Paying research subjects

Ethical issues in health research

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Disclaimer

- I have no conflicts of interest
- The content is solely the responsibility of the author and does not necessarily represent how the UNM HSC HRRC approaches compensating participants.

Research study seeking MALES who are on Parole (the Mind Research Network)

Research study seeking males who are on parole
Free taxi ride to and from appointments
Call or email

Compensation: Earn $300 at $20/hour for 15 hrs of your time.

Craigslist posted 2 days ago

Unmotivated? Diagnosed with schizophrenia? Smartphone Research Study

- Feeling Unmotivated? Recently diagnosed with schizophrenia
- Smartphone Research Stud
- Are you between 14-30 years old? *
- Were you recently diagnosed with schizophrenia, schizoaffective, or schizophreniform disorder in the last 5 years?
- Are you interested in helping pilot a new digital health intervention for young people with schizophrenia?

  WHAT THE STUDY IS ABOUT: The research team at the UCSF DRIVE Lab developed a mobile application called PRIME to help young people with schizophrenia achieve their goals and improve quality of life.

  WHAT IS PRIME: A personalized mobile experience that helps you make and achieve goals, a safe community for users with similar interests and struggles to connect, and support provided by motivational coaches via messaging

  IF YOU'RE ELIGIBLE: The study will be over a period of 6 months and involves the following procedures: clinical interviews, self-report questionnaires, a computerized task, and using the mobile application, PRIME for 3 months

- Participants can receive up to $280

- (1Sept2015)

Are you up to date with your TdaP (Tetanus, Diphtheria, and Pertussis) vaccine?

Lovelace Scientific Resources invites you to learn about a research study for adults and adolescents

You may be eligible if you are:

- Adults: age 19-40 years
- Willing to attend all visits and comply with all study procedures

For more information, call:
Lovelace Scientific Resources
505-348-9700
or go to
www.LSRtrials.com

No medical insurance required. All study related exams, study medication, and laboratory tests are provided at no cost while participating in the study. Compensation for time and travel may be provided to qualified participants.

Alcohol Drinkers 21 - 30 needed for UNM / MRN Research Study

We are seeking healthy drinkers 21-30 years of age for a study of the effects of cognitive training and brain stimulation on brain functioning and drinking.

The study involves 8 appointments at the Mind Research Network and Department of Psychology at the University of New Mexico, for a total of approximately 10.5 hours. You will be compensated up to $225 for your participation.

The Mind Research Network is located on the North Campus of University of New Mexico and the Department of Psychology is located on the UNM campus off of Central Avenue.

If you would like to be considered for the study, please call 925-2368 or email show contact info

Please mention "Alcohol Training study". UNM-HSC HRRC #12-520.

Posted 5 hours ago (1 Sept 2015)

Walter Reed

- Yellow fever studies in Cuba (1900): intentional exposure
- Paid $200 in gold
- $500 bonus for successful infection
- Payable to family in the event of death.

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

$$$$ for research

- Advertisements in newspapers, the internet, and in hallways and bathrooms.
- Most research organizations and academic medical centers pay at least some some participants (24-80%) (Dickert et al Annals, 2002)
- Few have specific guidance about when or how to pay

$$$ response, willingness, motivation

- 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 Epidemiology2003; 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 Ethics2004)
- Money as motivation to participate
  - >90% of those surveyed said financial compensation was a main motivation (Bigorra & Banos 1990; vanGlederen et al, 1993; Hassar et al, 1993)
  - Healthy volunteers do have other motives: curiosity, altruism, knowledge, etc

$$$$Topics

- Payment types: reimbursement and inducement
- OHRP Guidance
  - Coercion and undue influence
- Payment for research subjects:
  - Population: minorities, marginalized, vulnerable, sick, children….
  - Payment practices for research participation
- IRB views
- Discussion

Payments: reimbursement and inducement

- Reimbursement refers to payments that remove financial deterrents to research participation by reimbursing for out of-pocket expenses.
- Inducement refers to payments that may encourage an individual to participate in the research:
  - *Appreciation* payments are given after completion of the research to thank the person for participating
  - *Compensation* pays participants for the time and inconvenience of research participation.
  - *Incentive* payment: offered to secure the needed number of participants for the research project

Paying for research participation

- When does compensating subjects undermine informed consent or parental permission? (OHRP FAQ #7)
- Human subjects often are provided payment for their time, inconvenience, and out-of-pocket expenses.
- Remuneration for risk, however, has been a source of controversy because it is challenging to assign a reasonable level of payment and because it is difficult to assess what constitutes undue influence.
- In reality, however, many subjects would not participate in research involving risk absent some level of remuneration.

Coercion and undue influence

- Payment of research subjects as an inducement to participate, compromising informed consent
- Violation of the ethical requirement that research participation should be voluntary
- Could compromise the scientific integrity of research; possibly motivating prospective subjects to withhold important information?
- May wrongly commodify a practice that should be based on altruism
- Lead to injustice if some groups are more likely to respond to financial incentives than others.

Views

- Conceptual and ethical confusion to regard the offer of financial payment for research participation as *coercive*, since it is an offer and not a threat. (Wertheimer & Miller 2007)
  - "Genuine offers are not threats";
  - Requires: (1) right violation if non-compliant, and (2) Having no reasonable alternative.
- Why would payment compromise 'voluntariness' in research if it doesn't in other situations/settings?
- Freedom-enhancing offers
- If financial offers can result in invalid consent: eg., if the prospective subject is not able to make a competent and rational decision in response to the offer.

- Inducement is not necessarily ‘undue’.
- Inducement is undue when it predictably triggers irrational decision-making given the agent’s own settled (and reasonable) values and aims.
- “An offer is troublesome if it is so ‘‘attractive [that it] may blind prospective subjects to the risks or impair their ability to exercise proper judgment’’ about the risks of participation (OHRP)

Populations

- There are theoretical concerns that burdens of clinical research will be disproportionately experienced by the poor because they will be unduly influenced by compensation, and overlook risk.
- Minorities and disadvantaged patients are often under represented in research and clinical trials
- NIH guidelines: appropriate representation
  - To ensure health needs of diverse populations are met with accurate data

Research participation by race, SES[1]

	Weighted proportion of each group who reported prior participation *n* = 221% (95% CI)
Race/ethnicity	
Non-Hispanic white	14 (11–17)
Non-Hispanic black	2 (0.8–6)
Non-Hispanic other	14 (6–30)
Hispanic	4 (2–8)
Annual household income	
<$30,000	13 (9–18)
$30,000–$60,000	10 (7–15)
$60,001–$100,000	10 (7–15)
>$100,000	14 (9–21)

Table 2. Proportion of previous research participants by race/ethnicity and income.

Walter et al, Clin Trans Sci 2013. Research Participation by Low-Income and Racial/Ethnic Minority Groups: How Payment May Change the Balance

$$ Requested for research participation[1]

- Median requested payment for participation in the low-risk research was $300 (mean=$1,160; range $0–$10,000).
- Among those willing or unsure if they would participate: the median requested payment was $300 (mean=$1,119.
- Requested payment differed significantly by annual household income: the $30,000–60,000 group was requesting less payment ($500) than the lowest income group ($900)
- Requested payment differed by race/ethnicity: Hispanics requesting more payment ($500) than non-Hispanic whites ($300)

HIV

- HIV vaccine trial: small number join for money
  - 14% joined was for financial reimbursement; 56% reduce risk behavior; 46% to get protection from HIV.75% to receive services or compensation (Colfax et al, 2005)
- Monetary incentive works better than non-monetary incentive
  - Project Respect: enrollment, participation & retention (Kamb et al, 1998)
- African American drug users view payment for HIV research participation as “income” (Slomka et al, 2007)

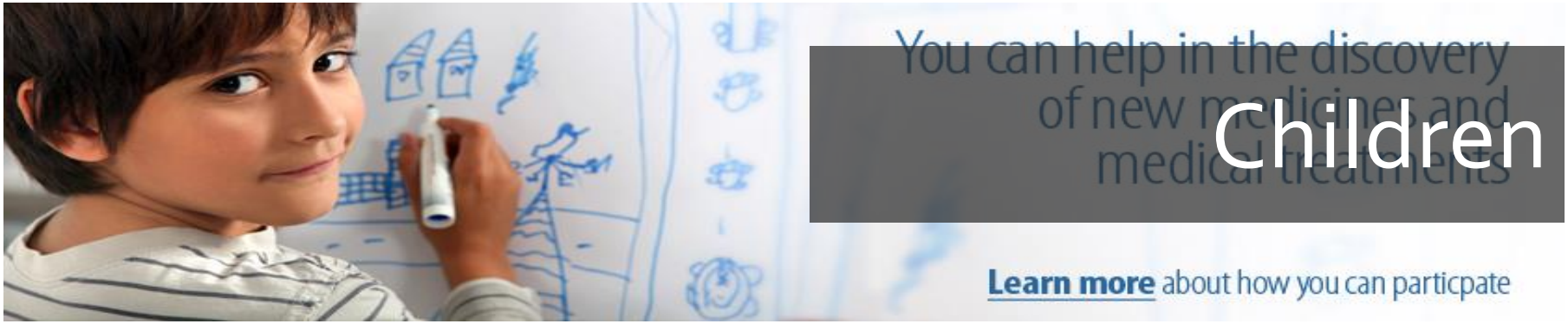
Drug users

- Many especially worry about paying drug users
  - What do you think the biggest concern is?
  - What are your views? Why?
- 99% of clinical researchers compensate; 86% pay cash[1]
- Neither the amount or the mode of paymet influences rates of relapse or new drug use[2]
- Financial incentive the strongest predictor of IDU willingness to participate in HIV vaccine trial[3]
- Financial incentives increase retention, tracking efforts, and participant satisfaction [4]

[1]McGrady et al., Ethical issues in informed consent with substance abusers; *J Consult Clin Psychol* 1999. [2]Festinger et al, Do research payments precipitate drug use or coerce participation? *DAD* 2005; [3]Golub et al Changes in willingness to participate in HIV vaccine trials among HIV-negative injection drug users AIDS&Beh 2005; 4 Festinger et al., Higher magnitude cash payments improve research follow-up rates without increasing drug use or perceived coercion DAD 2008

Other vulnerable, or marginalized groups

- Vulnerable: pregnant women, incarcerated, institutionalized, children
- Homeless
- Mental health problems
- Sex workers
- Illiterate populations
- Migrants, refugees



Children

- Children < 9 years of age generally have problems appreciating the role and value of money
  - *$68 because it's her "lucky number." Also requested "a million dollars*"
  - *Refuses to participate with no incentive. When offered an incentive ($91), changes mind and accepts it; expressing intent to buy a car with the money; would also accept $85 so he "could get a motorcycle"*
- Children => 9 years were able to appreciate the role and value of money.
  - $25-$30; $100; $20 or $25; $$75 or $100; Fifteen bucks

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Developing Countries

- Access to ARTs in preventive vaccine trials
  - Clearly desired by any subject participating
  - Raised concerns that it was too attractive to refuse
- Burial expenses for an autopsy study of Cerebral malaria in Malawi
  - Cultural views?
- Cell phones for study subjects in SA mine
  - Too attractive?

Mfusto-Bengo & Taylor Trends in Parasitology 2002

Developing Countries

- Access to ARTs in preventive vaccine trials
  - *Attractive but not a threat*
- Burial expenses for an autopsy study of Cerebral malaria in Malawi
  - *Attractive but not a threat*
  - *Cell phone issue: similar?*
- In neither case is the subject worse off for refusing than for never being asked
- People will enroll: predictable but not coercive

Developing countries

- Concerns about exploitation
- Local culture
- Local regulation: reimbursment, incentive and inducement

IRB Members

- Concern that any payment may be coercive or unduly influential of potential research participants, with increasing concern for higher payments used as incentives or as payment for risk.
- IRBs do NOT consider payment as a benefit
- Research to about how IRB members' perceptions may influence approval of protocols?
  - Investigators may be discouraged from offering payments if they think that they will be perceived to be incentives or payment for risk by IRBs.

- There is wide variation in payments for studies.
- There is no consensus regarding what is appropriate or fair payment for clinical research participation; most IRBs do not have written guidelines for determining how to pay[2,3]
- Members of IRBs demonstrate the broadest support for reimbursement of expenses or payment for time and inconvenience.[4]

2. Ripley et al, Why do we pay? A national survey of investigators and IRB chairpersons. J Empirical Res Hum Res Ethics 2010; 3; Grady et al, An analysis of U.S. practices of paying research participants; Contemp Clin Trials. 2005; 4 Largent et al, Money, coercion, and undue inducement: attitudes about payments to research participants. IRB . 2012.

Paying for research

- Non-monetary offers
- Medical care
- Gift cards
- Payments: cash, check

Largent et al, Money, Coercion, and Undue Inducement IRB: Ethics and Human Research 2012

Figure 1.
Percentage of Respondents Concerned about Influence on Participant Decisions and Behavior

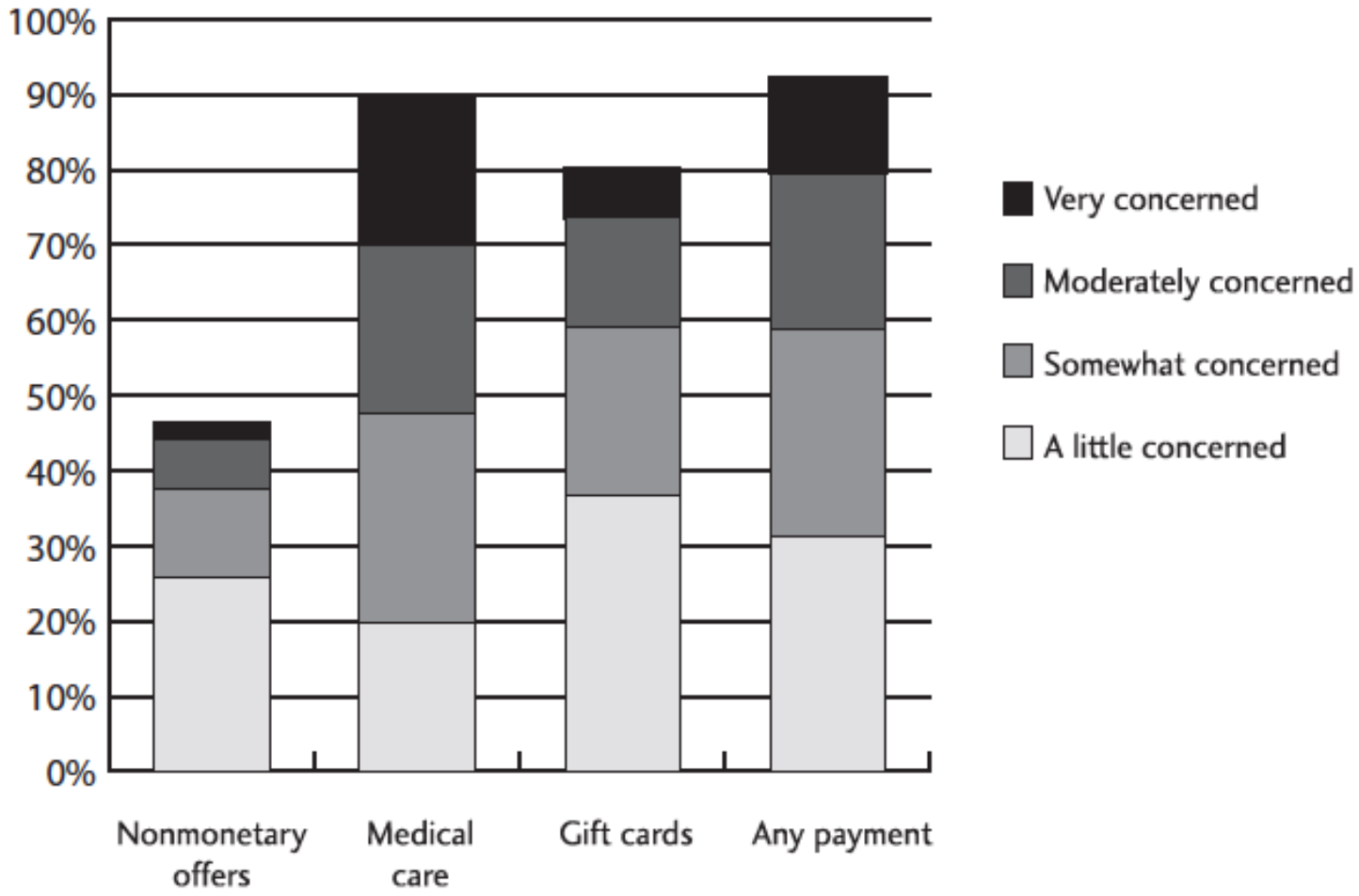
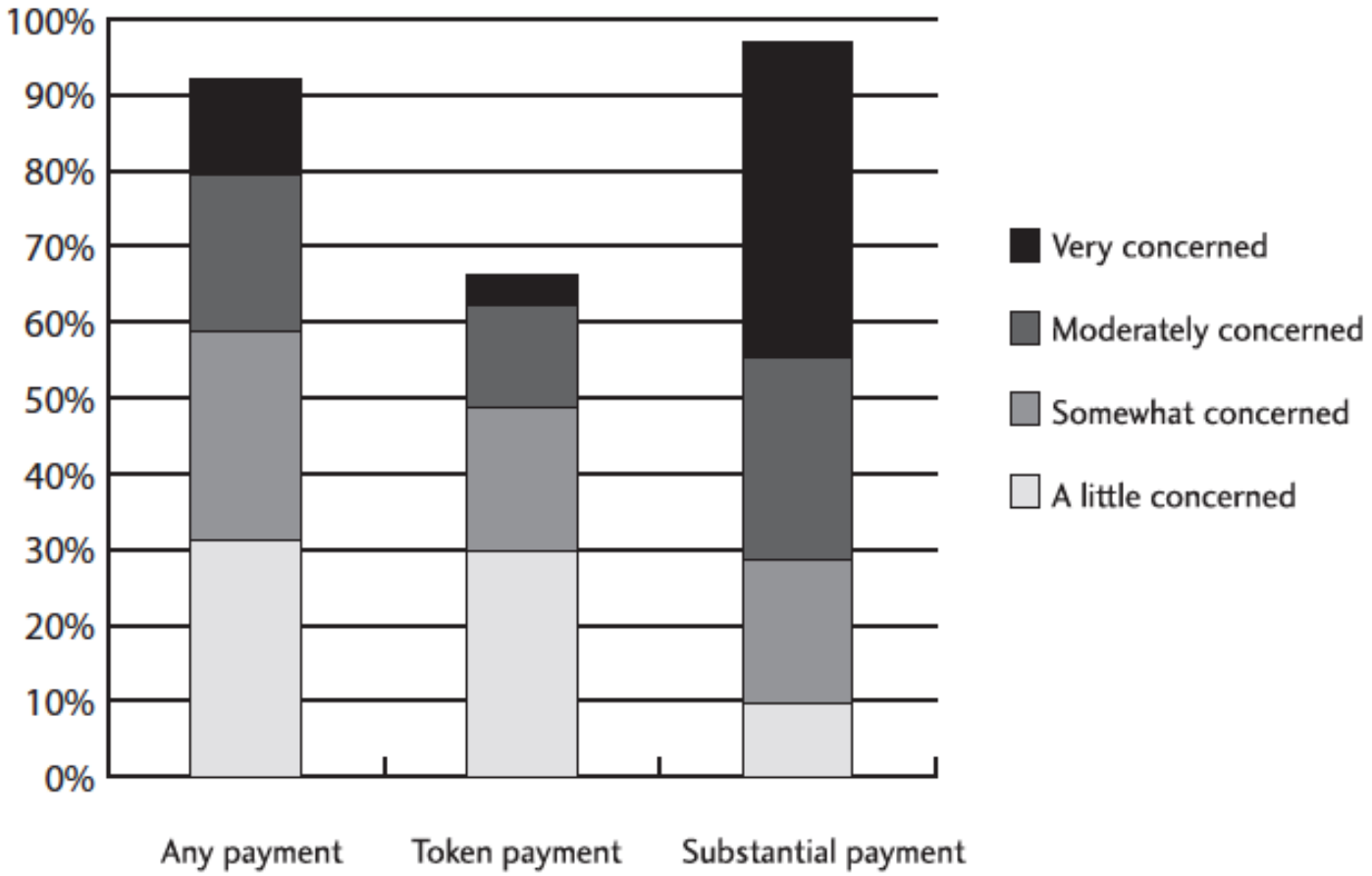


Figure 2.
Percentage of Respondents Concerned about Payment's Influence on Participant's Decisions and Behavior



- Lack of consistent standards emerged between and even on single IRBs.
- IRBs wrestled with defining of ‘coercion’ and ‘undue inducement’, often using the terms synonymously
- They rely on ‘*gut feelings*’, and seek compromises.
- Ambiguities regarding reimbursement vs. inducement
  - whether subjects should be paid differently based on income
  - Types of studies
  - providing free care in research,
  - whether and how recruitment flyers should mention compensation

Klitzman J Med Ethics 2013

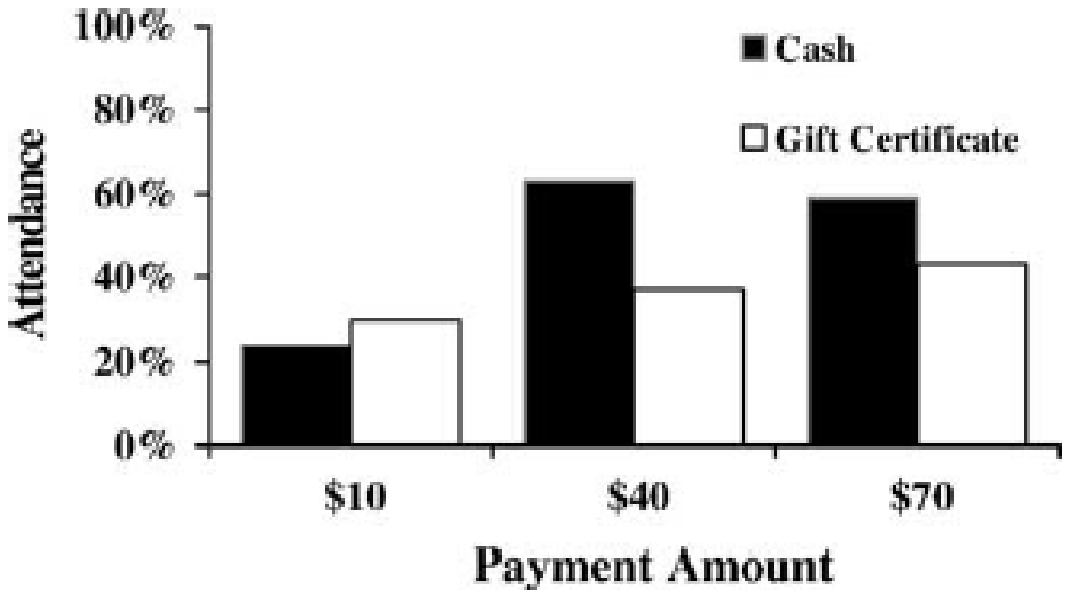


Fig. 1. Percentage of participants who attended their 6-month follow-up as a function of magnitude and mode of payment.

Festinger et al. DAD 2005

IRB and Children

- Attitudes vary widely on what is 'reasonable' compensation
  - Eg: For a single non-therapeutic blood test: 53% found reimbursement acceptable; 18% unacceptable; 28% would allow under some conditions.
- Views on: cash, toys, 'trust' or treasury bond, split between parent and child, only expenses
- Vary by length of service; research experience;
- ALL agree that more guidance would be useful

Crites et al, Payments to participants in pediatric research: variation in IRB members attitudes. IRB: ethics and human research 2013; Whittle et al,. IRB practices regarding assent in pediatric research. Pediatrics. 2004

OHRP guidance

- ORHP FAQ #7
- http://www.hhs.gov/ohrp/policy/consentfaqsmar2011.pdf
- *previously* noted
  - (1) In no case should remuneration be viewed as a way of offsetting risks; that is, it should not be considered a benefit to be weighed against study risks.
  - (2) The level of remuneration should not be so high as to cause a prospective subject to accept risks that he or she would not accept in the absence of the remuneration.

OHRP guidance

- The first sentence:
  - (1) In no case should remuneration be viewed as a way of offsetting risks; that is, it should not be considered a benefit to be weighed against study risks.
  - *BECAUSE: it focuses on potential undue influence in the consent process (45 CFR 46.116) rather than IRB considerations (45 CFR 46.111)*
  - OHRP continues to assert that IRBs should not consider remuneration as a way of offsetting risks.

OHRP guidance

- The second sentence:
  - (2) The level of remuneration should not be so high as to cause a prospective subject to accept risks that he or she would not accept in the absence of the remuneration.
  - *BECAUSE: research community noted that these sentences had the effect of implying that in most cases any level of remuneration based on research risks could be considered unacceptable*
  - In deciding whether to participate in research, subjects should have the opportunity to assess when risks and benefits (including remuneration) are balanced in light of their individual circumstances.

OHRP

- FAQ has been changed to clarify that:
- Remuneration to subjects may include compensation for risks associated with their participation in research and that compensation may be an acceptable motive for some individuals agreeing to participate in research

UNM HSC

- UNM HSC policy discourages “highlighting” compensation in study advertisements;
  - however, the FDA guidance simply states that “Advertisements may state that subjects will be paid, but should not emphasize the payment or the amount to be paid, by such means as larger or bold type.” (slide # 3)
- UNM strongly prefers that compensation be issued via a “merchandise” card; but no such requirement exists in the federal regulations

Payment is OK!

- 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

PARTNERS HUMAN RESEARCH COMMITTEE
Suggested Monetary Compensation

- Blood draw for research purposes from healthy volunteers …. $5 - 25
- Noninvasive psychological testing or memory tasks ……$5 – 30/hr
- Focus groups (1-3 hrs)……$20 – 75
- Skin biopsy ……..$50
- Muscle biopsy, at the higher end of the range ……$50 – 100
- MRI scan, depending upon duration and use of contrast agent $50 –200
- Oral glucose tolerance test or other infusion tests, more if special preparation or diet required ……$50 – 150
- Lumbar Puncture ……$100
- 24 hour stay in sleep center or clinical research center, for relatively non-invasive activities: blood draws, IV lines, vital signs or other non-invasive clinical monitoring…… $100 – 200/ 24 hour stay
- Bronchoscopy with lavage in healthy volunteer subjects ……..$150 – 300
- PET scan with radiolabelled material, more if arterial or IV line placed … ……$200 – 300

21 CFR 50.20
Payment to Research Subjects

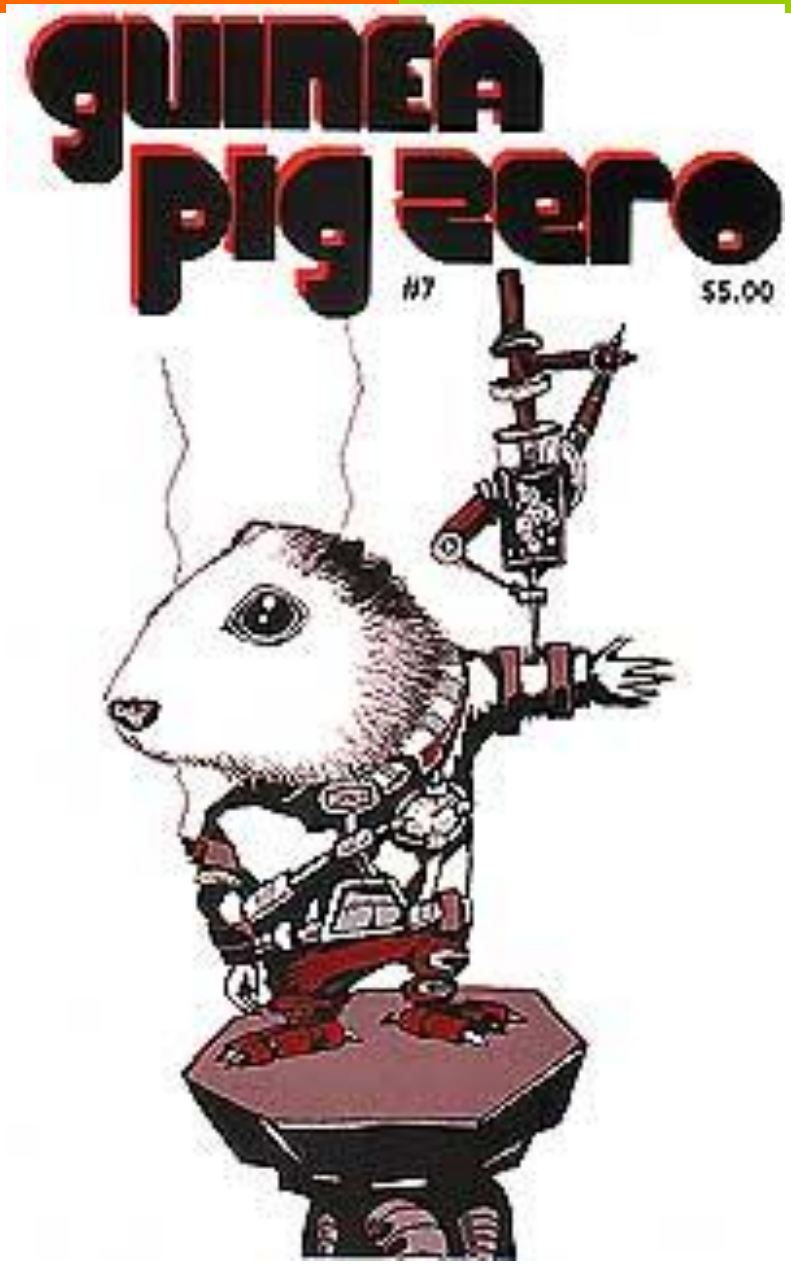
- Information Sheet Guidance for Institutional Review Boards and Clinical Investigators (http://www.fda.gov/regulatoryinformation/guidances/ucm126429.htm)

- The IRB should determine that the risks to subjects are reasonable in relation to anticipated benefits and that the consent document contains an adequate description of the: (1) study procedures; (2) the risks and benefits.
- It is not uncommon for subjects to be paid for their participation in research, especially in the early phases of investigational drug, biologic or device development.
- Payment to research subjects for participation in studies is not considered a benefit, it is a recruitment incentive.
- Financial incentives are often used when health benefits to subjects are remote or non-existent. The amount and schedule of all payments should be presented to the IRB at the time of initial review. 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.
- Any credit for payment should accrue as the study progresses and not be contingent upon the subject completing the entire study.
  - Unless it creates undue inconvenience or a coercive practice, payment to subjects who withdraw from the study may be made at the time they would have completed the study (or completed a phase of the study) had they not withdrawn. For example, in a study lasting only a few days, an IRB may find it permissible to allow a single payment date at the end of the study, even to subjects who had withdrawn before that date.
- While the entire payment should not be contingent upon completion of the entire study, payment of a small proportion as an incentive for completion of the study is acceptable to FDA, providing that such incentive is not coercive.
  - The IRB should determine that the amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn.
- All information concerning payment, including the amount and schedule of payment(s), should be set forth in the informed consent document.

Discussion points

- Minorities and poor population are underrepresented in research, not over-represented due to undue influence of monetary incentive
- Increasing payments could result in increased minority population involvement.
- Higher payment requests could reflect less trust in the research; less access to research opportunities.
- Better understanding of factors that influence minorities participation or lack of participation is needed

- Fears: historical legacy of abusive experimentation in which investigators have exploited human subjects continues to color the ethical appraisal of clinical research
- Human research evokes moral discomfort, as research participants are being used to advance science and promote the social good – or bad.
  - Incentives for research participation heighten moral discomfort.
- Models: Market; Wage-payment; Reimbursement
- Ethical review committees help to mitigate concerns and threats to the voluntariness of research participation but – they 'wrestle' with the issues, and there is WIDE variability and ambiguity!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