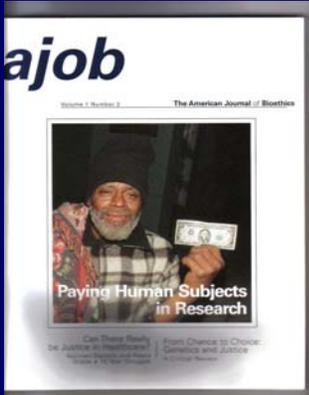


SUBJECT PAYMENT FOR RESEARCH: Current Controversies

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OBJECTIVES

- ✓ Is paying subjects for research participation ethically acceptable?
 - ✓ When / for what?
 - ✓ How much?
 - ✓ Who?
-
- Review regulation
 - Consider ethical norms and current views
 - Evaluate guidelines and general principles



ajob
Volume 1, Number 2 The American Journal of Bioethics

Paying Human Subjects in Research

Can There Really be Justice in Research?
From Choice to Coercion: Genetics and Justice

AMERICAN JOURNAL OF BIOETHICS (Vol 1: 2001)

(Permeth-Wey & Borenstein, "Financial Remuneration for Clinical and Behavioral Research Participation. *Ann Epidemiol*, 2009)

CONCLUSION

- There are potential ethically problematic aspects of the practice of paying research subjects IF the payment is intended as an inducement (ref. Tuskegee, prisoner research)
- Even so, the practice of offering payment as thank you or compensation is not, in itself, ethically objectionable and may be ethically obligatory.

Regulatory Guidance

- Belmont Report:
Nat'l Commission, 1976
- 45 CFR 46
- 21 CFR 50 (FDA)
- OHRP IRB Guidebook

Belmont Report

III -C -1. Informed Consent: *Voluntariness*:
“An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence....Undue influence...occurs through an offer of an excessive, unwarranted, inappropriate, or improper reward or other overture, in order to obtain compliance.”

Code of Federal Regulations

45 CFR 46.116: Informed Consent

“An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.”

(adopted verbatim in 21 CFR 50)

OHRP IRB Guidebook

Chap III – G: Incentives for Participation

- Permits payments to subjects
- Recommends standard fees
- Cautions:
 - amount of payment
 - influence on risk assessment
 - vulnerable populations (poor)
 - use of normal volunteers

OHRP Guidebook

“undue influence: an offer one could not refuse”

Concerns:

- may blind or influence the subject in assessing risks
- may prompt the subject to lie about eligibility

Regulations: Summary

- ▶ Payment to subjects is permitted
- ▶ IRB must determine if payment constitutes "undue influence"
- ▶ Undue influence may be present if payment is:
 - excessive,
 - unwarranted,
 - inappropriate
- ▶ No specific rules, definitions, or guidelines
- ▶ In particular, no advice on how to distinguish "coercion" (controlling degree of influence) from "inducement" (incentives that motivate)

MORAL DEBATE

- Autonomy
- Nonmaleficence (beneficence)
- Justice

Concerns Related to Autonomy

Money = inappropriate influence on willingness to participate

Response:

- a) decisions, even about treatment, are influenced by many factors
- b) money has never been shown to be a strong reason for participation in surveys
- c) autonomy requires us to refrain from interfering in decisions to use participation as a means to earn money
- d) excessive amounts are rarely offered
- e) this may be relevant to inducement, but not to thank you

Concerns Related to Nonmaleficence

Money = possible interference with ability to assess risks

Response:

- a) none of the known egregious instances of research ethics violation, associated with significant harm to subjects, are related to sole influence of money
- b) evidence suggesting risk appraisal is unaffected by monetary inducement (Halpern, 2004)

Empirical Assessment of \$\$ as Inducement (Halpern, Arch Int Med, 2004)

126 hypertension patients
Hypothetical drug research protocol, with varying level of risk and varying payments (\$100, \$1000, \$2000)

Willingness-to-participate decreased with higher risk of adverse effect, higher risk of being assigned to placebo, and lower payment (thus payment is an inducement)

No interaction between factors (thus increasing payment does not make subjects more willing to tolerate risk)

Wealthier subjects rate payment as more important (contrary to assumptions)

Subject Perception of the Effect of Payment

(Slomka et al, J Gen Int Med 2007; 22:1403-9)

37 adult, economically disadvantaged, cocaine smokers; qualitative interviews

Denied payment would encourage drug use
Denied that payment would change risk assessment

Concerns Related to Justice

Money = means to exploitation of most vulnerable (poor)

Response:

- a) it is unfair to withhold payment justly earned through willingness to bear inconvenience, discomfort, etc (compensation)
- b) if we are concerned about exploitation, we should focus on the influence of providing access to care rather than small payments

Conceptual Analysis: Definitions

Compensation: providing money to replace that spent or forfeited through the subject's participation (e.g. parking, lost wages) or as payment for assumption of risk, burden, or inconvenience

Thank-you: gesture of appreciation

Inducement*: reward intended to encourage participation

(only "inducement" raises ethical concerns)

Conceptual Analysis: Models

- Free market: appropriateness of payment rests on assessment of what it takes to encourage participation
- Wage payment: appropriateness of payment rests on current wage scales and time commitment of participation
- Reimbursement: appropriateness rests on match with actual expenses
- Fair benefits: appropriateness related to proportionality of reward to burden, risk
- Appreciation: amount reflects gratitude

Average Payments to Subjects
(Latterman, AJOB, 2001)

Review of 10 journals, 1997-8, offering payments (n=126 studies)

Research Activity	Mean \$	Range
Survey	\$13	1-25
Interview	\$24	10-100
Intervention	\$445	160-730
Mult. Tasks (>3)	\$190	8-600

Average Payments to Subjects
(Grady et al, Contemp Clin Trials 2005; 26: 365-375)

467 studies, 11 IRBs

Subjects:

- patients: 61%
- healthy subj 24%
- both: 15%

Wide variation in totals (\$5 - \$2000)
 No discernible relationship to time, procedures
 Generally modest: median = \$155
 Usually pro-rated

Other Concerns:
"inappropriate reward"

Offering money changes the MD-patient relationship into a contractual model

Response:

- a) enrolling normal volunteers is properly seen as a contractual relationship
- b) enrolling patients is subject to the traditional expectation of nonmaleficence and fidelity, thus fair compensation does not change the terms of MD-patient relationship, any more than patient fees to MD

“inappropriate”

Research participation = gift from subject to researcher and to society; adding money changes this from gift to employed service

Response:

- a) those who participate are making a valuable contribution, even if not a “gift”
- b) the point of the enterprise is not to provide an opportunity for gifting, but rather to contribute to science, better care of patients

Special Problems: Children

Concern: proxy decision-maker stands to gain from payment while subject bears the burden

Response:

- a) AAP: don't reveal payment until after consent obtained
- b) require payment be in form that will only benefit subject (e.g. gift certificate)
- c) require payment be split

PRACTICE

- **Ittis et al, J Law Med Ethics, 2008:**
Survey of 81 investigators in Peds studies
52% paid subjects; 43% of these gave cash
positive correlation of # of visits and amt.
- **Bagley et al, Pediatrics, 2007:**
interviews with 42 children, ages 4-16 yr
children <9 yr could not understand “wage-
payment” model; recommend age-appropriate
gifts for this age

Special Problems: Economically Disadvantaged Countries

Money: excessively influential; exploitation

Response:

- a) maintain limits on amounts
- b) use “local context review” to assure appropriate form of reward or compensation

The other side of the coin....

- It is “unfair” to impose burden and inconvenience on subjects without compensation
- Subjects are always accepting burden for the benefit of others – hence they “deserve” at least a “thank you”
- At least in Western societies, we do use money as reward, to encourage desirable behavior

IRB IMPLICATIONS

1. Fairness: consistency, publicity, policy

Weise, et al, Pediatrics, 2002:

- 7% (6/84) had policy about payment
- 69% used harms, inconveniences as factor in determining payment; 30% do not
- 42% approved payment for child and parent; 31% only parent; 19% only child

IRB IMPLICATIONS

2. Clarity

- a) Which kind of payment is allowed (compensation, thank you, inducement)?
- b) which factors are relevant to determining amount (risk, inconvenience, discomfort)?
- c) are there different rules for paying normal volunteers vs. patients?

IRB CONSIDERATIONS

3. Procedural rules

- a) guidelines for amounts for each form (e.g. hourly wage rate, \$x for hospitalization, \$25 as thank you, etc)
- b) restrictions / guidelines for special cases (children, demented, etc.)
- c) partial payment
- d) in-kind vs. money

SUMMARY

- Payment is at least permissible and arguably obligatory.
- While large monetary amounts seem to present the theoretical threat to voluntariness, there is no evidence that this occurs.
- Inability to at least compensate may impair subject recruitment, particularly in studies involving some discomfort, thus slowing discoveries that could benefit many.
- The most likely source of inequities and inappropriate practice is the lack of clear and consistent policies and practice.

ADDITIONAL GUIDELINES

- ✓ Clarity of consent (amount and type)
- ✓ Reasonableness
- ✓ Consistency
- ✓ Pro-rated
- ✓ Small completion bonuses
- ✓ Split payments (in kind) to children

Suggested Rules of Thumb

- If children are subjects, children should receive at least part of payment
- Basis for compensation for “costs” of participation: transportation
lost wages (~\$15/hr)
- Thank you = \$5 – \$50
- Inducement: discomfort
inconvenience
NOT risk
<\$500

Remaining Questions (OHRP)

- Are “conditions” in keeping with community standards?
- Are the incentives “reasonable” in relation to inconvenience, complexity?
- Are there “special” standards for studies that present significant risk or for vulnerable subjects?
- Should the IRB monitor subject recruitment to evaluate coercion or undue risk?
