

Coercion and Undue Inducement in Research

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Disclaimer and Acknowledgement

- The views expressed are my own. They do not necessarily represent any position or policy of the National Institutes of Health or the Department of Health and Human Services.

The basic problem

- Research requires subjects
- In some cases, recruitment is easy
- But in some cases, recruitment is difficult
- Participation may be risky, inconvenient, painful
- Altruism is limited
- Subject accrual is often slow. Many studies do not complete. More studies are not proposed.

The basic problem

- “Lack of study volunteers hobbles cancer fight”
(NYT Headline, August, 2009)
- 3% of adult cancer patients participate
- More than 1/5 trials sponsored by NIC failed to enroll a single subject and only half reached minimum needed for a meaningful result

Recruitment as Collective Action Problem

- It is in everyone's interest that research be conducted
- It is sometimes in an individual's interest NOT to participate
- In some areas of social life we use government coercion to solve a collective action problem
- Not in research

The basic problem

- Consent is required
- We may use incentives to get people to participate
- Not a new phenomenon

Walter Reed

- Yellow fever studies in Cuba (1900).
- Intentional exposure.
- Paid \$100 in gold.
- \$100 bonus for successful infection.
- Payable to family in the event of death.



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

Payment Today

- “**Make \$1,000's...** Get paid hundreds weekly in additional cash income, part-time, while relaxing in a million-dollar, get paid research study... Yes, there are thousands of cash paying studies and even free medical care available!”
- “Get paid up to \$1,000 weekly for safe sex research?”

<http://www.rxgetpaid.com>

| PROGRAM DIRECTORY | |
|--|---|
|  Easy Sleep "ZZZ" Research |  Drive Cars Get Paid |
|  Alcohol+Medical Marijuana Studies |  Plasma+Blood Donation |
|  Eat and Shop Get Paid |  Health+Weight Loss Studies |
|  Safe Sex+Condoms +Sperm Donor |  Surrogates+Egg Donors Wanted |
|  Anxiety+Depression Bi-Polar Treatment |  Look at Email Get Paid |
|  Free Samples Get Paid |  Tobacco Smokers +Non-Smokers |
|  Focus Groups+Product Opinions |  Free Health & Dental Care |
|  Experimental Drugs and Medications |  PreExisting Condition Studies |

Advanced Search

Other Incentives

- Free treatment (or chance of treatment)
- Free medical examinations
- Experimental Treatment
- Post-trial treatment
- Ancillary Care or Incidental Findings

Payment in the U.S.

- Payments made in Phase I, II, III
- At least 23% of protocols at academic institutions paid subjects.
 - Few have any method of tracking paid studies
- Frequency of payment higher at independent IRBs and pharmaceutical companies.

Dickert, Grady, and Emanuel. *Annals of Int Med.*
2002

Amount of Money Being Paid (n=467 studies)

| | |
|---------------|-------|
| < \$100 | 30.4% |
| \$100-249 | 33.6% |
| \$250-499 | 21.2% |
| \$500-999 | 10.5% |
| \$>1,000 | 4.3% |
| <i>Mean</i> | \$266 |
| <i>Median</i> | \$155 |

Amounts shown in U.S. dollars

Grady, Dickert, Jawetz, and Emanuel.

Why do we pay research subjects?

- Reimbursement
- Compensation for time and burdens
- Compensation for risk
- Avoid exploitation
- Incentive for recruitment
- Some reasons are more accepted than others

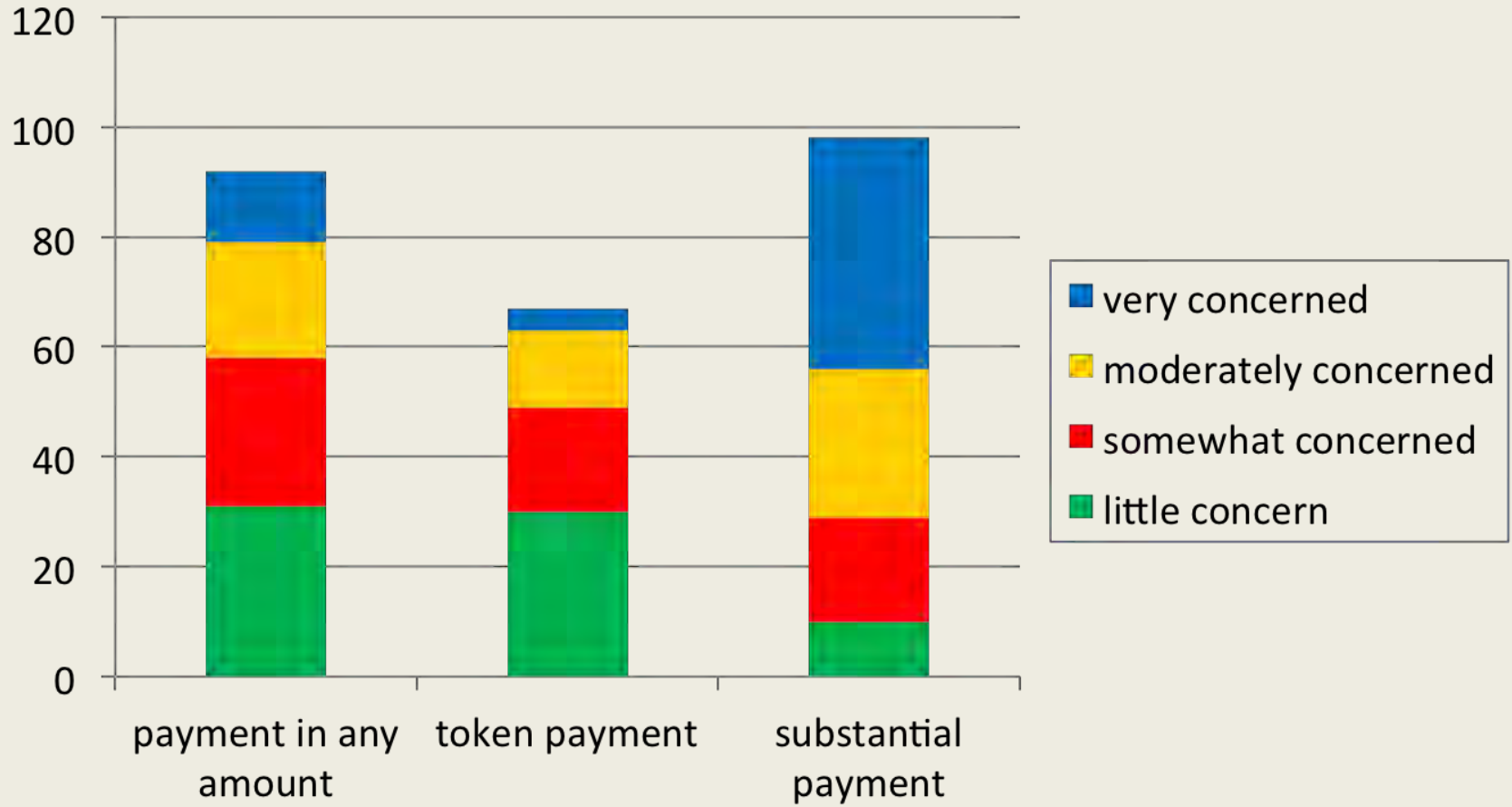
Results: Reasons for paying and views about paying healthy and patient volunteers

| % who agree or strongly agree that it is acceptable to... | Healthy Volunteer | Patient-subjects with no prospect of benefit | Patient-subjects with a prospect of benefit |
|---|-------------------|--|---|
| Offer Money | 86.8% | 78.7% | 71.1% |
| Reimburse for expenses | 97.9% | 95.4% | 92.8% |
| Compensate for time, effort, inconvenience | 94.5% | 90.7% | 86.2% |
| Offer money as an incentive | 58.3% | 56.2% | 50.2% |
| Offer money to compensate for risk | 36.4% | 36.9% | 34.6% |

The State of Payment in the U.S.

- Payment is very common.
- All types of subjects are paid.
- Payment is erratic with little institutional guidance or consistency.
- Payment is generally modest.
- Significant disagreement over payment as incentive or for risk.
- Lots of worrying

Results: concern about payment



What are the worries?

- Consent
 - Coercion
 - Undue Influence
- Other
 - Commodification – Guinea Pigging
 - Trust in research enterprise
 - Scientific
 - Conceal information
 - Feign illness (psychiatric research)
 - Reporting adverse events
 - Skewing population

Anecdotal Evidence

- Anecdotal evidence suggests that many IRB members think that payment or offers of medical care do or can coerce or constitute undue influence
- Our study showed that this hypothesis is correct

What's the problem?

- To the extent that IRB members' attitudes regarding payment are ethically sound, they appropriately influence payment practices
- studies should not be approved if participants' consent is likely to be compromised by coercion or undue influence.
- If IRB members' concerns are based on conceptual or ethical misconceptions, unnecessary limits may be placed on payments to research participants and impede valuable research without ethical cause.

Consequences of the worries

- Fact that payments are frequently made does not show that worries make no difference (speed limits)
- Not how many protocols are disapproved
- But how many protocols that would otherwise pass muster are not proposed or even considered?
- Does research progress more slowly?

Our Thesis

- Many of the prevalent concerns about payment *are* largely misguided.
- Payment never coerces.
- Payment raises ethical concerns with respect to consent only when it unduly influences participants by distorting their perception of research risks and benefits.
- In the absence of evidence that such distortions occur, IRBs should be reluctant to conclude that offers of payment undermine the validity of consent

Emily A. Largent, Christine Grady, Franklin G. Miller, and Alan Wertheimer, "Misconceptions about Coercion and Undue Inducement: Reflections on a Survey of IRB Members, *Bioethics forthcoming*."

Regulatory Statements

The Common Rule

“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.”

45 CFR 46, 116

FDA

“The IRB should review both the amount of payment and the proposed method and timing of disbursement to assure that neither are coercive or present undue influence.” FDA Information Sheets, 1998

OHRP

“... the IRB should review both the amount of payment and the proposed method of disbursement to assure that neither entails problems of coercion or undue influence. Such problems might occur, for example, if the entire payment were to be contingent upon completion of the study or if the payment were unusually large. Payments should reflect the degree of risk, inconvenience, or discomfort associated with participation.”

Office of Human Research Protection. IRB Guidebook.

How do IRB members understand coercion?

Results: Respondent views on coercion and undue influence

| % of respondents who agreed or strongly agreed that <i>if</i> the research participants ... | <i>Then</i> ...it is coercion | <i>Then</i> ...it is undue influence |
|---|----------------------------------|---|
| ...are threatened with harm | 91.2% | ----- |
| ...will participate with payment when otherwise they would not | 64.8% | 81.0% |
| ...feel they have no reasonable alternative but to participate because of payment | 81.6% | 79.2% |
| ...ability to accurately perceive risks and benefits is distorted when offered payment | --- | 98.2% |

Coercion

- Some people think that offers of payment are coercive if and when they get someone to agree to participate in research when they would otherwise not.
- There are numerous ways of motivating people to do things that they would otherwise not do
 - A persuades B to give blood or go to a movie or invest in a mutual fund
 - A offers the teenager next door \$20 to mow his lawn.
 - As a general proposition, offers do not coerce.
 - Offers can be indecent and immoral but they do not coerce

Coercion

- A coerces B to do consent to do X in a way that invalidates B's consent only if A proposes to harm B if B does not consent to do X
- The *Belmont Report*: “Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance.”
- Examples
 - Gunman case
 - Extortion
 - The Godfather's Offer

Coercion

- Threats v. offers
- Threats reduce options
- Offers enhance options

Coercion

- Some people think that people are coerced to participate in research when they have no reasonable alternative but to consent to participate.
- Appeal to gunman case
 - “but we could not say that my handing over the wallet was an autonomous, let alone a consenting act since I was, after all, under threat. I had no other “real”, i.e. reasonable alternative.”

Thomas Schramme, “Coercive Threats and Offers in Psychiatry”

Lack of Income

- “Nevertheless, many in the field worry that lower-income patients who either need the money or cannot afford conventional treatment are subject to a different kind of pressure. It is ‘coercion through lack of income,’ explains David J. Rothman . . . ‘Monetary need may cloud a patient’s decision-making, exposing the individual to a greater level of risk than he or she might otherwise accept’.”

No Reasonable Alternative

- Attractive but mistaken view
- In most cases of coercion, target has no reasonable alternative but to agree.
- “Give me your money or I’ll beat you up.”
- But it does NOT follow that she is coerced BECAUSE she has no alternative but to agree.

Coercion

- We do *not* say that a patient who agrees to surgery or chemotherapy because the only alternative is death has been coerced to consent or that her consent to treatment is involuntary or invalid.
- We do *not* describe people as coerced if they take an unpleasant job in order to provide for their families.
- It is 'coercion through lack of income' (Rothman)

Coercion and Jesse Gelsinger

- Jesse Gelsinger, 18, had a mild form of a rare metabolic disorder
- In 1999, enrolled in Phase I gene-therapy trial at U Penn.
- On Sept 13, he was injected with a weakened cold virus carrying corrective genes. Four days later he died from an immune reaction to the virus vector

Coercion and Jesse Gelsinger

- Gene therapy not designed for treatment of people like Jesse who had mild form of disease, but for neonates with a more severe and almost always fatal form.
- Researchers had planned to test treatment on terminal neonates
- They were persuaded to test it on adults because adults could give consent

Coercion and Jesse Gelsinger

- Arthur Caplan: The parents of dying infants are incapable of giving informed consent – “They are coerced by the disease of the child”
- In my view, Caplan is wrong.

Coercion

- Issue is not merely semantic
- Issue is the regulatory and decisional effects of describing or labeling payment as coercive

Coercion is Rare in Research

- Cases where retribution is conceivable.
 - A physician may threaten to abandon a patient who refuses to participate in a study.
 - Explicit v. tacit threats
- Perceived coercion is possible.
 - Patient participates in a study run by his PCP because the patient mistakenly fears his care is contingent on participation.

A clear answer?

- “How large a payment constitutes “undue influence” or a coercive offer to participate in research is a question . . . for which no clear answer is forthcoming.” (Ruth Macklin)
- A clear answer is forthcoming: offers of payment do not coerce
- Stop worrying about coercion

Undue Influence

- When do offers of payment constitute undue influence?
- A different question

Inducement

- Inducements are offers that get people to do things they would not otherwise do.
- Inducements are typically unproblematic
 - Jobs
 - Market transactions
 - Parenting

Undue Inducement

“...monetary inducements may be undue if they alter patients’ decision-making processes such that they do not appropriately consider the risks of participating.” Halpern, et. al. Arch. Intern Med. 2004

Undue Inducement

“An offer one could not refuse is essentially coercive (or "undue"). Undue inducements may be troublesome because offers that are too attractive may blind prospective subjects to the risks or impair their ability to exercise proper judgment”

Office of Human Research Protection. IRB Guidebook.

The Core of Undue Inducements

- Inducements are problematic when they distort the target's decision-making.
- Tunnel Vision
 - Focusing on gain
 - Ignoring cost
- Myopia
 - Overweighting short term gains
 - Underweighting long term costs
 - Hyperbolic discounting

Undue Influence

- “Monetary need may cloud a patient’s decision-making, exposing the individual to a greater level of risk than he or she might otherwise accept” (David Rothman)
- Half right

Risky Jobs

- Coal mining
- Logging
- Commercial fishing
- Structural Steel
- Fire fighters
- Soldiers
- Is research different?

How much should subjects receive?

- Level
 - Reimbursement
 - Inconvenience
 - Time
 - Risk
 - Market or opportunity cost
- Equality
 - Everyone receives the same absolute payment
 - Everyone receives payment tied to opportunity cost

Wage Payment Model

- Opportunity cost model would not be accepted
 - Jury compensation
- Treats research as a form of unskilled labor
- Standardized payment for time and for procedures.

Wage Payment Model-Advantages

- Provides consistency.
- Treats research participation as labor.
- Offers appropriately limited protection from undue inducement.
- Prevents unfair advantage exploitation by ensuring reasonable standard payment tied to the nature of the work
- Controls research costs.

Wage Payment -- Disadvantages

- Insufficient incentive
- Unfair to high wage earners
- Fair subject selection and demographic disproportionality

Conclusion

- Does payment or paying more compromise the voluntariness of consent? It might, but probably less than is often thought.
- Does non-payment or paying too little increase the likelihood of exploitation? It might, but stay tuned.