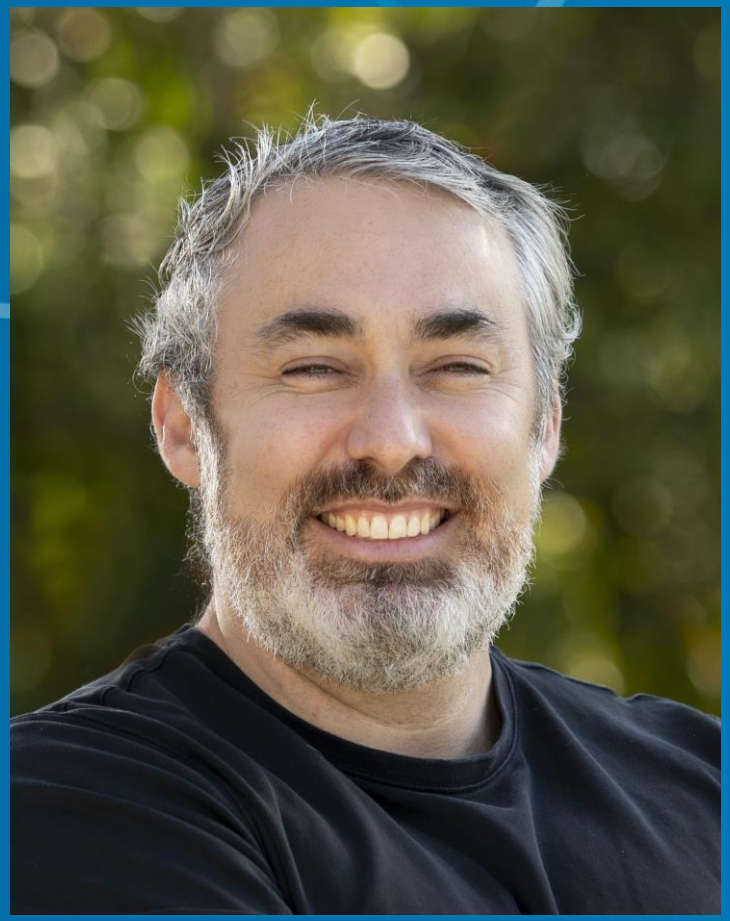
New Investigators Working Group Webinar Series

Payment to Research Participants: Regulations, Stakeholder Perspectives, and Data



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June 22, 2023, 10:00 - 11:00 AM PDT

Case Study: High Risk Research

"We are conducting a HIV cure related research study among people living with HIV who inject drugs. You may not directly benefit from participation in this study. For more information, please contact the study coordinator."

- We will pay you
  - $5
  - $100
  - $10,000
- What if the study is:
  - 1 visit
  - 5 visits
  - 2-year duration with multiple visits

Case Study: Issues in Deciding Payment

- What was provided in similar studies?
  - Disease state
  - Location, #visits
  - Risk
  - Funding amount
- Which hat are you wearing?
  - Study participant
  - IRB
  - PI of the study
  - Study Sponsor

Case Study: Decision Making

- Perfect world
  - Review previous studies
  - Contact other PIs
  - Ask participants what amount or type of payment is fair
- Real world
  - Quick decisions
    - Meet deadlines
  - Budget, beliefs, standards
  - Costs of participation (barriers)
  - Ethics committees rely on PI

Definitions of Payment

Reimbursement	Payment for out-of-pocket expenses incurred as part of research participation
Compensation for Time/Burdens	Participants paid for time and undertaking burdens of research
Recruitment Incentives	Offered to improve recruitment and participation rates

Most Ethically Problematic = Incentives

Incentive types

- Money
- Snacks
- Health care
- Gifts

Ethical issues

- Encouraging participation?
- Skewed sample selection?

Example 1
Join a study!
$6,875
Males between 18-45 years old who are generally healthy and willing to provide up to 8 sperm samples

Example 2
Do you have Hepatitis C?
Ages 18-60
Men and women needed!
Includes time and travel compensation

Example 3
Healthy men and women needed!
$1,800
Ages 18-55
Cocaine & Opiate Abuse Study

Example 4
A $17,000 Sleep Study!
Wow! Need some easy cash? Check out this high-pay sleep study. This government funded study will pay YOU up to $17,000 to participate.

No Federal Regulations Specifically Address Participant Payment

- Regulations do not require payment to participants for participation
- FDA (2018) guidance states:
  - Payment is considered a recruitment incentive not a benefit
  - IRBs should consider payment in relation to potential undue influence
    - IRBs should review the amount and plan for disbursement
  - Researchers need to disclose amount, frequency, and type of payment to the IRB at initial review

Federal Regulations

- Office for Human Research Protections (OHRP) Informed Consent FAQs
  - "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.

(HHS nd)

Coercion and Undue Influence

- **"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."
  - Payment as undue influence = "**compromise a prospective subject's examination and evaluation of the risks or affect the voluntariness of his or her choices**."

Evaluation of Payment at a Single Institution

Sample IRB Reviewer Checklist for Evaluating Subject Payments

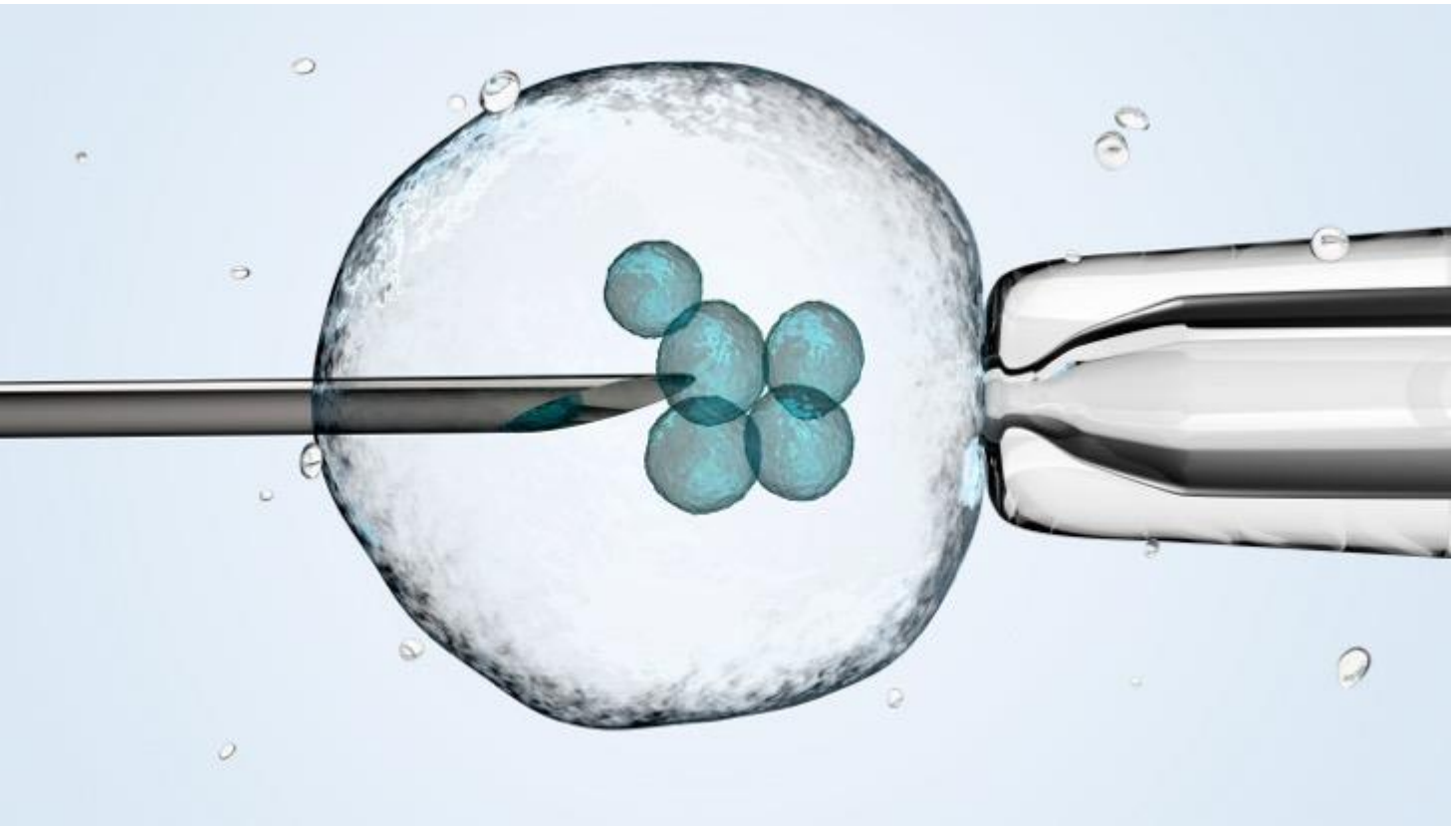
- ❑ **If payments are included, does the protocol specify (all must be checked as "Yes"):**
  - ❑ **Amount is specified**
  - ❑ **Amount is not so large as to be coercive nor does the amount present undue influence**
  - ❑ **Type or form of payment is specified (gift card, cash, check, etc.)**
  - ❑ **Timing/schedule of payment(s) is specified**
  - ❑ **Payment is not contingent upon subject completing study (i.e. prorated payment)**
  - ❑ **Any bonus for completion is reasonable and not presenting undue influence**
  - ❑ **All payment information is included in the consent form**
  - ❑ **Compensation does not include a coupon or discount voucher for the price of the product once it has been FDA approved**
  - ❑ **If payment is $600 or over per calendar year, the consent form includes statement re: taxable income and reporting to IRB**

Common arguments against providing incentives

- Impact research outcomes
  - Enthusiasm to join, not adhere
- Professional research subjects
  - Fabricate/conceal-symptoms/behaviors
- Research studies “monetizing” health actions

http://betablog.org/croi-2013-voice-trial-results-on-daily-hiv-prevention-for-women/
http://www.hivequal.org/hiv-equal-online/prep-works-for-transgender-women-but-only-if-they-use-it

Gene Edited Babies in China



- Gene edited babies study in China
  - CRISPR to remove CCR5
- Must pay 100,000 Chinese Yuan if they exit the study

(Bai 2018)

Pay to Participate in Research

- P4 Studies

(Shaw et al. 2017)

Get Paid for Risk

During the COVID-19 global pandemic, some vaccine researchers advocated for "human challenge trials" that would present high risks of harm to participants.

Should participants be paid to join a research study in which they will be knowingly exposed to COVID-19 to test a vaccine's efficacy?

(Cohen 2020)

So how do we solve this problem?

Data!

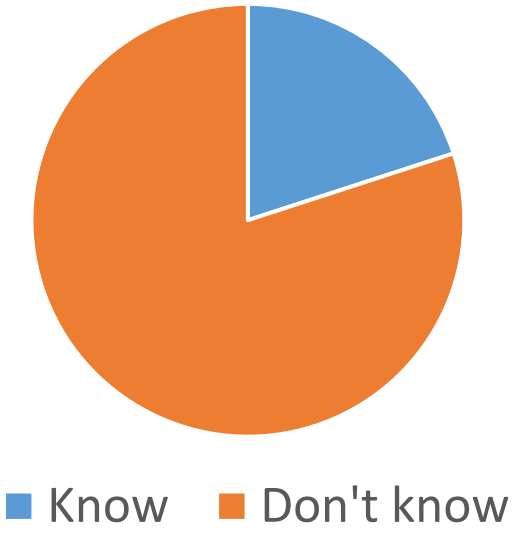
"When you two have finished arguing your opinions, I actually have data!"

Data on Payment

- No public record of participant payment
- Not easily searchable, even within 1 institution
- Nothing on clinicaltrials.gov
- No guidance on what types/amounts to provide
- No working definition of excessive payment

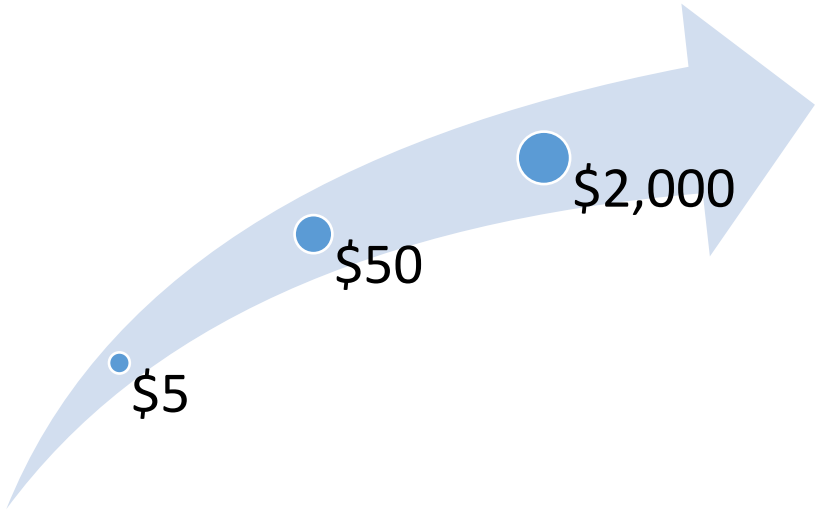
Few publications report incentives/payment

- 20% of orgs knew what % of their studies paid



(Dickert, N., Emanuel, E., and Grady, C. 2002)

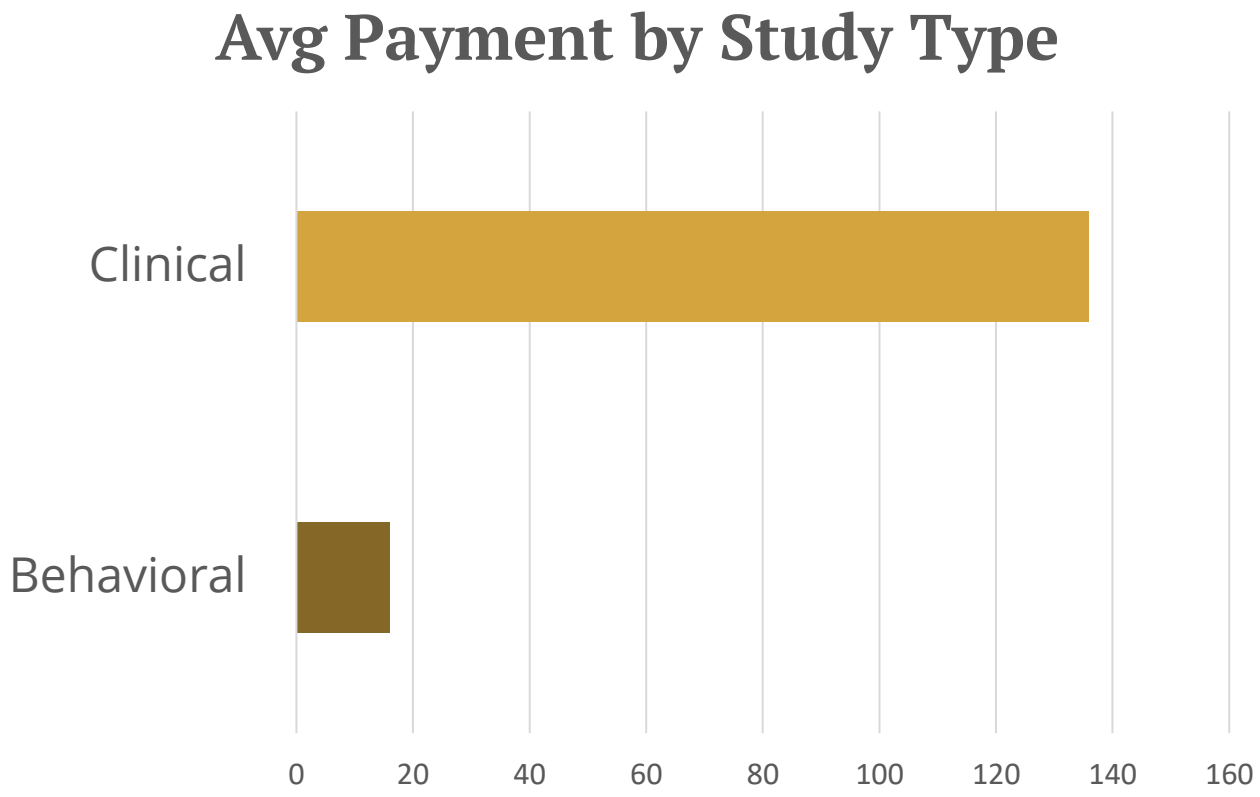
- Variation in payment for the same study at different sites



(Grady, C., Dickert, N., Jawets, T., Gensler, G., and Ezekiel, E. 2005)

Institutions Can Report Payment Data

- We published on data from UCR
- Payment and amount differed by:
  - Types of research
  - Study population
  - Visits
  - Time
  - Risk
- Norms may be different at each institution



(Brown et al. 2021)

Payment in HIV research

- Among participants living with HIV
  - 80% - payment plays a role in participation
  - 70% - there should be a standard policy for payment
  - 96% - people should receive payment to participate
  - 91% - payment is a benefit of participating

(Polonijo et al. 2022)

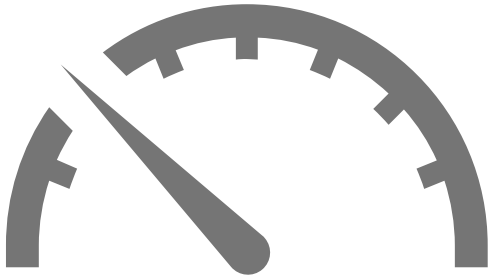
Views from Multiple Stakeholders in HIV Research

1. **People living with HIV**
2. **Researchers**
3. **IRB members and analysts**

- Most participants from the three stakeholder groups view research incentives as positive
- More study risk/invasiveness deserves more pay
- Larger funding=larger incentive
- People with lived experience should be involved in decision making

"oh, it makes me feel like they value my participation. Like they are cognizant of the fact that even though I'm doing this on a volunteer basis, that my time is valuable. What they're taking away from my body is valuable. And although I, you know, I'm glad to be helpful and help science move forward, it makes me feel like a part of the team too, because all of them are getting paid." -PLWH

Impact of Incentives -Too Low



- PLWH: this is unethical
- Decreased participation
- Decreased retention
- Participants don't feel valued
- Many PLWH view $25 as the lowest research incentive they are willing to accept, $10 or less is "insulting"

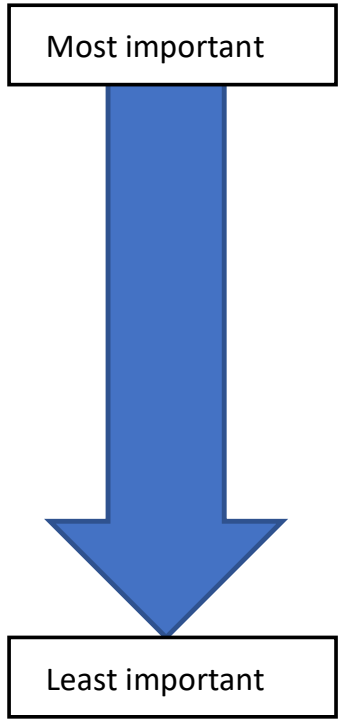
"If you don't compensate participants enough.....in order to avoid coercing people, you are actually shunning them."
(IRB Member)

Impact of Incentives -Too High

- IRB and researchers: this is unethical
- Not answering study questions truthfully
- Low-quality study results
- Poor adherence to study intervention
- Participating solely for the incentive
- Lower SES individuals accept more risks

"I have a very hard time coming up with examples where I'm really uncomfortable with an incentive being too high, because I think we're just underestimating people's conviction of values. I think there are so many reasons why people participate in high risk research." (IRB Member)

Conjoint analysis



Attribute importance segmented by participant type		
IRB Members/ Ethicists	**PLWH**	**Researchers**
Invasiveness	Amount paid	Invasiveness
Amount paid	Invasiveness	Amount paid
Whether ART needed to be stopped	Whether ART needed to be stopped	Time commitment
Whether first in humans	Time commitment	Whether ART needed to be stopped
Time commitment	Whether first in humans	Whether first in humans
Whether ancillary costs reimbursed	Whether ancillary costs reimbursed	Whether ancillary costs reimbursed

Sample Vignette

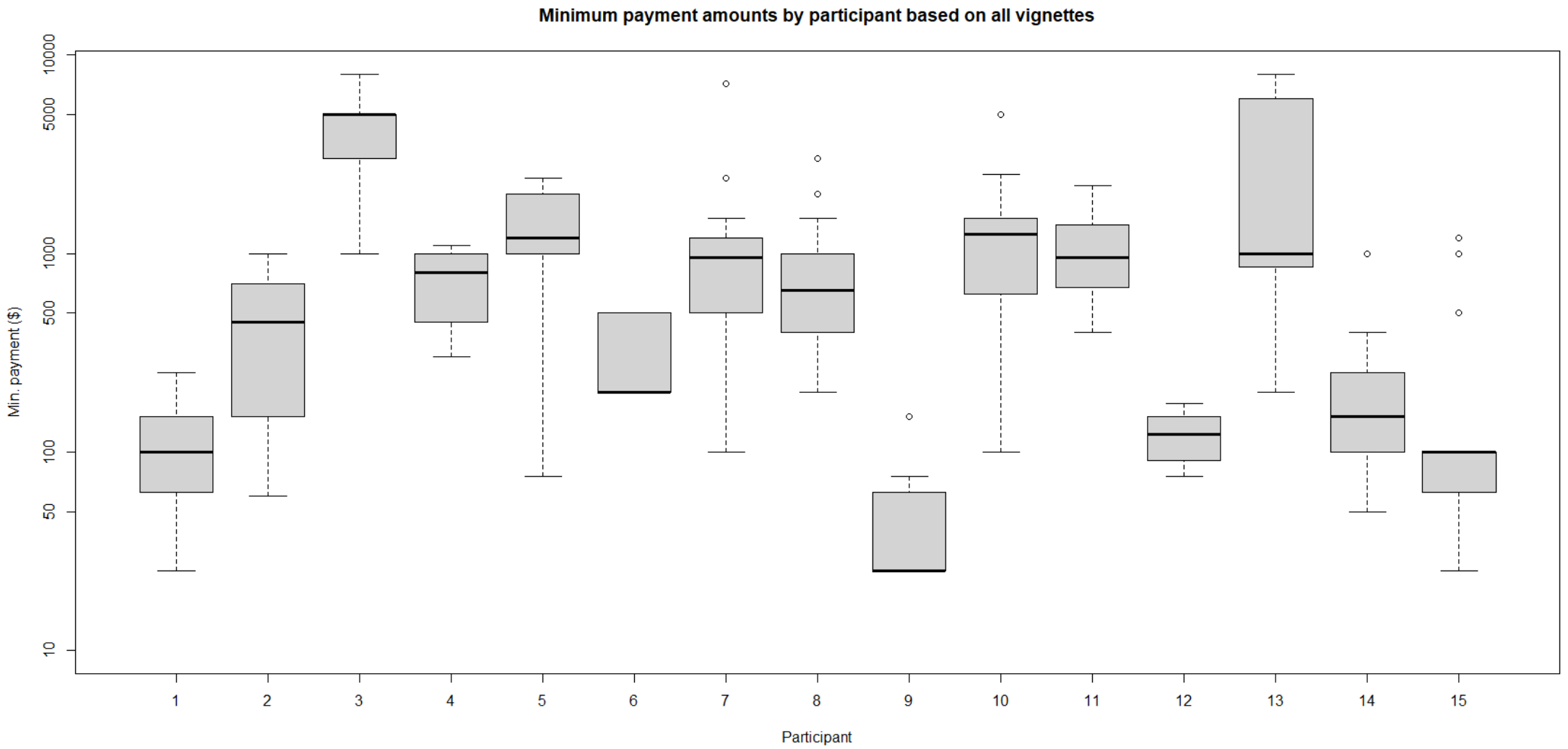
- Researchers are recruiting people with HIV who also have **mild depression** for a HIV cure-related study which is **first in humans**. The study procedures are **moderately invasive**, and there are **potential long-term risks** from the required HIV analytical treatment interruption. The overall time to participate has **some impact on daily activities**, and **ancillary medical care is provided** as part of the study. As with any early-stage HIV cure-related study, the prospect for direct benefit is low.

What would you recommend as a range for an appropriate payment for the participant in this study?

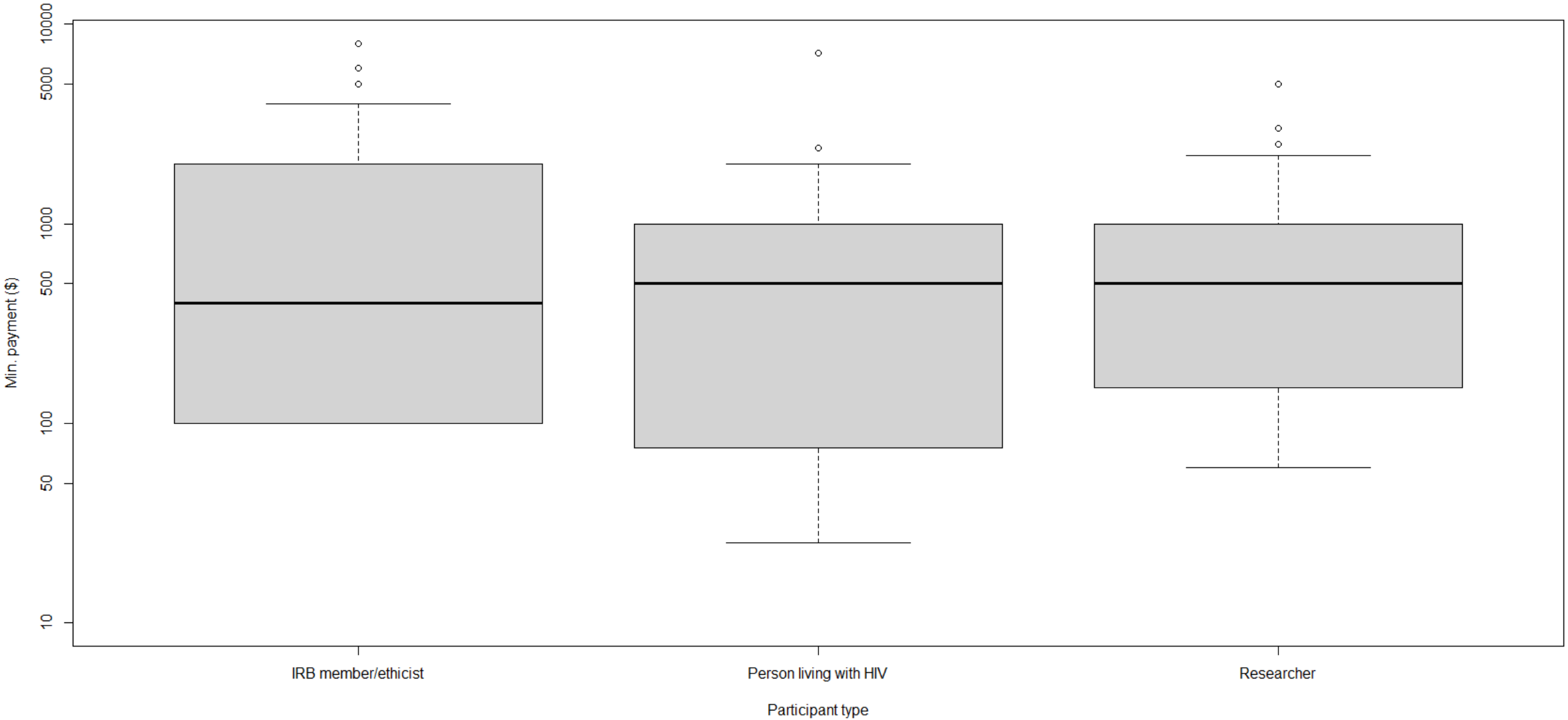
Vignette Options

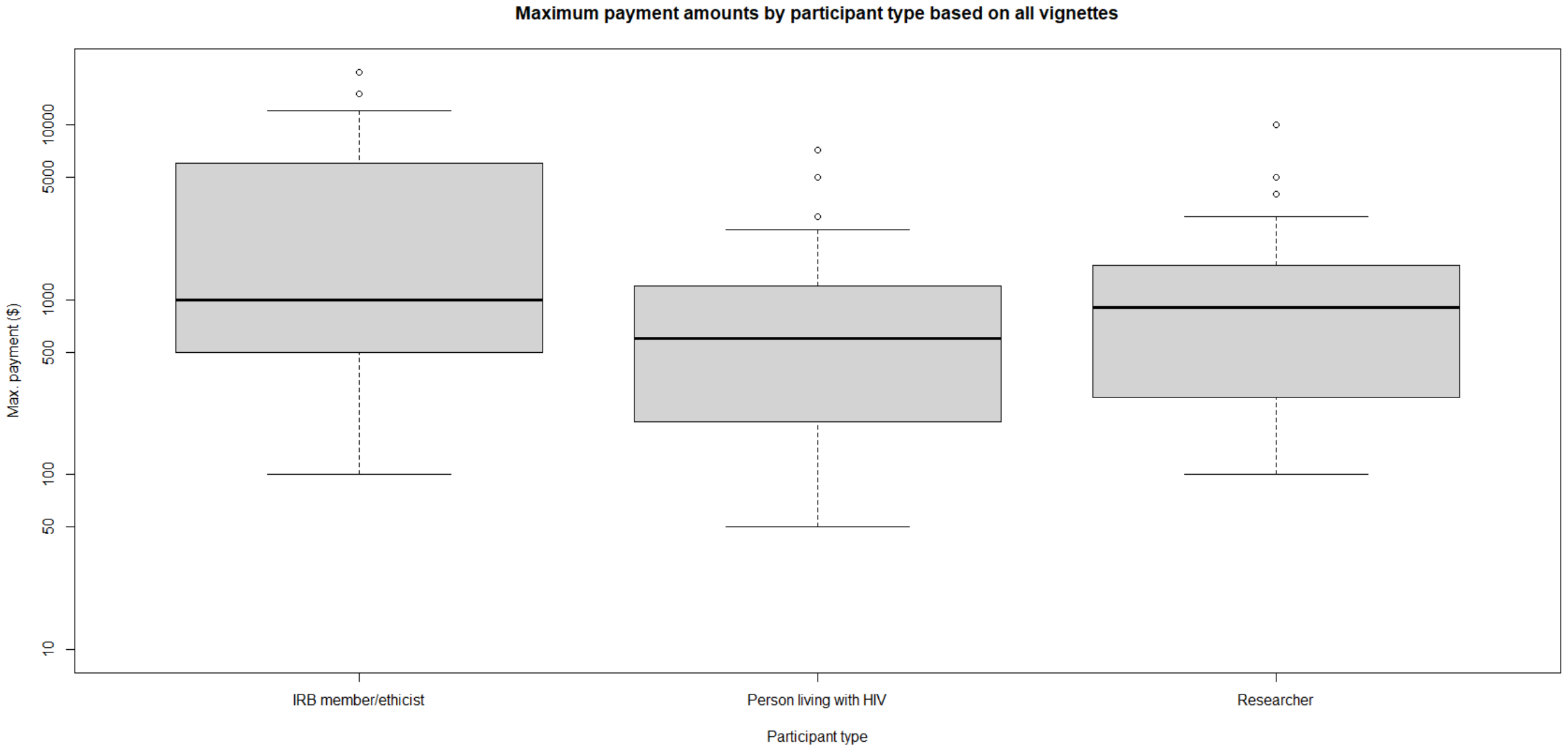
Factor	Factor Details	Attribute 1	Attribute 2	Attribute 3
A	Comorbidity	Arthritis	Mild depression	Heart disease
B	First in humans (proxy for risk)	Yes	No	
C	Invasiveness (proxy for pain/burden)	Low (blood draw)	Moderate (lumbar puncture/spinal tap)	High (chemo, bone marrow transplant)
D	HIV analytical treatment interruption risks	Yes	no	
E	Overall time burden to participate	Little impact on daily activities	Some impact on daily activities for 3 months	Significant impact on daily activities for 12 months
F	Ancillary care	Yes	no	

Preliminary vignette data



Minimum payment amounts by participant type based on all vignettes




Maximum payment amounts by participant type based on all vignettes
Max. payment ($)
10000
5000
1000
500
100
50
10
IRB member/ethicist
Person living with HIV
Researcher
Participant type

Closing time

- Participant payment decision-making is a major gap in all research
  - We may be underpaying or overpaying
  - First step=track current payment data
- Benefits to having access to data
- Potential risks to having access

Recent work on the topic

- A Penny for Your Thoughts? Moving Research Payment Transparency from Idiom to Policy. National Academy of Medicine
- Cash Transfer Apps are a Feasible, Acceptable, and More Equitable Method for Compensating Participants in HIV Research. Journal of Acquired Immune Deficiency Syndromes
- Improving Representation in Clinical Trials and Research. National Academies Report
- Letter to the editor: considerations for ethical incentives in research. Med Health Care Philos
- Attitudes Toward Payment for Research Participation: Results from a U.S. Survey of People Living with HIV. AIDS and Behavior
- CITI training webinar on paying participants in research
- CAB members must be paid. PRIM&R Ampersand

Acknowledgements

- Thanks to the Considerations Around Study Honoraria (CA$H) multi-site study team and study participants for their time and energy and guidance on the topic of payment in HIV research participation
- Appreciation to the HIV+Aging Research Project-Palm Springs (HARP-PS) and our national community advisory board for guiding us at each step of our journey to prioritize the participant perspective
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