

Coercion and Undue Inducement in Research

Alan Wertheimer, Ph.D.
Professor Emeritus of Political Science
University of Vermont

Research Scholar
Department of Bioethics
National Institutes of Health

CAREB
May 1, 2010
Montreal, QC

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.
- Actually, some of the material presented is not my own. Christine Grady and Neal Dickert have been kind enough to allow me to use slides that they developed.

Bioethics Worries About Money

- Selling Organs
- Commercial surrogacy
- Payments to Research Subjects
- Payments to Referring Physicians

- Payments to Researchers?

The basic problem

- Research requires subjects
- Participation may be risky, inconvenient, painful
- Altruism is limited
- Subject accrual is often slow

Reasons for Payment

- Reimbursement for expenses
- Compensation for inconvenience, burdens
- Compensation for risk
- Incentives

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>

Other Incentives

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

TGN 1412

- TeGenero AG
- Lymphocytic leukemia and rheumatoid arthritis
- Phase I trial by Parexel, American CRO
- Subjects paid £2,000
- 6 subjects had catastrophic system failure

TGN 1412

- Unethical or Bad Luck?
- Consent form?
- Simultaneous Administration
- Undue Inducement/Coercion

TGN 1412

- The consent document stated that “If you leave the study and exercise your right not to give a reason or are required to leave the study for noncompliance, no payment need be made to you.” Greg Koski, former director of the U.S. Office of Human Research Protections, remarked, “That’s very coercive language.”
- Bloomberg. Parexel misled subjects sickened in London study, ethicists say. April 10, 2006. Available at <http://www.bloomberg.com/apps/news?pid=7100000&refer=germany&sid=aG3sg1rIkL4U>

Overview

- Canonical Statements
- State of payment in the US
- Coercion
- Undue Inducement
- Exploitation

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

“Payment to research subjects for participation in studies is not considered a benefit, it is a recruitment incentive... 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.

Toronto Academic Health Sciences Council (TAHSC) GUIDELINES FOR RESEARCH ETHICS REVIEW INVOLVING HUMAN SUBJECTS

PAYMENTS TO SUBJECTS

- Subjects should not be expected to incur expenses as a direct result of participation in a research study; reimbursement for out-of-pocket expenses (e.g. travel) is encouraged. Payment should not be used in such a way that it could be construed as an undue inducement to participate (e.g. unreasonable amount, payment tied to completion of study). Reimbursement should be for expenses, time or inconvenience, but should not be used to encourage subjects to accept increased risk. If reimbursement for time is proposed, please explain. It is expected that any payments will be pro-rated.

Is Money a Benefit?

- The IRB should not view remuneration as a benefit to offset research risks in deciding whether a protocol should be approved. As in all cases, the IRB is charged with determining whether research risks are justified by the potential benefits of doing the research. Risks that are otherwise unacceptable cannot be made acceptable by offering increasing amounts of money to subjects. (Office of Human Subjects Research, NIH)

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

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.

What are the worries?

- Subject Protection
 - Coercion
 - Undue Inducement
 - Fair Subject Selection
 - Exploitation
 - Fairness in Payment Schedules

What are the worries?

- Non-subject protection
 - Commodification
 - Trust in research enterprise
 - Scientific
 - Conceal information
 - Reporting adverse events
 - Skewing population

What are the Worries?

- Payment as a necessary evil
- Reluctance to view research as a job or economic transaction
- Some institutions have specific rules about completion bonuses

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?

Coercion

“By now it is an unquestioned ethical precept of biomedical and behavioral research practice that subjects should not be coerced into participating... Those who choose to participate in research should be capable of choosing freely; they must do so voluntarily, willingly, without duress, and without being subjected to threats or the promise of too great a reward.”

Macklin, IRB, 1981

Coercion

- Concept used in many different circumstances.
- Often misunderstood as simply meaning under strong influence.
- Particularly misused to refer to situations in which there are no good options.
- We must be careful.

Advertisement



Coercion: Two Views

- A coerces B to do X only if A proposes (threatens) to render B worse off unless B does X. (Threat view)
 - Belmont Report view
- A coerces B to do X when A's proposal leaves B with no reasonable alternative but to do X. (No Reasonable Alternative view)

What is Coercion: Threat View

- A coerces B to do X when A threatens to make B worse off if B does not do X.
- Threats v. offers
- Threats reduce options
- Offers enhance options

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.

No Reasonable Alternative

- Surgery. Doctor tells patient that unless she agrees to surgery, she will die within a year. Patient agrees.
 - Does patient have a reasonable alternative?
 - Has patient been coerced?
 - Can patient give voluntary consent?
 - Has doctor committed battery?
 - Is patient obligated to pay?

Coercive Offers

- Are there coercive offers?
 - “Is it not a coercive offer to force terminally ill pregnant women to choose between joining a placebo-controlled trial which gives them a shot at an established HIV intervention, and no treatment at all?” Udo Schuklenk
- Offers enhance range of options
- So it seems that offers cannot coerce
- But what about an offer that can't be refused?



Godfather's Offer (Revised)

After original offer of \$10,000 is rejected, Don Corleone raises the offer to \$100,000.

The bandleader accepts the proposal.

Can Payment be Coercive?

- Payment is an offer and not a threat.
- To be coercive, a subject who refuses must be made worse off than if he or she would have been if never asked.
- Payment for research is not coercive.

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 do not coerce
 - A payment constitutes “undue influence” only if it distorts the agent's judgment or reasoning

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.

Inducement

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

TGN 1412

- Those who participated were members of an “economically vulnerable population; members who, presumably, would have made a different decision had they been in a position in which their personal valuations of the incentive were not *clouded* by their economic standing.” (emphasis added)
- Benjamin Hale, Risk, Judgment, and Fairness in Research Incentives, *American Journal of Bioethics* (2007) 7:2, 82 - 83

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: (1) offers that are too attractive may blind prospective subjects to the risks or impair their ability to exercise proper judgment; and (2) they may prompt subjects to lie or conceal information that, if known, would disqualify them from enrolling -- or continuing -- as participants in a research project.”
Office of Human Research Protection. IRB Guidebook.

Undue Inducement

“Payment in money or in kind to research subjects should not be so large as to persuade them to take undue risks or volunteer against their better judgment. Payments or rewards that undermine a person’s capacity to exercise free choice invalidate consent.”
CIOMS, 2002, Guideline 7.

Fallacies about Inducement

- It’s problematic to get someone to do something that they would otherwise not do.
 - Give blood
 - Give to charity
- It’s problematic to get someone to do something against their better judgment
 - Against better judgment NOT COUNTING value of inducement.
 - Against better judgment, counting value of inducement

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

Risky Jobs

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

Payment Schedules

- Assume that patients have a right to withdraw from research at any time
- “the subject may discontinue participation at any time without penalty or loss of benefits *to which the subject is otherwise entitled.*” The Common Rule
- Do completion bonuses compromise that right?

Payment Schedules

- “Incentives must not be provided on a schedule that results in coercion or undue influence on an individual's decision to continue participation. That is, incentives must not be withheld as a condition of an individual completing the research. If an individual withdraws early, payments or incentives must be prorated to reflect the time and inconvenience of the individual's participation up until that point.”
 - Syracuse University IRB Handbook

Are completion bonuses problematic?

- Voluntariness worries
- Fairness worries
- Scientific worries

Conclusion

- There may be other – legitimate – ethical worries about the practice of payment to research subjects
- But there is no reason to be particularly worried about coercion and undue inducement