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Compensating Participants in Research

School of Nursing
University of Maryland Baltimore
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James Campbell, MD, MS

UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE
CENTER FOR VACCINE DEVELOPMENT
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Compensation/Payment

- **Why pay research participants?**
  - Incentive to enhance recruitment/retention
  - Enable them to participate without financial sacrifice
  - They are contributing to societal good

- **Why all the ethical/regulatory fuss?**
  - Can it/will it ***unduly*** influence participation?
  - Can it/will it obscure risks? Exploitative?
  - Is the incentive so great as to cloud judgment?
- **Can't we just rely on federal regulations? (Is there a calculator?)**
  - Guidance is sparse
  - No formula

US Department of Health and Human Services

- **January 2018, FDA updated its information sheet**
  - Old language: “Other than reimbursement for reasonable travel and lodging expenses, IRBs should be sensitive to whether other aspects of proposed payment for participation could present an undue influence, thus interfering with the potential subject’s ability to give voluntary informed consent.”

  - **OHRP FAQs and FDA guidance**
    - define undue influence as “an offer of an excessive or inappropriate reward or other overture in order to obtain compliance.”
    - “difficult for IRBs to draw a bright line”, “use discretion”
    - paying subjects is common and, in general, acceptable; remuneration should be just and fair

https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-september-30-2019/index.html

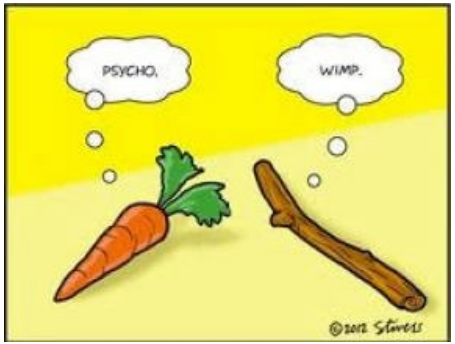
US Department of Health and Human Services

- **OHRP FAQs and FDA guidance - continued**
  - Payments should not be so high as to "compromise a prospective subject's examination and evaluation of the risks or affect the voluntariness of his or her choices"
  - Consent should have a detailed account of terms of payment, when less or no payment will be given, and be prorated for time in the study rather than delayed until completion, but permits payment of a small proportion as an incentive for completion of the study, as long as not coercive.
  - Compensation should not be deemed as a means to offset risk
  - Payment is not considered a benefit (as in benefits and risks) although it is an acceptable motive for joining
- **The only regulatory codes pertaining to this topic**
  - 21CFR50.20 and 45CFR46.116 (FDA and HHS sections on informed consent)
  - "minimize the possibility of coercion or undue influence."
  - Not surprising investigators and IRBs get confused

https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-september-30-2019/index.html

US Department of Health and Human Services

- **SACHRP (Secretary's Advisory Committee on Human Research Protections) states that current guidance is "problematic"**
  - Most payments do not lead to undue influence
  - Payments are ethically important – to complete trials, to lead to diverse participation, and to acknowledge the value of participant contribution
  - Tasked with providing advice on how to improve
- Separate 2 concepts: coercion and undue influence



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US Department of Health and Human Services

- **SACHRP (Secretary's Advisory Committee on Human Research Protections) states that current guidance is "problematic"**
- Undue influence= when there is
  - An excessive offer of something valuable or desirable that leads to
  - poor judgment or a compromised decision-making process, which in turn leads to
  - a decision to engage in harmful activity that seriously contravenes the decision-maker's interests or obligations.
- The mere fact that payment influences a decision does not make that decision involuntary or due to undue influence

https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-september-30-2019/index.html

US Department of Health and Human Services

- **SACHRP**
- Payments that do not raise concerns about undue influence
  - Reimbursement- such as transportation, lodging, childcare, additional medical expenses, meals outside of home.
    - Expected to minimize financial impact of joining
    - Presumably no “net benefit” to reimbursement
  - Compensation- recognizes the societal value of participant time and burden
    - Presumably makes participation as attractive as other ways of spending time
    - May be adjusted based on time and inconvenience/burden
    - IRBs should not make determinations in the abstract- but rely on investigators to justify
    - Benchmarks include average working wage and purchasing parity ratio
    - “full compensation” vs “equitable compensation” – SACHRP favors equitable.
  - Appreciation- small payments/gifts not intended to meaningfully reimburse or compensate

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US Department of Health and Human Services

- **SACHRP**
  - Payments that could raise concerns about undue influence
    - Incentive payments- attempt to make participation more attractive than alternatives
      - Not inherently impermissible, but should be reviewed
      - Participant 1: risks worry me, but I need the $ and I have thought through risk/benefit
      - Participant 2: desperate for $, don't want to hear about risks, just sign me up and pay me.
      - Should IRBs err "on the safe side" to avoid Participant 2 scenarios?
        - No, reasonable incentive payments are encouraged
        - Available evidence suggest payments increase levels of caution and perception of risk, not vice versa. They also draw a clear distinction between research and clinical care.
        - Rather, review incentive, consent process, disclosure of risks/benefits
        - Some examples of approaches: sufficient time, comprehension "tests", waiting period to discuss with loved ones, cogent consent forms/discussions
    - The goal is to minimize, not eliminate, the possibility of undue influence

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US Department of Health and Human Services

- **SACHRP**
  - **Timing**: Recommend prorated payments paid at periodic intervals
    - Purpose is to minimize the effect backloading reduces autonomous choice to withdraw
    - May not apply for short studies
    - Completion bonus is acceptable as an incentive, when not excessive
      - Encourages completion and data are most valuable to all if most participants complete
      - Large completion bonus or sole payment at the end also may encourage participants to deceive researchers by not divulging things that could force withdrawal
  - **Advertising payment**: SACHRP recommends allowing this
    - Since the purpose is to facilitate enrollment, participants need to be made aware
    - Truthful, clear, appropriately contextualized

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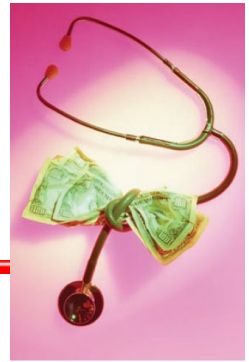
Payment of clinical research subjects

Christine Grady

Department of Clinical Bioethics, Clinical Center, NIH, Bethesda, Maryland, USA.



- **Why compensate?**
  - Biomedical and behavioral research are necessary to improve human health
  - This research relies on human participation
  - Payment encourages participation
  - It may make participation revenue neutral, compensate for a societal contribution
  - May improve racial, ethnic, social, and gender diversity

The Journal of Clinical Investigation http://www.jci.org Volume 115 Number 7 July 2005

Ethical concerns about the payment of research participants

Payment may be perceived as:	Related comments and questions
Coercion	Coercion involves a threat of harm. Thus, an offer of money in return for research participation is not coercion.
Undue inducement May compromise informed consent by: (a) reducing interest in understanding risks related to research; (b) reducing the voluntary nature of the decision to participate Money may unduly influence individuals to misrepresent themselves	Undue inducement is not well defined Limited data suggest that payment does not affect understanding or perception of risk. The adequacy of understanding as part of informed consent can be assessed. Voluntary decisions can be made when inducements are offered, even in the setting of limited or poor financial options There are limited data on the influence of money on informed consent Other incentives may be as powerful as money Careful eligibility screening can minimize risk of misrepresentation
Disproportionate research burden on the poor	Sociodemographics of research participants are not well known Inadequate financial reimbursement might disproportionately exclude the poor Paid participation may be an opportunity, not a burden
Commodification	Services offered as part of research participation are not the same as "selling" body parts or sex and may be of little risk to the health and well-being of the participant

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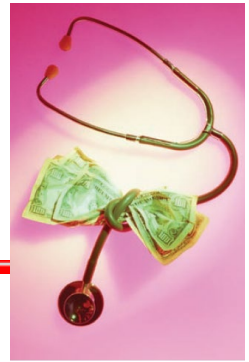

- **Other points**
  - No data to show that payment obscures risk perception; some data to show it does not
    - One study Would $500 impair judgment? 50% said yes, others, but only 20% said yes for themselves
  - The idea of undue influence is thought by some a misplaced worry and possibly “unwarranted paternalism”
  - Other of our voluntary decisions are motivated by a variety of factors, including money (salary, purchase price), but decisions are complex

The Journal of Clinical Investigation http://www.jci.org Volume 115 Number 7 July 2005

Table 1
Models of payment for the participation of research subjects

Model	Payment serves as	Amount determined by	Potential advantages	Potential disadvantages
Market	Incentive	Supply and demand; market rates	(a) More rapid recruitment. (b) Completion bonuses encourage subject retention and high completion rate. (c) Possibility of profit for participants. (d) Little or no financial sacrifice by subject.	(a) Undue inducement possibly resulting in: incomplete assessment of risks and benefits by subject; subject concealing information to ensure enrollment/retention. (b) Competition between studies; better-funded studies more likely to meet recruitment goals. (c) Different levels of payment at different locations for multicenter trials.
Wage-payment	Compensation	Standardized "wage" for time and effort, suggested to be commensurate with wages for unskilled, but essential jobs; additional payment for extra burdens such as endurance of uncomfortable procedures	(a) Recognizes contributions of participants. (b) Uniform payment across studies. (c) Equal pay for equal work. (d) Less risk of undue inducement.	(a) May have little impact on recruitment. (b) Might undercompensate some subjects in relation to regular wage and preferentially attract others.
Reimbursement	Reimbursement	Expenses incurred (transport, meals, lodging); with or without reimbursement for lost wages	(a) Makes research participation revenue neutral. (b) Little risk of undue inducement. (c) Little or no financial sacrifice for subject if lost wages are reimbursed.	(a) May have little impact on recruitment. (b) Uneven reimbursement from subject to subject. (c) Reimbursement costs for high-salaried subjects may result in the targeting of low-income populations. (d) Financial sacrifice for subject if lost wages are not reimbursed.
Appreciation	Reward	Token of appreciation given at the conclusion of study	(a) Expresses gratitude for contribution made. (b) Not market dependent. (c) Avoids undue inducement.	(a) Likely to have no impact on recruitment. (b) No basis for consistency.

Table modified from *The New England Journal of Medicine* (46).

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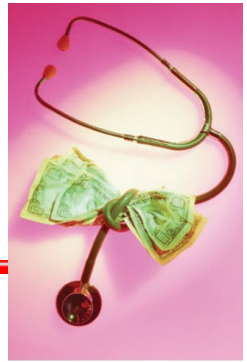

- **Healthy volunteers vs patient-participants**
  - Some argue ok to pay healthy volunteers but not patients
  - Healthy volunteers may be considered independent contractors, may get little to no benefit, and are motivated partially by money
  - Some worry about paying patients because they are “vulnerable”
    - Possibly true for a few reasons, especially because their physician may be their researcher- therapeutic misconception
    - Also possible that payment would help mitigate the misconception
  - If payment is to reduce personal costs, in some cases reasonable

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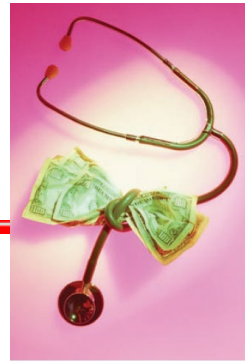

- **Children**
  - Concern that payment to parents could sway their decision
  - Concern that parents are using their child as a commodity
  - However, cost, inconvenience, time off work for parent to bring child to study is similar to if they brought themselves
  - Risks to children are carefully controlled/reviewed/regulated in studies
  - Some argue that children should get gifts for participation (appreciation)
  - *(Our group uses the wage-earner model for parents, adds reimbursement for parking, and, when sponsor sanctioned, small tokens of appreciation to the children. We also encourage parents to "share" the compensation.)*

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Paying Research Participants: Regulatory Uncertainty, Conceptual Confusion, and a Path Forward

- 67-page treatise on the topic
- Most still are concerned about too much or any pay; they believe we may be considerably underpaying
- CIOMS (Council for International Organizations of Medical Sciences) says “participants should be reasonably reimbursed for costs directly incurred… and compensated reasonably for their time and inconvenience… Compensation must not be so large as to induce participants to consent to participate against their better judgement. A local research ethics committee must approve reimbursement and compensation…”

Yale J Health Policy Law Ethics. 2017 ; 17(1): 61–141.

The ethical anatomy of payment for research participants

- Argue “researchers have a *prima facie* moral obligation to offer payment to research subjects, which stems from the principle of social beneficence.”
- Biomedical research is a social practice aimed at a common good- generalizable scientific knowledge and improved health – personal and public. These aims are highly valued. They are critically dependent on enrolment and retention.
- Belmont Report Principles
  - Autonomy- reduced if high pay; also reduced if no or low pay? And what about autonomy to choose which activities to be paid for?
  - Justice- allow those of all means to participate
  - Beneficence- allows for revenue-neutral participation

Medicine, Health Care and Philosophy (2022) 25:449–464
https://doi.org/10.1007/s11019-022-10092-1

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WORKSHEET: Payments

NUMBER	DATE	PAGE
HRP-313	10.29.2020	1 of 1

The purpose of this worksheet is to provide support for the convened IRB or Designated Reviewers when evaluating payments to subjects or their legally authorized representatives. This worksheet is to be used. It does not have to be completed or retained.

1 Requirements for Payments (All must be **"Yes"**)

☐ Yes ☐ No	All payments are described in the protocol including:	
	☐ Yes ☐ No	Amount
	☐ Yes ☐ No	Method
	☐ Yes ☐ No	Timing of disbursement
☐ Yes ☐ No	Credit for payment accrues as the study progresses.	
☐ Yes ☐ No	Payment is not contingent upon completing the entire study.	
☐ Yes ☐ No	The amount of payment and the proposed method and timing of disbursement is neither coercive nor presented undue influence.	
☐ Yes ☐ No	Any 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.	
☐ Yes ☐ No	All information concerning payment, including the amount and schedule of payments, is in the informed consent document.	
☐ Yes ☐ No	Compensation does not include a coupon good for a discount on the purchase price of the product once it has been approved.	

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Practical summary

- It is ok to pay (and often ok not to pay)
- Choose your “model” and adopt it
- If using “wage earner” base your pay on time and inconvenience, not risk
- Prorate and keep bonus, if used, reasonable
- For children, pay parent and give appreciation gift to child
- For international, work with partners on reasonable compensation within your “model”- review by CAB, local IRB
- For prisoners, work with experts on reasonable compensation, if appropriate (only about half of states allow for compensation, many require superintendent approval)
- Use balanced advertising when stating your compensation

Reading

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Thank You

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