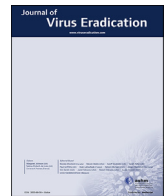




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Review

Altruism: Scoping review of the literature and future directions for HIV cure-related research



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ABSTRACT

Introduction: The question of what motivates people to participate in research is particularly salient in the HIV field. While participation in HIV research was driven by survival in the 1980's and early 1990's, access to novel therapies became the primary motivator with the advent of combination antiretroviral therapy (cART) in the late 1990s. In the HIV cure-related research context, the concept of altruism has remained insufficiently studied.

Methods: We conducted a scoping review to better contextualize and understand how altruism is or could be operationalized in HIV cure-related research. We drew from the fields of altruism in general, clinical research, cancer, and HIV clinical research—including the HIV prevention, treatment, and cure-related research fields.

Discussion: Altruism as a key motivating factor for participation in clinical research has often been intertwined with the desire for personal benefit. The cancer field informs us that reasons for participation usually are multi-faceted and complex. The HIV prevention field offers ways to organize altruism—either by the types of benefits achieved (e.g., societal versus personal), or the origin of the values that motivate research participation. The HIV treatment literature reveals the critical role of clinical interactions in fostering altruism. There remains a dearth of in-depth knowledge regarding reasons surrounding research participation and the types of altruism displayed in HIV cure-related clinical research.

Conclusion: Lessons learned from various research fields can guide questions which will inform the assessment of altruism in future HIV cure-related research.

Introduction

The question of what motivates people to participate in research has been central to the ethical development of scientific knowledge.¹

Although participation in research may benefit individual participants,² research is ultimately intended to improve health outcomes for future patients.^{3,4} Participation motivation remains particularly salient in the HIV research field. While participate in HIV research was initially driven

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by survival in the 1980's and early 1990's,⁵ access to novel therapies became the primary motivator with the advent of combination antiretroviral therapy (cART) in the late 1990s.⁶ Today, in HIV cure-related research, which can often be of high-risk and low direct benefit to the individual participant, altruism is increasingly cited as a reason people living with HIV (PLWHIV) participate.⁴ Yet, the concept of altruism has remained insufficiently studied in this context.

With over 250 completed or active HIV cure-related clinical studies worldwide,^{7,8} we have yet to understand the altruistic motivations underlying research participation. Altruism is frequently invoked as the main driver for participation in this type of research,⁴ but is typically treated as a static concept with limited nuances. A more complete awareness of altruism is necessary to better understand how and why it so strongly influences participation within the context of HIV cure-related research.

In this scoping review, we seek to better understand altruism as a construct driving research participation. We surveyed various fields, including altruism in general, clinical research, cancer, and HIV to extract altruism-related themes that may be directly or potentially applicable to the field of HIV cure-related research. We reviewed the growing socio-behavioral science literature on HIV cure-related research and examined how altruism underpins decision-making. We also summarized lessons learned and suggest possible future directions to guide the assessment of altruism in HIV cure-related research.

Methods

We used a scoping review approach to organize pertinent background information about a topic that has been under-explored.⁹ We reviewed a broad evidence base related to the construct of altruism, drawing on the precedent of examining related research fields and lessons learned.⁴ We focused on research fields with empirical similarities to HIV cure-related research. The fields of oncology and HIV cure-related research are similar in that overlapping research strategies are pursued, such as immune-based approaches¹⁰ and stem cell transplants.⁴ People who participate in HIV prevention research are healthy volunteers, while those joining HIV treatment and cure-related trials are living with HIV. Importantly, in some HIV cure-related trials, PLWHIV are asked to interrupt safe and potent cART to test the efficacy of new interventions. Despite differences between these types of research, altruism-related themes apply to the field of HIV cure-related research and can result in a better understanding of the motivations influencing research participation.

Our scoping review is based on a search of articles from the English-language, peer-reviewed literature. Using PubMed, we searched terms such as 'altruism AND clinical research', 'altruism AND cancer', and 'altruism AND HIV.' We also pursued references within the articles we reviewed and integrated the additional suggestions of peer reviewers. In total, we included 117 review papers, original research articles, and commentaries. Articles were selected because they specifically addressed altruism or contained information with direct or potential relevance to high-risk/low-benefit HIV cure-related clinical research. We did not employ strict criteria to adjudicate the literature given that our objective was to map existing literature to inform future research. For each topic, we extracted salient definitions, altruism types, related themes, and important findings. We used narrative synthesis to integrate findings into descriptive summaries and lessons learned.⁴

Discussion

General literature on altruism

A basic understanding of the history of altruism is critical to contextualize how altruism is conceptualized in clinical research. The term altruism (from Latin *alteri*—others) was coined in 1851 by the French philosopher Auguste Comte to denote placing the needs of others above

one's self-interest.^{11,12} Since then, altruism has captured the interest of philosophers, biologists, and theorists who have debated about whether humans are naturally selfless.¹¹ Technological advances in biology, genetics and neuroscience have increased our understanding of the human brain and revealed fundamental differences between altruists and non-altruists with regard to emotional processing.¹¹ Psychologists also recognized that cross-culturally, humans are moralistic and evaluate one another's actions, using the dimensions of right or wrong.¹³ Altruism has also been the object of several theories aimed at explaining prosocial behavior.¹³ Some theorists have considered empathy the prime emotion driving altruistic behavior.^{13,14} Others regard altruism as contextualized by different social norms, including reciprocity,¹⁵ giving,¹⁶ social responsibility¹⁷ and gratitude.¹⁸

Uncontestably, the greatest challenge in areas like evolutionary biology has been to determine the conditions that define behaviors as altruistic.¹⁹ West and colleagues have argued that altruism is "a behavior which is costly to the actor and beneficial to the recipient¹⁹". Theorist Ma has suggested that altruism "must be enacted voluntarily without expectation of a benefit".²⁰ From here, Ma proposed a complex 10-stage taxonomy of human relationships in terms of altruism.²¹ Regarding measurement, Sawyer proposed in 1966 an altruism scale to measure cooperative, altruistic, and competitive interpersonal orientation,²² arguing that altruism was not necessarily opposed to egoism in that it is possible to be concerned with both one's own and others' welfare.²² Lee and Kang developed the Altruism Scale of Adults,¹² whereas Rushton and colleagues developed the Altruistic Personality and Self-Report Altruism Scale.²³ Varied measurements likely reflect the challenges of identifying a common conceptual definition.

Individuals who behave altruistically do so in a social context. As social scientists have noted, altruism has contextual, social-cognitive, affective, and relational roots. It may be motivated by social conditions, such as natural disasters, war and genocide,^{24,25} by socio-political factors, such as social class and entrenched ideology, and by established relationships with particular individuals or social identity groups, such as parents or religious communities.^{26,27}

Altruism in clinical research

Altruism is a key motivating factor for participation in clinical research but is often suffused with the desire for personal benefit.^{3,28–32} Altruism may also be tied to research design factors, such as the trial design itself, presentation of safety information,³³ quality of life, and financial issues.³⁴ Luchtenberg and colleagues noted that intergenerational solidarity, or the desire to benefit future patients, motivated research participation in young people.²⁸ Verheggen coined the expression 'personal balance account' to describe the emotional and physical net value patients hope to gain from research participation.³⁵

In recognizing the various conceptual definitions of altruism, research is available to explain how specific types of altruism drive research participation.^{3,30,36} A fundamental difference in approaching various types of altruism lies in relation to other decision-making motivational factors. In one qualitative study, altruism was defined as pure altruism (true selflessness), hypothetical altruism (selfless behavior stated but not tested since participants were assigned to their preferred treatment), weak altruism (no active intention to benefit others), contingent or conditional altruism (participation dependent upon receipt of personal benefits), and sense of duty (a strong desire to give back).^{30,31} The nuances reflected in these wide-ranging definitions of altruism suggest more research is needed to validate different types of altruism.

In reviewing ethical issues associated with altruism, Jansen asserted that altruistic intent was central to assessing valid informed consent.³⁶ Researchers must distinguish between primary altruistic motivations from subsidiary ones.³⁶ The strength of altruistic motivation holds ethical import because weak altruistic motives may not be genuinely altruistic.³⁶ Establishing whether participants have genuine altruistic motivations is not easy nor without cost.³⁶ Nonetheless, the presence of strong altruistic

motives can alleviate concerns around exploitation that may otherwise exist, particularly for trials involving high risk for participants.³⁶

Altruism in cancer research

The field of cancer research may help inform our understanding of altruism in HIV cure-related research, as it tests similar modalities and follows a ‘remission’ model.³⁷ In cancer research, however, motivation for participation usually is in response to worsening health caused by progressive disease.¹ Existent cancer literature on motivations present a mixed picture regarding study participants’ altruistic intentions. Some studies suggest that self-interest often motivates participation in early-phase cancer trials.^{38–42} Others, however, emphasize that the desire to advance therapeutic options plays a role in motivations to participate in this type of trials.^{43,44} A systematic review of participation in breast cancer research among women has revealed that participation is usually motivated by a diversity of reasons, including personal, study and physician-related factors.⁴⁵ Studies from the cancer field have shown that altruism alone is rarely the only driving force for participation.

The trial phase, either Phase I (assessing safety of new compounds) or Phase III (evaluating efficacy and tumor response), may be a key factor in influencing altruistic intentions, as studies that offer reasonable expectations of direct therapeutic benefits may render altruism less a motivating factor than those that do not.³⁶ However, the issue is not straightforward. A study has reported that participants in early-phase cancer clinical trials and those with the poorest prognosis were less likely to cite altruistic motivations than those in later-phase trials.¹ The authors explained that participants with poorer prognosis often lacked “the luxury of altruism when making treatment decisions.^{1”} Similarly, research with cancer research participants has shown that participation motivation included accessing the best medical care while contributing to scientific knowledge.⁴⁶ Similarly, hope for a cure combined with altruism can serve as catalysts for participation.⁴³

A literature review synthesizing reasons why patients do not take part in cancer clinical trials found that less than optimal clinician-patient relationships and communication, as well as the burden of trial participation, played fundamental roles in thwarting altruistic intentions.⁴⁷ A study conducted in the U.S. found racial/ethnic differences in cancer trials participation rates, but not in willingness to participate or altruistic intentions.⁴⁸ The authors have postulated that psychosocial variables that may be associated with race and ethnicity—such as anxiety and optimism—could also serve as pertinent mediating factors.⁴⁸ This brief review of cancer studies suggests that altruism is potentially bidirectional and multiplicative with other research design factors, especially additional clinical monitoring.

Altruism in HIV prevention research

Altruism appears to be an important motivator for participation in HIV prevention trials, particularly for vaccine studies.^{49–53} HIV prevention research, however, is fundamentally different from the HIV cure-related one in that it involves participants without HIV. As scientists continue to test similar interventions in both HIV prevention and cure-related research, e.g. broadly neutralizing antibodies, differences between the two fields may decrease.

Socio-behavioral studies have revealed strong altruistic intentions among participants to advance the HIV prevention field.^{50,51} The HIV prevention field offers various ways to organize altruism, either by the types of benefits achieved or the origin of the values motivating research participation. For example, Dhalla and colleagues have developed an altruism typology consisting of perceived benefits, societal benefits, and individual ones, which, along the lines of historical debates about the conditions of altruism, were not perceived as genuinely altruistic. Furthermore, social benefits to participation were classified as either microsocioal (benefits pertaining to one’s immediate network), mesosocioal (benefits pertaining to one’s larger social world), and macrosocioal

(benefits pertaining to society as a whole).^{52,54} Another group has proposed a typology with ten categories of altruistic intentions: 1) cultural (culture values of altruism), 2) community (community values influencing the spirit of giving back), 3) familial (family values pertaining to helping others), 4) religious (religion-related values pertaining to helping others), 5) professional (values related to improving the health care system), 6) political (HIV activism in response to the epidemic), 7) experiential (altruism based on having personal experiences with HIV), 8) moral (making up for past wrongs), 9) existential (providing meaning and purpose), and 10) psychological (altruism as a vessel for emotional gratification).⁵³ While many typologies are available, there are limited data to determine whether they are entirely unique and differentially affect decisions around research participation.

In HIV cure-related research, some healthy PLWHIV are asked to stop their treatment. These analytical treatment interruptions may cause viral rebounds during which they are at greater risk of transmitting HIV to their sex partners.^{56–58} Importantly, HIV prevention altruism offers a unique theme that centrally aligns with a concern in HIV cure-related research: “the values, motivations, and practices of protecting sexual partners from HIV transmission.^{55”}

Altruism in HIV treatment research

HIV treatment literature can inform how altruism is understood in HIV cure-related research given the overlapping participation of PLWHIV in both types of trials. However, in HIV treatment research, particularly later-phase trials, therapeutic benefits are usually expected.⁵⁹ Early HIV treatment literature contains few mentions of altruism as a motivator to participation. Instead, early HIV treatment trials were about “access to the most promising experimental therapies” in the hopes of staying alive.^{5,6} Additional influential factors to HIV treatment research participation include the HIV doctor’s behavior, clinic conditions, and trust in the research team.⁵⁹ The late 1990’s witnessed major breakthroughs in HIV therapies with the advent of highly effective HIV suppressing cART.^{6,60}

There are limited socio-behavioral studies exploring motivations to participate in HIV treatment trials. One study, conducted among 657 PLWHIV in Canada, has revealed that the strongest motivators for HIV treatment research participation were the specific antiretroviral regimens studied and the quality of clinical interactions.⁶¹ Balfour and colleagues have studied altruism as a catalyst for participation in therapeutic HIV vaccine trials.⁶² Their cross-sectional survey among 49 participants has indicated that all participants were hopeful for societal benefits, and most respondents also reported high levels of existential well-being and quality of life.⁶² Another therapeutic HIV vaccine trial in China has found a higher level of willingness to participate between those who had acquired HIV sexually compared to those who has acquired it from injection drug use or blood transfusions.⁶³ A review on barriers to participation in HIV treatment trials has found that the main barriers to participation were related to side-effect or trial design concerns, distrust of researchers, interference with daily activities, and social discrimination.⁶⁴ These factors are pertinent because they can neutralize altruistic motivations in HIV treatment trials based on the personal experiences of potential participants. Future research could elucidate why these differences exist, given that the most vulnerable populations may have competing needs that prioritize the reporting of other intentions before altruism.

Altruism in HIV cure-related research

Despite the growing socio-behavioral research related to HIV cure, there remains a dearth of in-depth knowledge regarding reasons surrounding participation decisions and the types of altruism displayed in HIV cure-related research. This body of research shifts the focus of participation from potential therapeutic benefits to altruism in that cure studies often involve health risks.⁶⁵ These risks can be related to

interventions, monitoring procedures, or interruption of HIV treatment, without perceived personal benefits.⁶⁵ In this regard, current early-phase trials represent a reversal from the early days of the HIV epidemic because most PLWHIV are now stable on cART.⁶⁶ HIV cure-related research protocols in general follow a healthy-first pharmacology model as opposed to the sickest-first model.^{67–69} Social scientists and bioethicists have argued that it is increasingly important to understand the role of altruism in these high-risk/low-benefit trials.^{70–74} Altruism has been described as a benefit,⁷¹ since the standard risk-benefit calculus does not account for participants' own motivations and the emotional gratification they receive from participation.^{72,75–78} However, altruism has also been designated a limiting factor, because there are ceilings on acceptable study risks to ensure that they remain ethical.⁷² Whether altruistic sacrifices are acceptable will largely coincide with whether the risks to individual participants are reasonable in relation to the anticipated social and scientific benefits.^{65,79}

A number of socio-behavioral studies have been conducted to examine hypothetical willingness to participate in HIV cure-related trials. These studies found that altruism and the desire to advance towards an HIV cure to be participation motivators.^{66,70,71,73,74,80–85} These altruistic motivations are often contingent upon several participant-perceived barriers and facilitators. On one hand, the most commonly cited barriers have been potential side-effects of high-risk interventions and loss of viral load suppression and CD4 T cell count increases.^{81,82} For acutely-diagnosed individuals, e.g. Fiebig stage I, there is an added risk of HIV seroconversion.^{86,87} On the other hand, facilitators include the desire to contribute to the HIV community⁸⁸ or to gain knowledge about one's health⁷⁰(83), receipt of psychological support,⁸⁹ and hope for health benefits.^{70,83} Additional facilitators may also include perceived physical burden and/or psychological burden of living with HIV, accessibility to high quality clinical service, and sense of acceptance offered by non-judgmental care, especially among those with vulnerability factors who are often discriminated and/or marginalized due to their race/ethnicity, sexual orientation, job, and substance use status.^{75,90} Because both barriers and facilitators are at play, the topic of mixed altruism has gained significance in HIV cure-related research, in that potential participants perceived both societal (advancing science) and personal benefits (receiving compensation or feeling uplifted by making a contribution to research).^{66,71} In examining attitudes towards HIV treatment interruption trials specifically, scholars have argued that recruitment efforts should focus on long-term scientific benefits of participation, with more attention being allocated towards altruism-based motivations of study participants.⁹¹ But PLWHIV may experience deep tension between altruistic desires to advance HIV cure-related science and protecting their personal safety and not transmitting HIV to their sexual partners during HIV treatment interruptions.^{66,84,85}

Further, altruism may not adequately capture the role committed HIV activism plays in advancing trial participation.^{66,92} It is highly possible that the overwhelming stigma that HIV engenders coupled with the history of HIV activism, including the social, medical, and political response to the virus, has created a culture of 'giving' that facilitates altruism in the field of HIV cure-related research.^{93–95} The stigma surrounding HIV has arisen from the fear that surrounded the 1980's AIDS crisis when very little was known about HIV transmission. PLWHIV were and are often ostracized from society because of the fact that having a positive diagnosis was/is often seen as the result of a type of illicit behavior caused by an inherent moral fault deserving punishment. Thus, PLWHIV were forced to come together into a community and advocate for themselves. The history of HIV activism is also one of altruism, a shared sense of responsibility to often marginalized communities, and a reaction to social injustices.

Socio-behavioral scientists are beginning to gain a better understanding of how altruism influences participation in HIV cure-related trials.^{75,87,90,96} In addition, a growing number of these participants have written personal accounts about their experiences. All of them cited

a sincere desire to help advance the HIV cure-related research field.^{97–100} However, more quantitative research is needed to better understand what can be extrapolated in regards to the larger population of participants. For one, few rigorous studies on measurement development have been conducted, especially within the context of HIV, to identify if there are multiple types of altruism in effect. Secondly, more often than not, measuring altruism is performed by simply asking participants to report on the reasons for their participation through survey questions which may prime them to report in socially desirable ways. Lastly, there is consensus that we need to better understand participants' altruistic motives as well as their psychological experiences as they proceed through these complex trials.^{86,101} As HIV cure-related research strategies begin exhibiting safety and efficacy signals, scientists will need to determine how these novel regimens present clinical and therapeutic benefits above other anti-viral agents.^{83,102} It will be illuminating to study the degree to which altruism influences PLWHIV's participation as HIV cure-related trials move to later stages or as interventions begin to present clinically meaningful effects. Prevention altruism, which is discussed above, will also be affected by the critical need to mitigate the risk of HIV transmission to sexual partners during cART interruptions.⁵⁶

A new HIV cure-related research approach involves PLWHIV donating their bodies to science at the time of death.^{103–105} Modeled after similar research in oncology,^{106,107} the Last Gift study involves terminally ill PLWHIV who are willing to donate their bodies for rapid research autopsies to advance knowledge on HIV reservoirs.^{103,104,108} In the specific context of the evolving ethics of organ donation at the end of life, Rosenbaum used the expression 'altruism *in extremis*' to describe this deep manifestation of selflessness, i.e. a 'purer' form of altruism.¹⁰⁹ Several PLWHIV have taken part in early HIV treatment trials, but for decades have been denied the opportunity to participate in trials due to their age or co-morbidities. In the empirical research conducted within the Last Gift study, via in-depth participants' interviews, HIV-specific altruism was found to be nested within the context of the community, scientific advancement, and a moral obligation to participation.¹¹⁰ Altruistic motivations also included love for humanity and desire to give back to past and future patients.¹¹⁰ Altruism in death and existentialism, as a form of activism, was a prominent theme throughout the interviews with next-of-kin/loved ones of the Last Gift study participants.¹¹¹ In discussing how theories of altruism can explain patients' desire to participate in rapid tissue donation programs, Quinn and colleagues distinguished between gifting relationships (full body donations), reciprocal altruism (involving some expected returns for the donor and next-of-kin/loved ones, as emotional support), and empathy-induced altruism (emerging from the sense of community and loyalty to a disease group).¹¹²

Lessons learned and possible future avenues for the field of HIV cure-related research

Table 1 summarizes lessons learned on altruism from our scoping review. Themes explored have implications for future socio-behavioral sciences related to HIV cure and underpin the ethical framing of biomedical sciences regarding participants' benefits and expectations.¹¹³ In particular, we have found that valuable lessons can be learned from the fields of cancer and HIV prevention and treatment research to inform how we assess and contextualize altruism in HIV cure-related research. In cancer, participation is often motivated by the hope for clinical benefit and contingent on disease progression. We realize that cancer cannot be equivalently equated with HIV because of the omnipresence of ever-present stigma and strong cultural bonds created by the shared trauma within the HIV community. In the HIV cure-related research field, most otherwise healthy volunteers will not experience personal clinical benefit, yet, some studies may be 'high-risk/high-reward' when the risk is justified. In the HIV prevention field, altruism has been motivated by the need for improved biomedical interventions and altruism has emerged within several contexts (e.g., community, political, experiential,

Table 1
Lessons learned from scoping review of altruism.

General literature on altruism
<ul style="list-style-type: none"> • Humans are cross-culturally moralistic and evaluate actions on the basis of right and wrong. • Altruism is related to the themes of empathy, reciprocity, giving, social responsibility and gratitude. • For true altruism to occur, it must be done voluntarily without expectation of a benefit. • People may be concerned with both their own and others' welfare. • Altruistic behaviors occur within social contexts.
Altruism in clinical research
<ul style="list-style-type: none"> • Decisions to participate in clinical research are complex and multi-faceted. The link between altruism and decision-making is nuanced and complex. • In clinical research altruism is rarely pure as participants expect some degree of benefits. • It is important to distinguish between primary altruistic and subsidiary or secondary motives.
Altruism in cancer research
<ul style="list-style-type: none"> • The cancer literature reveals a mixed picture regarding whether research participation is motivated by altruistic intentions. • Altruism is often associated with the desire for clinical benefit (e.g., hope for tumor response). • Clinician-patient relationships and communication strategies as well as burden of trial participation play a vital role in shaping altruistic intentions. • Psychosocial variables, such as anxiety and optimism about trials, may serve as influential mediating factors in participation.
Altruism in HIV prevention research
<ul style="list-style-type: none"> • Societal benefits to participation are often altruistic and can be categorized as microsocial (pertaining to one's immediate network), mesosocial (pertaining to one's larger social world), or macrosocial (pertaining to society as a whole). • Altruistic intentions can also emerge within several contexts, including community, political (e.g. HIV activism), experiential, moral, existential, psychological and other factors.
Altruism in HIV treatment research
<ul style="list-style-type: none"> • Therapeutic benefits are usually expected in HIV treatment trials, particularly those testing potentially better therapies. • Early HIV treatment trial participation was driven by survival in the hopes of staying alive by accessing experimental therapies. • Mediating factors such as the reputation of the HIV/AIDS clinician/researcher, positive clinic conditions and the quality of clinical interactions are important. • Factors neutralizing altruistic intentions can include concerns about side-effects, trial designs and time commitments.
Altruism in HIV cure-related research
<ul style="list-style-type: none"> • Most HIV cure-related studies involve high risks with limited prospects of direct clinical benefits. • While there are several references on altruism in the HIV cure-related research literature, it has not been well characterized in this research context. • Altruism has been discussed as a benefit but also as a limitation as it imposes a ceiling on acceptable risks. • Altruism remains a motivator for HIV cure-related research participation in both hypothetical and actual research. • More research is needed to better understand how altruism influences intentions to participate in HIV cure-related research. • Prevention altruism will also be affected by the critical need to mitigate the risk of HIV transmission to sexual partners during treatment interruptions. • HIV cure-related research at the end of life involves a more extreme form of altruism. Three types of altruism may exist: 1) gifting relationships, 2) reciprocal altruism, and 3) empathy-induced altruism.

psychological and others), which may also be true in the field of HIV cure-related research. In the HIV treatment field, while early research participation was driven by survival, PLWHIV now participate in research with the hope of improving therapeutic interventions and health outcomes. Because of the high potency, lower risk threshold and ease of administration provided by current cART, some PLWHIV may be unwilling to participate in high risk cure-related trials.

Our review revealed various pre-supposed types of altruism as well as mixed methods to assess altruistic intentions. In the future, adequate formative and qualitative research will be necessary to better define altruism and fully understand the breadth of the construct of altruism, how altruism motivates PLWHIV to participate in HIV cure-related research, and how participants may weigh different motivations. For instance, building on previous work conducted on altruism scales,^{12,22,114} an HIV cure research-specific altruism scale could ensure

that patient-participants' perspectives, decision-making processes and motivations to participate in research are captured quantitatively in a standardized manner. Such a scale would inform HIV cure-related studies' development in a holistic and ethical way, by centering patient-participants' experiences and prioritizing quantified altruistic motivations, psychosocial variables and extrinsic factors, among other variables associated with the altruism continuum. An HIV cure-related research-specific altruism scale could be used by biomedical and social scientists in the design of HIV cure studies to ensure for example that recruitment strategies accommodate various personality types as demonstrated by the scale. To assess altruism intentions, it will also be imperative to interview participants in actual HIV cure-related trials, either prospectively or retrospectively, in order to comprehend their decision-making processes regarding participation, and how they perceive these decisions during and after participation.^{115,116} These assessments will require a closer collaboration of biomedical researchers, socio-behavioral scientists and bioethicists.^{4,101,117} Such findings could inform aspects of study design, such as recruitment strategies, informed consent processes, as well as retention and psychosocial support for participants.

Table 2 provides possible research questions on altruism for the field of HIV cure-related research.

Limitations

This scoping review has important limitations worth noting. First, we have relied on evidence from altruism-specific research in related fields, such as clinical research, cancer, HIV prevention, and HIV treatment, and inferred applicability to the field of HIV cure-related research. Second, selection biases may have occurred due to the scoping methodology. Third, research on altruism is fraught with social desirability bias influencing individuals' responses on questionnaires. Fourth, due to the scoping review methodology, we did not assess the quality of studies or the strength of evidence. Fifth, the papers reviewed varied greatly with respect to designs, trial phases, sample sizes and other parameters.

Table 2
Possible research questions on altruism for the field of HIV cure-related research.

- What are the types of altruism displayed in HIV cure-related research? Which type(s) drive(s) participation the most?
- Do altruistic motivations differ between HIV cure-related study accepters and decliners?
- What factors might be predictive of altruistic (intrinsic) motivations to participate in HIV cure-related research (for example, sex/gender, age, race/ethnicity, sexual orientation, time since HIV-positive diagnosis, self-perceptions of health, risk propensity/aversion, etc.)?
- What extrinsic factors might predict altruistic motivations to participate in HIV cure-related research (e.g., social support, financial stability, etc.)?
- What factors influence altruistic motivations in trials specifically involving HIV treatment interruptions?
- How do altruistic motivations correlate with other psychosocial variables such as quality of life?
- To what extent is altruism specific to the condition of living with HIV?
- What is the relationship between altruism and knowledge or understanding about a specific study?
- What are the potential ways researchers could assess altruism as a motivator to participation in a standardized process?
- Should an HIV cure research-specific altruism scale be developed? If so, what HIV cure-specific elements should be included in it?
- How do we develop recruitment strategies that appeal to people with altruistic intentions that specifically include diverse populations that remain under-represented in HIV cure-related research?
- To what extent does altruism influence retention in HIV cure-related trials?
- What are the ethical implications of studying altruistic motivations—particularly related to ensuring adequate informed consent?
- How will prevention altruism be affected by the critical need to mitigate the risk of HIV transmission to sexual partners during HIV treatment interruptions?
- What are the psychological characteristics that motivate terminally ill PLWHIV to donate their bodies to science in the context of HIV cure-related research at the end of life?

Finally, our review may have missed relevant bodies of research. These limitations notwithstanding, we believe the themes extracted remain highly relevant to inform possible future directions in HIV cure-related research.

Conclusion

Our scoping review makes clear that more attention should be paid to altruism in the PLWHIV's decision-making processes in the context of high-risk/low-benefit HIV cure-related research. Despite several mentions of altruism in this field, the construct has remained insufficiently studied while utilizing sub-optimally measured, divergent conceptual definitions. There is high value in pursuing new research on altruism and moving beyond singular notions to appreciate the various types of altruistic intentions and behaviors within this growing research enterprise. Efforts to better understand the nuances of altruism will allow biomedical researchers and socio-behavioral scientists alike to incorporate perspectives into the trial design process. This will result in improved, more sensitive and ethically designed studies. Substantial scientific progress has been made since the beginning of the HIV epidemic owing to the unyielding vision and strong partnerships between the HIV research community and PLWHIV. The selfless desire to benefit humankind on the part of clinical trial participants has been critical to these successful research partnerships.

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Authors' contributions

K.D. drafted the manuscript.

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Declaration of competing interest

The authors declare no conflict of interest.

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