

Ethical Issues in Providing Payment for HIV and Drug Use Research

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Objectives

Case study

Personal interest

How incentives are used in research

Why should we care

Potential solutions



Case Study

“We are conducting a HIV cure study among HIV positive people who inject drugs. You may not directly benefit from participation in this study. For more information please contact Brandon Brown at 951-990-9899”

Text: We are conducting a ¹ HIV cure study among positive injection drug users. You may not directly benefit from participation in this study. ²

| | Including text | Proposed amount |
|---|--|-----------------|
| 1 | No additional text | \$0 |
| 2 | biomedical, multiple visit, 2 year | \$2,000 |
| 3 | biomedical, multiple visit, 2 year In order to participate, you must halt the use of your antiretroviral treatment, which may make you sick or infectious | \$15,000 |

Case study-what are the issues?

There is diversity in decision making

- Wording+details
- altruism
- experience in research
- Perceptions
 - Payment & safety

Case study-other issues

Would knowing what has been provided in past studies help your decision?

Is there something other than monetary payment that should be considered?

If your role changes, does your suggested payment change?

- the participant
- the IRB
- the PI of the study
- the study sponsor (funder)

Regulatory Parameters

The regulations instruct IRBs to minimize the possibility of coercion and undue influence during informed consent.

- Neither the Common Rule nor FDA regulations explicitly connect payment with 'coercion' or 'undue influence' or discuss payment at all

OHRP, Informed Consent FAQs

‘When does compensating subjects undermine informed consent?’

- “Paying research participants in exchange for their participation is a common and, in general, acceptable practice.”

“IRBs should be cautious that payments are not so high that they create an ‘**undue influence**’ or offer **undue inducement** to participate in research.”

‘Coercion’ and ‘Undue Influence’

OHRP’s definitions...

- “**Coercion** occurs when an overt or implicit **threat of harm** is intentionally presented by one person to another in order to obtain compliance.”
- “**Undue influence**, by contrast, often occurs through an **offer of an excessive or inappropriate reward** or other overture in order to obtain compliance.”

What Is 'Undue' Influence?

OHRP: undue influence occurs when payment **distorts** an individual's decision to participate in research

- Payment as undue influence = “**compromise a prospective subject's examination and evaluation of the risks or affect the voluntariness of his or her choices.**”
- Empirical question; some data that payment **increases** perception of risks and caution among subjects

Three Main Payment Categories

Reimbursement

- Payment for out of pocket expenses incurred as part of research participation

Compensation for time/burdens


- Subjects paid for time and undertaking burdens of research

Recruitment incentives

- Offered to improve recruitment and participation rates

COMMENT | VOLUME 3, ISSUE 10, PE456-E457, OCTOBER 01, 2016

Transparency of participant incentives in HIV research

Brandon Brown  • Jerome T Galea • Peter Davidson • Kaveh Khoshnood

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Applying the Ethical Payment Framework: We Need Data

Tags: ethical considerations, human subjects research, incentives, paying research subjects, payment

 Comments: 3

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Providing payment for participation in research studies is an **accepted practice**¹, but until recently little guidance existed on the ethical aspects when deciding research payments. Gelinas et al² recently **presented a framework** that researchers

Incentives are everywhere

Sometimes acceptable, sometimes not

Sometimes you pay, sometimes get paid*

Initial Interest in incentives

Incentives provided to similar participants in three studies of infectious diseases in Lima, Peru

| | Study 1 | Study 2 | Study 3 |
|-----------------|--|---|---|
| Money | None | U.S.\$7.00 | None |
| Gifts | Watch, makeup, purse, wallet | Annual birthday present, watch, perfume, makeup purse, wallet, hair dryer, lunches | Nothing |
| Health services | Birth control, genital wart removal, condoms and lubricants, and HIV testing | Birth control, genital wart removal, condoms and lubricants, STD treatment and medical attention for participants and family , annual breast exam and Pap smear, and HIV testing | Genital wart removal, HIV testing, annual Pap smear, and syndromic treatment |

Retrospective analysis of participation in clinical trial

| Measure | Agreed | Disagreed |
|---|--------|-----------|
| Study well described in consent | 14 | 2 |
| Participation is voluntary | 16 | 0 |
| Felt they could withdraw at anytime without loss | 13 | 3 |
| Enjoyed participating in the study | 15 | 1 |
| Primary reason for participating was CC screening | 16 | 0 |
| Study should have paid us | 3 | 13 |

Incentives History: Tuskegee Experiments

1932-72, Tuskegee, Alabama

Public health doctors (NIH) followed African American men with syphilis

- Goal of learning about the disease history

Did not tell participants they had syphilis

When Penicillin became available (1947), did not treat

- Prevented trtx. Elsewhere
- “It was important that they were untreated, and it would be undesirable to go ahead and use large amounts of penicillin to treat the disease, because you’d interfere with the study”



For participants: free medical care, meals, and burial insurance

Incentives in research

money, snacks, health care, gifts
means of encouraging participation*

- Skewed sample selection?
- Marginalized-risk*

"High-Pay" of the Day ®

A **\$17,000** Sleep Study!

Wow! Need some easy cash? Well, check out this High-Pay sleep study. Yes, this program will pay you **\$17,000** to participate in this unique sleep study being conducted by a government sponsored agency. One of many "High Pay-Get Paid" opportunities listed with NRG.

[Sign up](#) and check it out.

Latest Opportunities

- \$6,875.00
Males Between
18-45 years old
Generally healthy
Willing to provide up to
8 sperm samples.
- \$3,820.00
Do you have Hepatitis C?
Ages 18-60
Men & Women Needed!
Includes time and travel
compensation
- \$1,155.00
Healthy Men & Women
Needed!
Ages 18-55
Profile: Cocaine & Opiate
Abuse

Hypothesis-‘going rate’ of incentives in research

Market forces for going rate

- How much to pay someone for a FG in Riverside, California

Ex outside research

- short trip from Los Angeles to New York City
- Oversold flight
 - Offers for taking later flight-incremental incentives
 - \$200+flight
 - \$250+dinner voucher+flight
 - \$300+dinner voucher+flight

Planning a new HS research study*

What are appropriate incentives?

- Who should be making the decision?
- How should this decision be made?*

We have few incentive data

Currently no public record of incentives

- Not easily searchable-IRB

No guidance on what types/amounts to provide*

No working definition of excessive incentives

- Undue inducement*

The Belmont Report

**Ethical Principles and Guidelines for the Protection of
Human Subjects of Research**

**The National Commission for the Protection of Human Subjects of Biomedical and
Behavioral Research**

April 18, 1979

Why should we care about incentives?

Impact research outcomes

- Enthusiasm to join, not adhere
 - Examples of this in HIV research

Professional research subjects

- Fabricate/conceal-symptoms/behaviors*

Research studies “monetizing” acts-HIV testing*

Incentives in the literature

Few publications report incentives/payment

Dickert et al 2002 'Paying research subjects'

- 37.5% of orgs had policies on payment
- 20% of groups knew what % of their studies paid

Grady et al. 2005 'Analysis of US Practices'

- 467 clinical studies with range of payment \$5-\$2000
- Unexplained variation

Brown et al. Forthcoming in JERHRE (UCR IRB data)

The Need to Track Payment Incentives to Participate in HIV Research

By Brandon Brown, Jerome T. Galea, Karine Dubé, Peter Davidson, Kaveh Khoshnood, Lisa Holtzman,
Logan Marg, and Jeff Taylor
July-August 2018
Volume: 40, Issue: 4

Abstract: Providing incentives is an accepted and common practice in human subjects research, including clinical HIV research. While we know that financial incentives among similar studies can greatly vary, surprisingly little research exists on how to determine when such incentives are excessive or constitute an “undue inducement.” Multiple factors, such as risks and benefits, study procedures, study budget, historical precedent, recommendations from institutional review boards, advice from other investigators, and local regulations may influence decisions about appropriate incentives, but little empirical data exist about what incentives are offered to potential research participants. Rules for acceptable gifts, services, and compensation should consider study location and population, but without a clearer understanding of currently offered incentives and how these practices match up to ethical beliefs of appropriateness, we continue to follow perceived trends without critical assessment. Here, we present one potential approach to explore the impact of financial incentives on biomedical HIV research and to further clarify undue inducement: the development of a framework to support ethical decision-making about payment to participate. This framework is based on input from people living with HIV, biomedical HIV researchers, ethicists, former study participants, and IRB members and includes a database that allows for tracking payment practices.

Incentive Decision Making

Perfect world

- study team engages potential participants beforehand
- Review of previous studies, contact PIs
 - Lengthy process

Real world

- Make quick decisions, deadlines
- depends on budget, beliefs, standards

IRBs review incentive amounts proposed by investigators

- Approve or deny
- May rely on investigator to do 'due diligence'

Ex: How payments are evaluated (IRB)

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 (Check if “Yes”. All must be checked)

| | |
|--------------------------|---|
| <input type="checkbox"/> | All payments are described in the protocol including: (Check if “Yes”. All must be checked) |
| <input type="checkbox"/> | Amount |
| <input type="checkbox"/> | Method |
| <input type="checkbox"/> | Timing of disbursement |
| <input type="checkbox"/> | Credit for payment accrues as the study progresses. |
| <input type="checkbox"/> | Payment is not contingent upon completing the entire study. |
| <input type="checkbox"/> | The amount of payment and the proposed method and timing of disbursement is neither coercive nor presented undue influence. |
| <input type="checkbox"/> | 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. |
| <input type="checkbox"/> | All information concerning payment, including the amount and schedule of payments, is in the informed consent document. |
| <input type="checkbox"/> | Compensation does not include a coupon good for a discount on the purchase price of the product once it has been approved. |
| <input type="checkbox"/> | For studies that compensate subjects, the following statement is included in the consent form: ‘According to the rules of the Internal Revenue Service (IRS), payments that are made to you as a result of your participation in a study may be considered taxable income.’ |

Determining appropriate incentives*

- Query of incentive amounts/types across studies
- Full reporting DNE

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Trial record **1 of 21** for: brando

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The Role of Genital Warts in HIV Acquisition in Peru (VIVA)

This study has been completed.

Sponsor:

University of California, Los Angeles

Collaborators:

Espacio Comun

Universidad Peruana Cayetano Heredia

Information provided by (Responsible Party):

Brandon Brown, University of California, Los Angeles

ClinicalTrials.gov Identifier:

NCT01387412

First received: June 30, 2011

Last updated: November 30, 2015

Last verified: November 2015

[History of Changes](#)

So how do we solve this problem?

Data!!

Sample Vignette (variables from Table):

You have been living with HIV for X years. For the past year your health has been Y. You have the opportunity to participate in a phase II study of HIV cure including an intervention which has proved safe in phase I trials but with unknown efficacy, and with a Z risk of adverse health effects. In order to participate in the trial, you must halt your antiretroviral medications for the duration of the study period AA. Your income is BB. Would \$500 be an appropriate incentive to participate?

| <u>Years w/HIV</u> | <u>Health Status</u> | <u>Study Risk</u> | <u>Study Time in Years</u> | <u>Income</u> |
|------------------------|--------------------------|-----------------------|--------------------------------|---------------|
| X | Y | Z | AA | BB |
| 1 | Poor | High | 1 | Low |
| 5 | Okay | Medium | 2 | Medium |
| 20 | Excellent | Low | 10 | High |

Potential benefits of the results

Aid incentive decision making in HIV research

- Report results of tool

Empower participants/community leaders

Use incentive tool/database to.....

- analyze impact of incentives on recruitment/retention*

What about the risks

Transparency means access

- Participants say no to lower paying studies

Underfunded studies not allowed to proceed

If you don't think incentives are important

- HPTN
- PCORI
- IRB
- Harvard Payment Working Group
 - NIH, OHRP, IRB, CDC, pharma
 - NEJM article
- PRIM&R
- ASBH-JAB fellowship



Questions?



"We found the donut to be more of an incentive for him."

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