


Ethical and practical considerations of paying research participants

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Example

- Phase 2 study of a new anti-anxiety drug for those with high levels of stress on a validated screening instrument, no current anti-anxiety drugs, and no significant medical problems.
- Involves several blood draws, physical exams, and hour-long interviews over the course of six months.
- Participants will be paid \$500 on completion of the study.

Example

- Comparison of a long-lasting formulation of an antihypertensive drug and the standard version to see if the new version improves adherence.
- The participants are already taking the standard formulation and there are no additional risks.
- They will be paid \$25 each visit for a blood pressure check and other basic tests.

Example

- Study of neurophysiologic correlates of anesthesia in healthy volunteers
- EEG, serial bloods, and multiple diagnostic tests after the administration of different anesthetics at each of 4 or 5 clinic visits
- Compensation offered is pro-rated by visit, with total about \$2000

Ads in Real Life

- **Men's Sexual Health Research**
- Our physicians are studying the effect of an investigational oral medication on sperm function. If you are between the ages of 25 and 64, are in good general health, and have not had a vasectomy, we may need your help.
- If you qualify, you will receive financial compensation of up to \$1350. You will also receive all study-related care and services.
- Please contact us today

Ads in Real Life: Bar Coaster

Research Subjects Wanted

Earn \$50-\$1295

Call

555-555-5555

Christine's Research Institute

To pay or not to pay?



Walter Reed

- Paid \$100 in gold for participation.
- \$100 bonus for successful infection with yellow fever.
- Payable to family in the event of death.



<http://etext.lib.virginia.edu/healthsci/reed/commission.html#vol>

How common is it to pay research participants?

- Advertisements in newspapers, the internet, and in hallways
- Most research organizations and academic medical centers pay at least some participants (24- 80%*)
- Paying studies range from short term physiologic studies to long term phase 3 clinical trials

– *Dickert et al. Annals 2002

Table 1. Types of Paying Studies and Types of Subjects

Studies By Type Of Subject Enrolled	Type of Study							Total
	Phase 1	Phase 2	Phase 3	Phase 4	Physiologic	Behavioral	Other	
Studies That Enrolled Only Healthy Subjects	16	5	1 ^a	1 ^b	37	35	18	113 (24%)
Studies That Enrolled Only Patient-Subjects	10	52	97	35	21	39	32	286 (61%)
Studies That Enrolled Both Types Of Subjects	0	1	2 ^c	0	30	8	27	68 (15%)
Total	26 (6%)	58 (12%)	100 (21%)	36 (8%)	88 (19%)	82 (18%)	77 (16%)	467 (100%)

^a This phase 3 study was testing a preventive vaccine in uninfected persons

^b This phase 4 study was testing a fiber supplement in healthy subjects

^c One of these studies was evaluating an intervention to reduce heterosexual transmission of herpes simplex and enrolled both the healthy uninfected partner and the patient with herpes. The other study was evaluating an intervention to reduce transmission of ADHD and enrolled some healthy children as controls.

Payment in the U.S.

- Significant variation within and between institutions in amount of payment for particular procedures, inpatient days, outpatient visits.
 - Rarely itemized.
 - e.g. MRI with contrast 0-\$25-\$150
 - Wide variation in multi-site studies.
 - Up to \$840 difference for the same study.
- Grady et al. *Cont. Clinical Trials* 2005

Why pay research participants?

- Facilitates Recruitment
 - Helps make participation a revenue-neutral experience
 - Compensation for time and contribution
 - Incentive to overcome barriers



TOM'S SHELL

*Self
Serve*

*Cash or
Credit*

Regular

ARM 9

Plus

LEG 9

Premium

**First 9
Born**

Why pay research participants?

- Money enables participation and can be a sign of respect
- “It is reasonable to pay someone for their work. If you gain, how much are you gaining? Telling someone their community is gaining is a stretch. How much time does it take? Time is money. What is the value of time for the person in the study?”

To what extent does payment facilitate recruitment?

- Data on survey response rates
 - Small amounts of money (e.g. \$5) increase response rates
 - Asch et al. *Med Care* 1998
 - Church *Public Opinion Q* 1993
 - Doody et al. *Am J Epidemiology* 2003
 - Ulrich et al. *Nursing Research* 2005
- Data on hypothetical willingness to participate
 - Money increases willingness to participate
 - Halpern et al *Arch Int. Med* 2004
 - Bentley and Thacker *J Med Ethics* 2004

Does money enhance recruitment of healthy volunteers?

- Motivations

- Money

- >90% of those surveyed said financial compensation was main motivation for participation

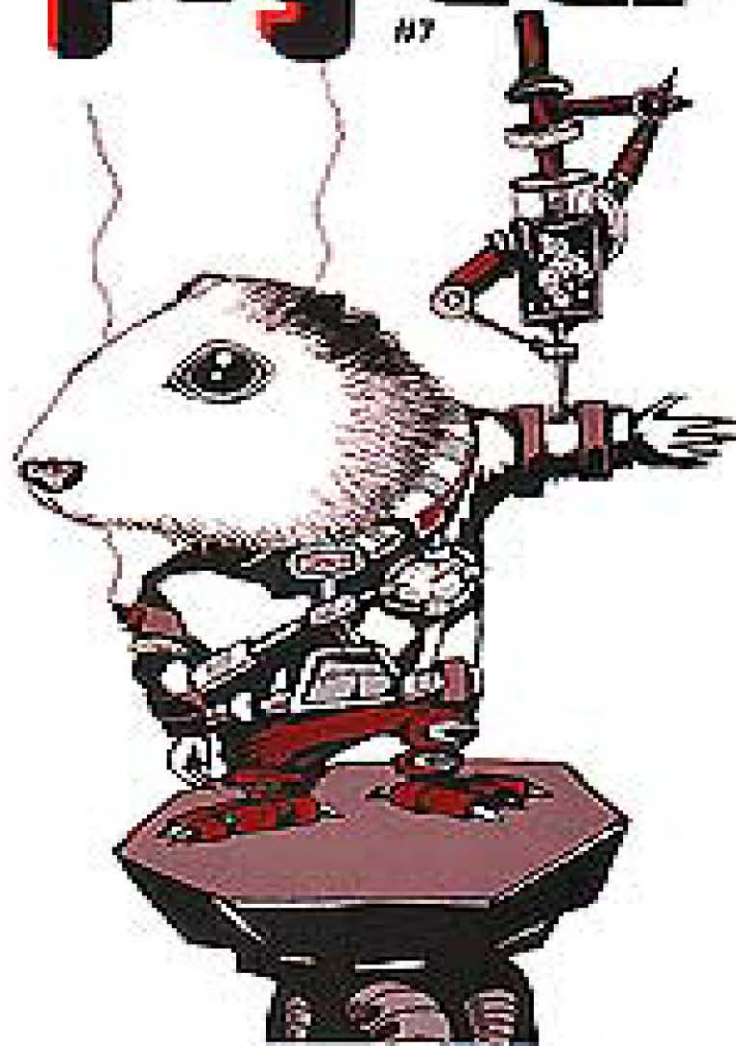
- e.g. Bigorra and Banos 1990; vanGlederen et al 1993; Hassar et al. 1977

- Healthy volunteers also have other motives, including curiosity, altruism, sensation seeking, knowledge, etc.

GUINEA pig zero

#7

\$5.00



Does money enhance recruitment of patient-subjects for clinical research?

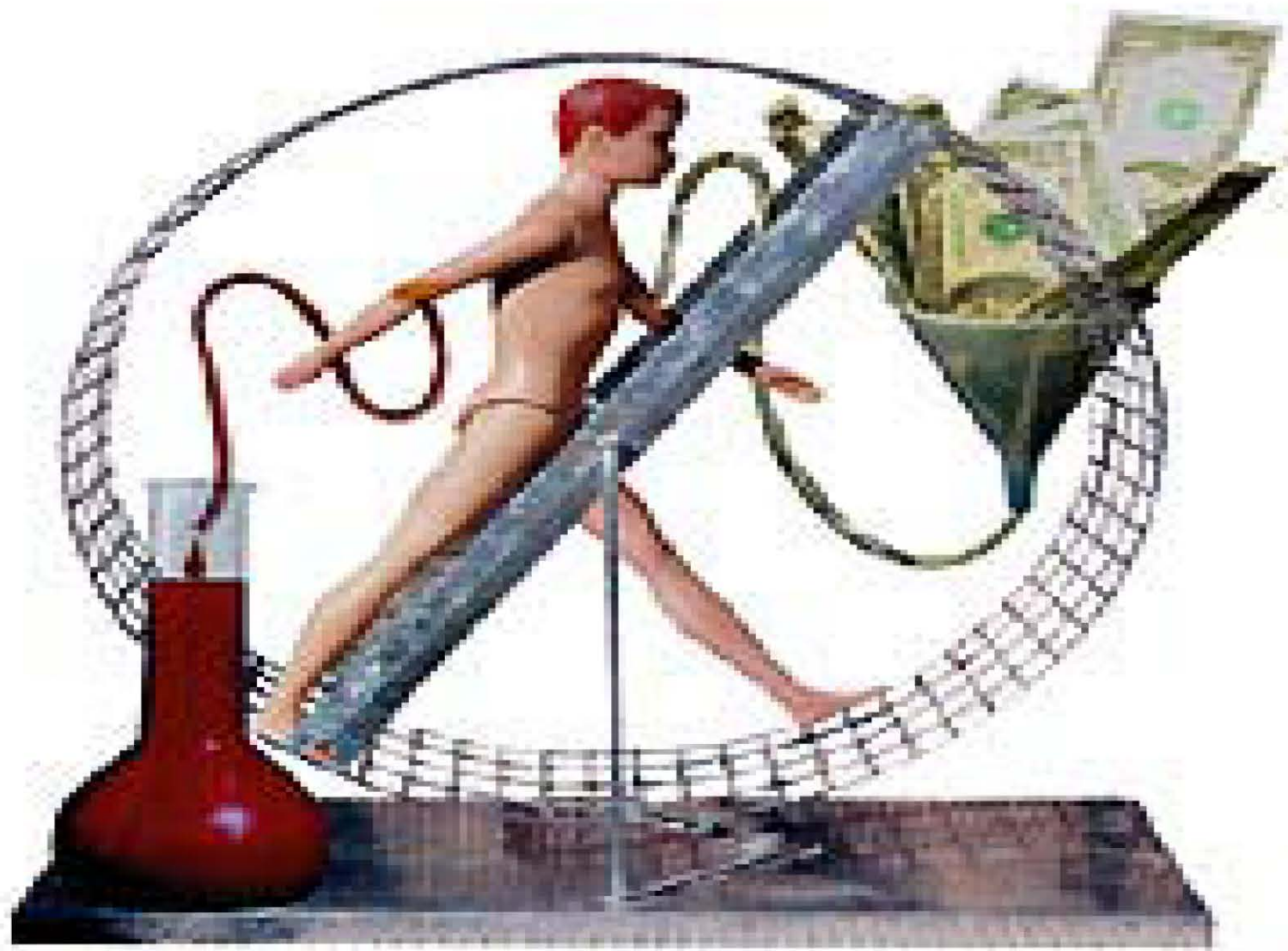
Motivations:

- Hope of personal therapeutic benefit
- Attention by/ trust of physician
- Knowledge
- Altruism
- Access to care

Why not pay research participants?

Ethical concerns

- Commodification
- Skewed sample
- Coercion
- Undue inducement



Skewed sample

- Worry: Money more attractive to lower income individuals
- Results
 - a skewed sample
 - and disproportionate burden on the socioeconomically disadvantaged
- DATA???
 - Who participates in research?
 - To what extent are subjects in paid studies different?

Coercion or undue inducement?

- US Code of Federal Regulations require that informed consent be obtained “under circumstances...that minimize the possibility of coercion or undue influence”
 - 21CFR.50
 - 45CFR.46

Can money be coercive?

- Coercion is a threat of physical, psychological, or social harm in order to compel someone to do something, such as participate in research.
- Money is an offer or an opportunity, and not a threat of harm.

Coercion

- Used in many different circumstances.
- Often misunderstood as simply meaning involuntary or under strong influence.
- Because coercion is not a benign accusation, the concept needs clarification and should be used carefully.

Coercion is Rare in Research

- Inmate whose care and treatment might be compromised for refusing participation.
- Patient may participate in a study run by his or her physician because of the fear or reality that care is contingent on participation.
- Recommendation: use “coercion” carefully and not regarding payment.

What is undue influence? (inducement)

- An offer one cannot refuse
- A controlling and irresistible influence
- Strong enough to compel someone to participate against their interests



Why worry about undue influence in research?

- An inducement is undue if it is “...so attractive [that it] can blind prospective subjects to potential risks or impair their ability to exercise proper judgment”
- [or] “prompt them to lie or conceal information that would disqualify them from enrolling--or continuing--in research”

Official IRB Guidebook OHRP

Do financial incentives blind prospective subjects to research risks?

- If risks are judged acceptable – is this a misplaced worry?
- Will subjects be asked to accept the same risks without financial incentive?
- Understanding of risks can be evaluated during the process of informed consent
- Limited data suggest payment does not obscure risk perception (eg. Bentley and Thacker 2004)

Do financial incentives impair judgment?

- *Voluntary* decisions are motivated by various factors, often including but not limited to money
- Money is one factor in research decisions of some participants
- Most participants (75%) in one study thought \$500 could impair the judgment of others, but fewer (20%) that it would impair their own judgment.
 - Casarett et al. *J Gen Intern. Med.* 2002

Should we worry about undue Inducement?

- An excessively *attractive* offer that leads people to exercise *poor judgment* about research participation that involves a *risk of serious harm*.
- IRBs should not approve studies that expose subjects to risk of serious harm
- Payment cannot be undue inducement in an appropriately approved study

Emanuel, *J Law Med Ethics*. 2004.

Undue Inducement



- Concern about undue inducement misdirected in a study with little risk.
- Concerns about payment obviating voluntariness are counter-intuitive.
- Concerns about problems with consent argue for improving the consent process.

Emanuel, *J Law Med Ethics*. 2004

Undue inducement



- “I’ll know it when I see it”
- Decisions left to investigators and IRBs
- Caution at the ends of the risk spectrum or in settings where subjects might have values that conflict with the research.

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- Subjects may be paid for inconvenience and time spent, and should be reimbursed for expenses incurred, in connection with their participation in research; they may also receive free medical services. However, the payments should not be so large or the medical services so extensive as to induce prospective subjects to consent to participate in the research against their better judgment ("undue inducement").
 - CIOMS International Ethical Guidelines

Models for paying research participants

- Market model
- Wage payment model
- Reimbursement model
- Appreciation model

Models of payment

	Market	Wage Payment	Reimbursement
<i>Justification</i>	Incentives to facilitate recruitment	Compensation for time, effort, uncomfortable procedures	Participation should be revenue neutral
<i>Approach</i>	Escalate payment to meet recruitment	Standardized wage-like payments	Reimbursement of out-of-pocket expenses

Dickert, N and Grady, C. (1999) *NEJM* 341(3):198-203

Wage Payment Model

- Participation in research requires little skill but takes time, effort, and endurance
- Payment should be based on a wage scale similar to other unskilled jobs
- Pay a standardized hourly “wage”, perhaps augmented by pay for particularly uncomfortable procedures or added inconvenience

Advantages of Wage Payment

- Greatly reduces the potential for undue inducement
- Provides valuable standardization across studies
- Adheres to the principle of justice by paying similar individuals similar amounts

Does/should who you are paying matter?

- Patient subjects
- Children

Payment to research subjects

- Common perception- Only healthy subjects in research are paid, patient-subjects are not
- Why might patient subjects be viewed differently?
 - They may benefit from the research
 - They are especially vulnerable

Patient-Subjects and Healthy Subjects

- These common perceptions appear not to be true:
 - 75% of paying protocols included ‘patient-subjects’ and paid all or some of them
 - 64% of those studies offered a prospect of therapeutic benefit to the patient-subjects
 - And, patient subjects are often asked to participate in research or research procedures that offer no prospect of benefit

- Grady et al. *Cont. Clinical Trials* 2005

Are patient-subjects more vulnerable?

- Special vulnerability of patients
 - “Therapeutic misconception”
 - Payment could reduce or eliminate it
 - Power differential
 - Payment could make it easier to refuse
 - Need data

Patient subjects

- For studies with a prospect of benefit, payment may be unnecessary as an incentive; but it does not follow that payment is unethical.
- In contrast, it may be unfair to not compensate or reimburse all subjects for similar contributions or expenses

Children

- Worry: Children do not provide their own consent. Money could sway parental decision making.
- Yet, research can involve cost and inconvenience to parents. And, risk to children in research is carefully evaluated and limited.
- Should children and/or their parents receive money or other payment as reimbursement, compensation, appreciation, or incentive??

Children

- Some support for at least reimbursing expenses of parents
- Some argue compensation for contribution should go to the children
- Child's age matters
- Need more data

Forms of Payment

- Payment may come in several forms:
 - Money
 - Gifts
 - Free care
 - Travel vouchers
 - Gift certificates

Considerations when deciding whether and how much to pay

- The nature of the study, including study risks and budget
- The nature of participant contributions and vulnerabilities
- Institutional or organizational guidelines
- Local societal and cultural norms

Practical considerations

- Proposal submitted to the IRB should describe rationale for payment, how dollar amount calculated, and how and when payment will be made.
- IRBs do not consider payment a benefit to offset research risks when deciding to approve a study

Need for more research

- How does payment affect recruitment?
- What trade-offs do participants make?
- To what extent do people participate in studies they find objectionable or against their interests?
- What are and what determines the sociodemographics of research participants?