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## Background

Benefits are sometimes portrayed as something positive that occur during study participation. Early HIV cure-related clinical trials will be proof-of-concept experiments with little to no direct clinical benefit anticipated for participants.

We assessed perceptions of benefits in HIV cure clinical research in the United States. We hypothesized that perceived personal benefits, clinical benefits and social benefits affect willingness to participate in HIV cure-related research.

## Methods

An extensive, online cross-sectional survey was conducted among 400 American adults (22% females; 77% males; <1% transgendered) in September – October 2015. The sample was ethnically diverse (65% Caucasian, 17% African-American, 12% Hispanic, 4% mixed and 2% Asian) and 38 U.S. states were represented. We also conducted key informant interviews with 36 people living with HIV, researchers, bioethicists, members of Institutional Review Boards (IRBs) and regulatory agencies to assess perceptions of benefits.

Using Likert scales, we asked participants to indicate which potential benefits would either be very important, somewhat important, barely important or not at all important in their motivation to consider participating in HIV cure-related studies. The graph below shows each factor in relation to the others, but also shows the relative importance of the “personal benefits,” “clinical benefits” and “social benefits” categories compared to each other.

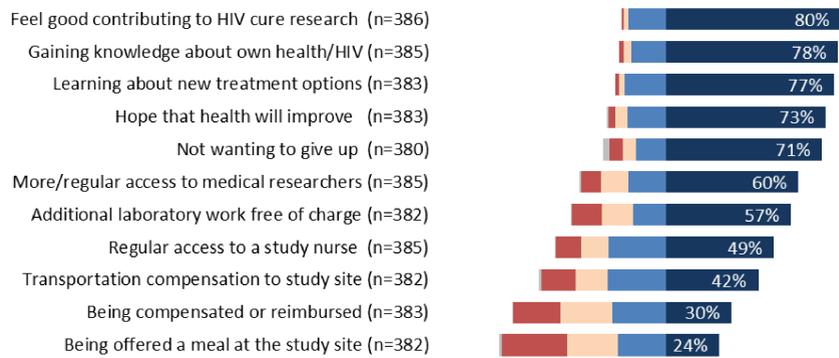
## Results

The perceived clinical benefits or social benefits appear to be more important motivators, on average, than personal benefits when considered as a category, in decision to participate in HIV cure-related research.

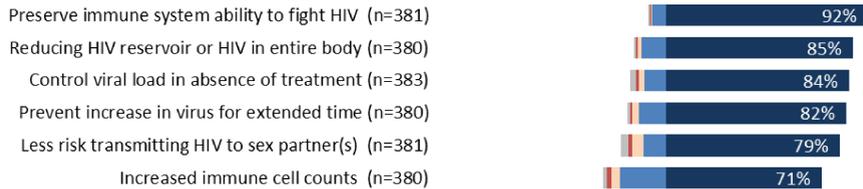
### Importance of Factors to Motivate Considering Participating in HIV Cure-Related Studies

■ Don't know/Not applicable ■ Not important ■ Barely important ■ Somewhat important ■ Very important

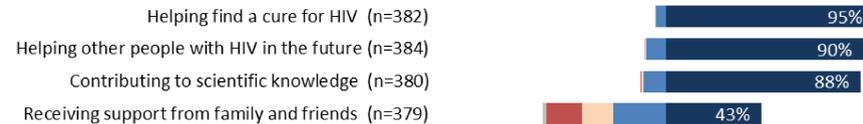
#### Potential Personal "Benefits"



#### Potential Personal Clinical "Benefits"



#### Potential Social "Benefits"



Percentages reflect "Very important". The remainder (up to 100%) includes the sum of "Somewhat important", "Barely important", "Not important" and "Don't know/Not sure".

The psychological benefit of feeling good about contributing to HIV cure research (80%, 95% CI: [75-85%]; n = 396) and gaining knowledge about one's health (78% [73 – 83%]; n = 385) were the potential personal benefits most likely to motivate participation in HIV cure-related research in the United States. Increasing one's ability to fight HIV (92% [87 – 97%]; n = 381) and reducing one's HIV reservoir (85% [80 – 90%]; n = 380) were the perceived potential clinical benefits most likely to motivate participation, although in reality there may be no direct clinical benefit accruing from a reduction in the size of the replication-competent HIV reservoir. Helping find a cure for HIV (95% [90 – 100%]; n = 382), helping others with HIV in the future (90% [85 – 95%]; n = 384) and contributing to scientific knowledge (88% [83 – 93%]; n = 380) were the most important perceived social benefits.

## Results (continued)

We delved deeper into these perceived benefits in the key informant interviews. Potential volunteers reported feeling empowered, contributing to stigma reduction, hope, education, bolstering one's advocacy work, financial compensation and ensuring participation of under-represented populations as motivating factors. Regulators and clinicians-researchers concurred that early HIV cure studies are unlikely to provide any direct clinical benefit, but indicated that participants may experience other types of indirect benefits.

Themes	Quotations
<b>Societal Benefits</b> Advancing scientific knowledge	<i>"I think all knowledge is important and the only way that we learn in this world is through failure (...) What has always motivated me is that every bit of information can help somebody else" – Patient-Participant</i>  <i>"The only tangible benefit that I am willing to talk about is the benefit of contributing to the greater good" – Clinician-Researcher</i>
<b>Personal Benefits</b> Psychological benefits	<i>"The benefits to me were emotional knowing and believing that I helped further medical knowledge. (...) The researcher said to me: "Do not underestimate... you have had a profound impact on medical research because we have found information that we would not have been able to know before. (...) I felt and still feel very satisfied that I participated (...)" – Patient-Participant</i>
Hope	<i>"The hope that one day I and others like me will not have to take all those HIV drugs" – Patient-Participant</i>
Information and education about HIV	<i>"I think that the benefit is education. We are not educated enough. And even though this thing has been around for years and years, we still need the education. There is not a lot of knowledge. There is a lot of stigma because there is a lot of ignorance. Because people don't know." – Patient-Participant</i>
Advocacy	<i>"Participating in studies (...) has helped me stay retained in care along with strengthening my knowledge around HIV/AIDS to be a better advocate" – Patient-Participant</i>

## Conclusions

Despite no expectation of direct clinical benefit from participating in early-phase HIV cure clinical studies, the majority of potential volunteers value the societal benefit of furthering science and believe they will experience psychosocial benefits from their participation. **Data show that we should not underestimate the importance of socio-emotional benefits in HIV cure research participation.** The perceived benefit of gaining knowledge about one's health raises questions about the need to communicate study data (in the aggregate) and advancements in science to study participants and highlights the importance of positive clinical contact factors. Hope that health will improve may be a strong motivating factors; yet early-phase research does not confer projected direct clinical benefits and there is the possibility of harm while advancing medical knowledge. Results highlight the importance of managing expectations and thoroughly exploring the potential for therapeutic misconception.

## Recommendations

- ✓ Researchers have the responsibility to report the associated lack of clinical benefits in early-phase HIV cure studies.
- ✓ Researchers need to appreciate that study participants may perceive tremendous psychosocial and mental benefits from being in a study.
- ✓ Researchers should clearly distinguish between benefits to society and benefits to participants in informed consent forms, including potential benefits from the interventions (if any), inclusion benefits (or indirect, collateral benefits).
- ✓ Examinations, study interventions and laboratory tests should not be considered benefits of study participation.
- ✓ HIV cure research participants should know that interventions are experiments that evaluate basic safety and they are meant to generate knowledge for the benefit of society.
- ✓ HIV cure researchers should be reminded that HIV cure research participation relies fundamentally on altruism of study participants.
- ✓ More empirical research is needed on actual benefits of participating in HIV cure clinical studies.

## Acknowledgements

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