors may be used and how requires an understanding of the legitimate purpose(s) of payments and an evaluation of whether payment should ever be required. To give

specific guidance on the appropriate relationship between a study's risk and payment of subjects and/or their parents, we must first determine whether it ever is appropriate to pay for the assumption of risk, and, if so, when – an issue that remains the subject of debate in the research ethics literature.[7] If payment will be offered for discomfort, pain, or inconvenience, how will payment be calculated?

Will subjects and/or their parents be compensated for their time and, if so, how will compensation be calculated? If it is to be calculated as a wage, as some have recommended,[8] will all subjects/parents be paid the same wage or will the wage be based on what an individual could earn in a given amount of time? To provide specific guidance, we must know not only what are the legitimate purposes of payments, but we also need additional empirical research, e.g., to determine what level and type of payment different groups recognize as reasonable compensation for their time and whether certain payment offers have negative effects that should be avoided.

Will subjects or their parents be paid for their time, pain, inconvenience, or discomfort when a study involves more than minimal risk? Some might worry that such payments in a study that involves more than minimal risk could lead people to assume risks they otherwise would not assume, lead people to give false information in order to be eligible for a study, or result in the over-recruitment of the less well-off. We have limited knowledge of how money influences research participation decisions in general, how it influences parental decisions about their children's participation, and how it affects children of different ages,[9] which makes it difficult to formulate specific rules about what is required for the ethical conduct of research.

Will payments be divided among parents and children, or will one party receive full payment? Specific rules should be informed by an account of the legitimate purpose(s) of payments, how payments affect research participation decisions, and whether any sub-group needs additional protections. For example, if the purpose of payments is to compensate people for their discomfort and time, then it seems that children, who experience discomfort in research and sacrifice their time, and their parents, who sacrifice their time when their children participate in research, should be compensated.

Major guidance documents in the U.S., Canada, and the United Kingdom that address payment in research involving children hold that payments meant to reimburse subjects/parents for expenses are permissible.[10] Insofar as reimbursements may prevent unfair subject selection by enabling people who otherwise could not afford to participate in research to enroll,[11] we must ask whether reimbursement ever should be required.

2. Will subjects/parents be paid equally?

If payments other than reimbursements are permitted, will subjects involved in comparable studies (e.g., studies with comparable time commitments, risks, potential benefits, discomforts) at the same location be paid comparably? Will subjects enrolled in the same study at different sites be paid comparably? Will persons involved in the same study at the same site be paid equally? To formulate specific rules on whether equal payments should be required and, if so, whether unequal payments might be acceptable or sometimes required to avoid targeting the less well-off, requires additional conceptual analysis of the purpose of payments and empirical research on the effects of payments.

3. When and how will payment information be disclosed?

The AAP Committee on Drugs stated that "[i]f remuneration is to be provided to the child, it is best if it is not discussed before the study's completion. This will help assure that the remuneration is not part of the reasons that a child volunteered or is volunteered for a

study."[12] Others disagree.[13] To provide specific guidance on when and how payment information should be disclosed, we must understand the legitimate purposes of payments and how different people, including parents and children of different ages, respond to advertisements and information about payments. For example, does knowledge of payment affect risk perception? Does awareness of payment help to mitigate the therapeutic misconception?[14] Does disclosure of payment or awareness that payment might be made but that such information will be shared after the decision to participate is made, put children who refuse to participate at risk for abuse?

4. What forms of payment, e.g., cash, toys, gift cards, will be used?

Rules on what kinds of payments are appropriate should be informed by the purpose of payments, who is to be paid, and for what are they to be paid. Answers to a number of relevant empirical questions should shape such rules as well. How do different forms of payment affect research participation decisions? Are some forms more likely than others to lead to undue influence? Are some offers more effective than others in avoiding unfair subject selection? Are some less likely than others to put children who refuse to participate at risk for abuse?

5. What payment schedule will be adopted?

It is widely held that longitudinal studies should pro-rate payment to avoid situations in which subjects/parents feel compelled to remain in a study to receive payment. Investigators and IRBs must determine if subjects/parents will be paid and, if so, whether payments will be pro-rated, whether payments will be increased over time, and whether they will offer completion bonuses. A special concern for children is the possibility that a parent will insist that a child remain in a study to receive full payment. Payment schedules that minimize this risk might be developed. Sound, specific rules cannot be crafted in the absence of knowledge about the purpose of payments, the permissibility of paying for the assumption of risk, and how payments affect voluntariness.

Payment policies will be expected to guide decision making on a wide range of issues, including those noted above. Yet it is not possible to develop sound, specific rules given the limited conceptual understanding of the purpose payments and the current empirical evidence we have. A policy that institutes a range of rules on payments, for example, specifying an amount that may be paid to children or parents per procedure, or how much children/parents should be paid per hour of research time, would not necessarily accomplish the goal of improving the protection of children who participate in research. Such a policy would presume knowledge and understanding we lack, making it uninformed and perhaps counterproductive. It also would be a blunt instrument potentially unable to account for special circumstances that might require us to treat somewhat similar situations differently. Over time, with the benefit of additional evidence, some specific guidelines may emerge. Even as our understanding and knowledge of issues related to payment practices evolve, to translate new information into ethical payment practices requires that data be interpreted in light of the principles of the ethical conduct of research. Payment policies that provide guidelines based on the principles for the ethical conduct of research but avoid the imposition of uninformed rules can and should be developed at this time.

A policy that institutes a range of rules on payments, for example, specifying an amount that may be paid to children or parents per procedure, or how much children/parents should be paid per hour of research time, would not necessarily accomplish the goal of improving the protection of children who participate in research. Such a policy would presume knowledge and understanding we lack, making it uninformed and perhaps counterproductive.

Payment Policies

We present a framework for developing payment policies concerning studies involving children or adolescents, as called for in the IOM's 2004 report. The proposed framework aims to promote the ethical conduct of research and improve the oversight of research involving children while respecting the circumstance that we lack much of the knowledge necessary to formulate and apply specific rules appropriately. An IRB or institution could develop a payment policy that describes seven principles of the ethical conduct of human research,[15] and explain some of the ways in which the principles might inform a payment plan. Investigators would then develop plans in light of the principles delineated in the policy and could be required to articulate how their payment plans meet each principle. IRBs would evaluate proposed payment plans based on those principles. Investigators, sponsors, and IRBs would have to rely on the limited data available on payment, their judgment, experience, and knowledge of local communities to apply the principles to specific cases. Like other aspects of research oversight, as new information becomes available, e.g., on the effect of payments on understanding risks, it should be taken into account and protocols revised as necessary.

> Sponsors, investigators, and IRBs should consider whether the ways in which payment information is disclosed might shape subjects' understanding and appreciation of information or in some other way affect the ability to give free and voluntary consent, permission, or assent.

1. Social or Scientific Value

The effect of payment practices on the social or scientific value of a study should be considered. For example, if a plan makes it difficult to recruit and retain an appropriately representative population, then the study will have less value than if the results were derived from a representative population.

2. Scientific Validity

The possibility that some payment practices might positively or negatively affect the scientific validity of a study should be considered. For example, if a payment plan makes it difficult to recruit and retain a sufficient number of subjects, then it will not be possible to gather sufficient data to draw generalizeable conclusions.

3. Fair Subject Selection

Payment plans should be designed to avoid targeting or under- or over-recruiting specific populations. It is reasonable to ask if an offer of payment is too low to attract anyone but the least well-off. If subjects will not be reimbursed for costs associated with research participation, then we should ask whether this will unfairly deny the less well-off access to study participation.[16]

4. Favorable Risk-Benefit Ratio

Evaluating the relationship between the risk-benefit ratio of a study and payment plans depends on how we understand the relationship between risks and payments, including whether it is permissible to pay subjects for assuming risks and whether payments may be considered a benefit of research participation. The former has not been defended with regard to children, and the latter is rejected by the FDA and NIH.[17] Other considerations include the obligation to ensure that payment plans minimize risks to potential and enrolled subjects. For example, if subjects/parents will not be reimbursed even for basic costs associated with research participation, then they may experience a financial loss. This is of special concern when subjects/parents and investigators incorrectly assume insurance will cover certain research related costs. Subjects/parents may then find themselves with substantial bills, which could be

considered a risk of participation; thus, financial risks, among others, are to be considered in determining whether study risks are proportionate to the anticipated benefits, and to be disclosed to potential subjects.

5. Independent Review

Payment plans must be evaluated and approved by the independent party responsible for reviewing research, such as an IRB.

6. Informed Consent

To give free and voluntary informed consent, permission for a child to participate in research, or assent, payment and cost information must be disclosed, and changes in such information should be reported during the course of the study. One of the concerns often raised about payments in research is the possibility that payment will unduly influence subjects or their parents, although in the absence of empirical information, we do not know when this influence occurs. An additional concern is whether payment may alter risk perception or lead individuals to discount risk information excessively. Sponsors, investigators, and IRBs should consider whether the ways in which payment information is disclosed might shape subjects' understanding and appreciation of information or in some other way affect the ability to give free and voluntary consent, permission, or assent. It also is reasonable to ask whether payment may help to decrease the therapeutic misconception or whether a particular way of disclosing payment information may have this effect.[18] If subjects will incur costs, particularly costs for medical procedures, as a result of research participation, then we should consider whether this might increase the therapeutic misconception.[19]

7. Respect for Persons

Respect for persons requires a number of practices to ensure that potential and actual subjects are treated appropriately throughout the entire research process, including that they be allowed to withdraw from a study and be provided with new information as it becomes available. Payment practices may demonstrate respect for persons by, for example, pro-rating payments to avoid situations in which parents/children do not withdraw to avoid losing pay they believe they have earned through their participation thus far. Pro-rating also acknowledges the value of sacrifices subjects and their parents make even if they fail to complete a study. If personal information is collected as part of the payment process, then respect for persons requires that such information be kept confidential.

A payment policy that identifies ethical principles aiming to guide payment plans and specifies some factors to be considered in developing and evaluating payment plans but that avoids a list of specific rules, will not satisfy persons who think only detailed requirements or an absolute prohibition of payments beyond reimbursements will protect children. However, a policy that focuses on the connection between payment practices and the ethical conduct of research would provide more guidance than what we found in many current policies.[20] It would call attention to the importance of considering the ethical conduct of research and not merely a rule-following compliance approach to research review, and avoid the imposition of potentially misguided rules that could do more harm than good. It also could broaden the scope of concerns IRBs consider in evaluating payment plans. Avoidance of undue influence could be seen as one among a number of important ethical considerations rather than the only concern. Situating the evaluation of payment plans within a framework for the ethical conduct of research will require critical analysis of individual situations and, over time, should be informed by new evidence to ensure that it serves the needs and interests of children who participate in research.

References

1. Institute of Medicine (IOM). The Ethical Conduct of Clinical Research Involving Children. Washington, D.C.: 2004. at Recommendation 6.1
2. Iltis AS, DeVader SR, Matsuo H. Payments to Children and Adolescents Enrolled in Research: A Pilot. Pediatrics 2006;118(4):1546–1552. [PubMed: 17015545]
3. *Id*., at 1547.
4. *Id*., at 1549.
5. *Id*.
6. *Id*., at 1550.
7. Menikoff J. Just Compensation: Paying Research Subjects Relative to the Risks They Bear. American Journal of Bioethics 2001;1(2):56–58. [PubMed: 11951895]Grady C. Money for Research Participation: Does It Jeopardize Informed Consent? American Journal of Bioethics 2001;1(2):40–44. [PubMed: 11951886]
8. Dickert N, Grady C. What's the Price of a Research Subject? New England Journal of Medicine 1999;341(3):198–202. [PubMed: 10403861]
9. Kirkpatrick MAF. Factors that Motivate Healthy Adults to Participate in Phase I Drug Trials. Drug Information Journal 1991;25(1):103–115.Bagley SJ, Reynolds WW, Nelson RM. Is a 'Wage-Payment' Model for Research Participation Appropriate for Children? Pediatrics 2007;119(1):46–51. [PubMed: 17200270]Tishler CL, Bartholomae S. The Recruitment of Normal Healthy Volunteers: A Review of the Literature on the Use of Financial Incentives. Journal of Clinical Pharmacology 2002;42 (4):365–375. [PubMed: 11936560]Bentley JP, Thacker PG. The Influence of Risk and Monetary Payment on the Research Participation Decision Making Process. Journal of Medical Ethics 2004;30 (3):293–298. [PubMed: 15173366]Rothmier JD, Lasley MV, Shapiro GG. Factors Influencing Parental Consent in Pediatric Clinical Research. Pediatrics 2003;111(5):1037–1041. [PubMed: 12728085]Hayman RM, Taylor BJ, Pearl NG, Galland BC, Sayers RM. Participation in Research: Informed Consent, Motivation, and Influence. Journal of Paediatrics and Child Health 2001;37(1):51–54. [PubMed: 11168870]McCarthy AM, et al. Psychological Screening of Children for Participation in Nontherapeutic Invasive Research. Archives of Pediatrics and Adolescent Medicine 2001;155(11): 1197. [PubMed: 11695927]
10. Royal College of Physicians, Research on Healthy Volunteers, a Report of the Royal College of Physicians. Journal of the Royal College of Physicians of London 20(4)1986;:243–257.257 [PubMed: 3772845] EU Clinical Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001, On the Approximation of the Laws, Regulations and Administrative Provisions of the Member States Relating to the Implementation of Good Clinical Practice in the Conduct of Clinical Trials on Medicinal Products for Human Use. Eckstein S. Manual for Research Ethics Committees Cambridge, U.K.Cambridge University Press2003:184–195.195 American Academy of Pediatrics, Committee on Drugs, Guidelines for the Ethical Conduct of Studies to Evaluate Drugs in Pediatric Populations. Pediatrics 95(2)1995;:286–294.294 [PubMed: 7838651] National Council on Bioethics in Human Research (NCBHR). Report on Research Involving Children. Ottawa, Ontario1993British Paediatric Association, Ethics Advisory Committee. Guidelines for the Ethical Conduct of Medical Research Involving Children. London1992 see IOM, *supra* note 1.
11. Iltis AS. Costs to Subjects for Research Participation and the Informed Consent Process: Regulatory and Ethical Considerations. IRB: Ethics and Human Research 2004;26(6):9–13. [PubMed: 15658017]
12. See American Academy of Pediatrics, *supra* note 10, at 293.
13. See, e.g., Fernhoff PM. Paying for Children to Participate in Research: A Slippery Slope or an Enlightened Stairway? Journal of Pediatrics 141(2)2002;:153–154.154 [PubMed: 12183703]
14. See Dickert and Grady, *supra* note 8.
15. Emanuel E, Wendler D, Grady C. What Makes Clinical Research Ethical? JAMA 2001;283(11): 2701–2711. [PubMed: 10819955]
16. Ramsey BW. Appropriate Compensation of Pediatric Research Participants: Thoughts from an Institute of Medicine Committee Report. Journal of Pediatrics 2006;149(1 Supplement 1):S15–S19. [PubMed: 16829236]

17. Food and Drug Administration (FDA). Information Sheets: Guidance for Institutional Review Boards and Clinical Investigators, 1998 Update. at Payment to Research Subjects *available at* <http://www.fda.gov/oc/ohrt/irbs/toc4.html> (last visited March 12 2008)Clinical Bioethics Department, Warren Grant Magnuson Clinical Center. Sheet 20: Guidelines for Remuneration of Research Subjects in the Intramural Research Program and Registration in the Clinical Research Volunteer Program Database. NIH National Institutes of Health Office of Human Subjects Research. *available at* <http://ohsr.od.nih.gov/info/sheet20.html> (last visited March 12, 2008)
18. See Dickert and Grady,*supra* note 8.
19. See Iltis, *supra* note 11.
20. See Iltis, DeVader, and Matsuo, *supra* note 2.

Biography

Mark A. Rothstein serves as the section editor for *Currents in Contemporary Ethics.* Professor Rothstein is the Herbert F. Boehl Chair of Law and Medicine and the Director of the Institute for Bioethics, Health Policy and Law at the University of Louisville School of Medicine in Kentucky. (mark.rothstein@louisville.edu)

Ana S. Iltis, Ph.D., is the Editor-in-Chief of the Journal of Law, Medicine & Ethics. She is also an Associate Professor of Health Care Ethics at Saint Louis University. **Hisako Matsuo, Ph.D.,** is an Associate Professor of Research Methodology at Saint Louis University. **Shannon R. DeVader, M.P.H.,** is currently a Centers for Disease Control and Prevention/Council of State and Territorial Epidemiologists (CDC/CSTE) Applied Epidemiology Fellow assigned to the Maine Center for Disease Control and Prevention, Division of Chronic Disease.

Table 1

Comparison of Payment Amount among Studies with Different Risks, Discomforts, and Funding Sources

Risks	**Physical***		**Psychological/Emotional**		**Social***	
Amount	***Number***	***Mean Rank***	***Number***	***Mean Rank***	***Number***	***Mean Rank***
No Risk	3	35.33	25	19.20	32	20.75
Minimal Risk	27	16.19	12	18.58	5	8.00
Minor Increase over Minimal Risk	7	24.29	—	—	1	34.50
More than Minor Increase over Minimal Risk	1	28.00	1	38.00	—	—
Discomforts			**Physical***		**Psychological/Emotional***	
Amount			*Number*	*Mean Rank*	*Number*	*Mean Rank*
None			22	15.02	25	15.84
Mild			12	18.58	13	24.12
Moderate			2	29.50	1	36.00
Funding Source						
Funding Source	*Number*		*Mean Rank*			
Industry	5		20.00			
Federal Governemnt	19		20.16			
State/Local Government	1		9.50			

*$p<0.05$

Table 2

Correlation of Payment with Number of Study Visits

	Number of Visits Required		Average Length of Time Per Visit	
Variable	***Correlation***	***p-value***	***Correlation***	***p-value***
Total Amount of Payment	0.546	<0.001	0.165	0.168
Number of Visits Required			-0.021	0.430