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"I Know That I Was a Part of Making a Difference": Participant Motivations for Joining a Cure-Directed HIV Trial with an Analytical Treatment Interruption

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Abstract

Analytical treatment interruption (ATI), defined as a closely monitored clinical pause in antiretroviral therapy (ART), is a core component of many HIV cure-directed clinical studies. ATIs may cause significant physical and psychosocial risks for people living with HIV and, as a result, integrating participant and community perspectives into clinical trial designs that include an ATI is crucial to ensuring a successful and person-centered trial. We conducted semi-structured interviews with participants enrolling in the BEAT-2 cure-directed trial (NCT03588715). Interviews elicited participant motivations and decision-making processes for trial participation along with participants' perceptions of the ATI. Interviews were recorded, transcribed, and analyzed using a directed content analysis. Fourteen of 15 trial participants completed interviews. The majority were Black (79%) cisgender male (79%). Participants noted several significant motivating factors contributing to their desire to enroll in the HIV cure-directed clinical trial, the most prominent being a desire to find a cure for HIV and help others in the HIV community. HIV care teams were the most commonly identified resource for patients when making the decision to enroll in the trial, and family, friends, and romantic partners also played a significant role. Altruism was a primary motivation for participation, although participants also shared interest in learning about HIV science and research. Participants had a strong understanding of trial procedures and displayed significant trust in the study team to keep them informed and healthy during their participation. The ATI was a significant source of anxiety for participants. Their primary worry was that their prior antiretroviral therapy (ART) regimen would no longer be effective once they resumed ART. Despite these concerns, participants shared considerable excitement for continued participation in the trial and being a part of the search toward an HIV cure.

Keywords: HIV cure research, socio-behavioral research, people living with HIV, patient voices, qualitative research, community advisory boards

Introduction

In July 2011, the National Institutes of Health (NIH) launched a pioneering initiative, the Martin Delaney Collaboratories (MDC) Toward HIV Cure Research. The goals of the MDC include studying the persistence of HIV in the body despite successful suppression of HIV replication during antiretroviral therapy (ART), and developing new curative strategies for managing HIV in the absence of ART and ultimately eradicating HIV from the body.[1] In

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this article, we report on clinical trial participants' experiences and motivations for joining an MDC-sponsored clinical trial.

Over the course of the trial, participants living with HIV interrupt their current ART regimen and engage in close clinical monitoring to study the effects of novel strategies seeking to cure HIV or lead to the durable suppression of viral replication in the absence of ART. Such analytical treatment interruption (ATI) studies are key to the development of novel HIV cure-related strategies.[2] Since persons on ART must take their treatment for their entire lives, ATI studies provide the ability to measure the effect of an investigational intervention on time to viral rebound and the immune system.[3] However, ATI studies present physical and psychosocial risks for trial participants[2,4] and risk of HIV transmission for their sexual partners.[5–8] We argue that these significant challenges to HIV cure research participation obligate researchers to integrate individual experiences and community perspectives from the beginning of all HIV cure-related clinical research; doing so respects current participants, honors the longer history of community involvement in the advancement of HIV research, and adheres to ethics in clinical research more broadly.

Community advisory boards (CABs) have been central to fostering community awareness about HIV research and development of clinical studies that are relevant and accessible to the diverse community of people living with HIV (PLWH). The role of CABs in HIV research has its roots in the activism of PLWH in the early 1980s. In 1983, the group *People with AIDS* produced a manifesto outlining social justice recommendations for biomedical and public health responses to the HIV crisis and a statement of rights for people with AIDS. This document, known as the Denver Principles,[9] and the subsequent Meaningful Involvement of People with HIV/AIDS guidelines,[10] are among the earliest examples of the patient empowerment movement that eventually evolved to encompass how participants are considered and treated in HIV clinical research.[11]

With input from HIV/AIDS activists, the National Institute of Allergy and Infectious Diseases (NIAID) mandated in 1989 that all HIV clinical research receiving funding from NIAID convene CABs to ensure that the perspectives of PLWH were incorporated into how HIV clinical trials are conducted. CABs provide mechanisms for community consultation with clinical researchers to foster more meaningful and equitable research.[12]

The BEAT-HIV Delaney Collaboratory (https://beat-hiv.org/) has established a community engagement group (CEG) composed of three distinct elements: the BEAT-HIV CAB, the BEAT-HIV community partner Philadelphia Fight, a comprehensive health service organization for PLWH since 1990, and BEAT-HIV investigators. In 2019, the CEG convened a working group to generate a document to support the HIV cure-directed clinical trial participant experience with defined rights and responsibilities for both participants and biomedical investigators conducting HIV cure clinical trials. Clinical trials conducted by the BEAT-HIV program have been conducted with CEG support and have been informed by the recommendations in the position article, *Joining Forces to Advance HIV Cure Research*.[13]

We report here on a BEAT-HIV community-led study of participant experiences nested within the parent clinical trial NCT03588715 ''A Pilot Phase I Randomized Study to Evaluate Innate Immune Activation Predictors of Sustained Viral Control in HIV-Infected Adults Undergoing a Brief Analytical Treatment Interruption after Administration of Pegylated Interferon Alpha 2b in Combination with Two Intravenous Broadly HIV-1 Neutralizing Antibodies 3BNC117 and 10–1074''[14] (hereafter referred to as ''the trial''). In this trial, participants are randomized to receive one of two interventions, but all participants undergo an ATI.

The participant experience study was CAB-led with the support of the overall BEAT HIV CEG. CAB members originally identified the need for a participatory study exploring the experiences of clinical trial participants undergoing HIV cure-directed studies. CAB members contributed to and helped to lead all phases of the research process. The purpose of this article is to describe participants' motivation to join a cure-directed study and enrollment experiences, using in-depth interviews administered after study enrollment. As well, the article demonstrates the importance of fostering partnerships between community members and clinical researchers to advance HIV cure-directed research. Such partnerships enable investigators of clinical trials to implement protocols that consider and prioritize participants' values, potentially enhancing trial recruitment, retention, and long-term impact.

Materials and Methods

Our study is informed by principles of Community Based Participatory Research (CBPR), a research model in which community members are actively engaged with researchers throughout the research process ranging from conceptualization, design, implementation, and analysis to communication of findings.[13]

All participants in the parent trial were eligible and offered participation in the participant experience study. Trial inclusion criteria were as follows: 18 years or older, spoke English, and able to give informed consent. Following an explanation of the participant experience study, participants signed a consent form agreeing to an initial interview and a second interview after completion of their participation in the parent trial. When a new participant was enrolled in the parent trial, a member of the clinical study team contacted our study team (Table 1) to schedule a telephone interview approximately 2 weeks after enrollment to discuss their initial experiences in the study.

Between August 2020 and February 2021, data were collected over the telephone through one-on-one, open-ended semi-structured interviews. The purpose of the interview was to elicit perspectives on participating in a cure-directed clinical trial that includes rigorous biologic and standardized survey data collection and a period of HIV treatment interruption. An interview guide, originally conceptualized and designed by the CAB and refined by the study team, was administered over the telephone by a research coordinator from the Mixed Methods Research Lab at the University of Pennsylvania (a copy of the interview guide can be found in Supplementary Appendix A1). Each participant was given $50 per interview. Interview transcripts were reviewed by team members on an ongoing basis for quality control. Interviews were audio recorded with participants' permission, transcribed, de-identified, and entered into NVivo 12.0 for coding and analysis.

We conducted a directed content analysis of the data. The study team developed a codebook by conducting a line-by-line

Table 1. BEAT-HIV-02 Study Scheme

	Time period	*Group 1*	*Group 2*
Step 1	0 weeks	ART+baseline evaluation (innate response measures, leukapheresis/rectal biopsy, ophthalmic evaluation), qualitative interview	
Step 2	4 weeks	ART+pegintron injections	ART
Step 3	26 weeks	ATI+pegintron injections+broadly neutralizing antibodies IV infusions	ATI+broadly neutralizing antibodies IV infusions
Step 4	12 weeks	ATI+follow-up	ATI+follow-up
Step 5	12 weeks	Return to ART, optional continued ATI	Return to ATI, optional continued ATI

ART, antiretroviral therapy; ATI, analytical treatment interruption; IV, intravenous.

reading of three transcripts to identify key concepts in the data. Two coders (R.N., Z.B.) established strong inter-rater reliability with three interviews; initial coding was validated by additional team members (K.D., C.R., N.L.J.). The remaining interviews were divided between reviewers and coded independently. After all data were coded, each code was summarized and examined for patterns.

The University of Pennsylvania Institutional Review board reviewed and approved this study.

Results

Fourteen of 15 participants in the parent trial completed an interview. One trial participant declined participation. The majority of participants ($n=9$, 64%) were 50–60 years old and cisgender male ($n=11$, 79%). Additionally, 11 participants identified themselves as Black (79%) (Table 2). Participants described motivating factors (Table 3) for participation, their study experience to date, and their expectations for the ATI.

Motivations for participation

Improve the lives of community members. Participants frequently described feeling a close connection to the HIV community and hoped their participation in the trial would directly and positively impact those who were also living with HIV. Recognition was given to past clinical trial participants for their contributions to making HIV medications more effective and medication routines easier to manage. Several participants shared that their participation was motivated by a desire to pay forward the efforts of past clinical trial participants to younger people in the HIV community.

> ''People before me got me [here]. So now it's like, I only have to take one pill once a day. This is nothing, giving blood and transfusions, or doing the biopsies. That's nothing. I mean, that's the least I can do to give back.''

> ''It's not about me, this is just to help somebody else that's coming aboard this thing, somebody else is going to be positive [for HIV]. And what I'm going through, if it would just make their life a little bit easier.''

Table 2. Participant Demographics (Age, Race, Sex)

Age		*Race*		*Sex*	
30–40	2	Black	11	Male	11
41–45	2	White	3	Female	2
46–50	1	Asian	0	Trans (MtF)	1
51–55	4	Other	0	Total	14
56–60	5	Total	14		
Total	14				

MtF, male to female.

One participant shared that their identification as Black contributed to their decision to enroll. This participant noted that limited Black representation in clinical trials, caused by a lack of trust in research, meant that certain medications were not effective for their community.

> ''It gives science the opportunity to be able to target and help people with different genotypes. Most African Americans are really spooked by clinical studies, because of the Tuskegee study. At the end of the day, we need more people with more genotypes to be able to find medicines that will help everybody.''

Involvement of Black participants in the trial felt particularly significant to this participant, as it would mean future HIV treatments would be effective for people who looked like them, making their contribution even more valuable.

Improve HIV treatments/move toward HIV cure. All participants believed that enrolling in the ATI trial could help advance the search toward a cure for their HIV; however, few expected personal benefit.

> ''When I think about all the people who died in the early stages of it, and now knowing all the newer research that has made a difference that they didn't get the opportunity to witness. That's one of [my] main influences to continue to be a part of something so major and know that, somewhere down the line, we will find a cure for this, and that people won't have to die anymore because of this illness.''

Participants held out much hope for the future of HIV science and shared a desire for their data to contribute to an eventual cure for HIV.

Desire to learn. Participants often referenced the ability to learn about their own bodies and HIV science in general as a motivator for participating in the trial. Undergoing extra procedures and check-ups, though not always comfortable, made participants feel secure in their health. Additionally, one participant shared that one of the study procedures had caught a medical issue long before it would have been found through regular screening.

Table 3. Motivations for Participation in BEAT-HIV-02

Improve the lives of community members	A desire to help others with HIV, particularly those who were recently diagnosed or have yet to be diagnosed, with the hope that their experience will be easier than the participants. Participants wanted to pay forward the efforts of previous study participants who had made their own experiences with HIV easier.
Improve HIV treatments/ move toward HIV cure	A desire to help find a cure for HIV and AIDS, whether it come from BEAT-HIV-02 or a future study.
Desire to learn	A desire to know more about HIV and the treatments scientists can offer and are hoping to offer to treat and/or cure it. Participants appreciated receiving laymen's terms explanations from researchers.
A good candidate for research	A desire to participate as a result of being healthy and able to do so.

Several participants felt that it was difficult to learn about HIV research on their own, as resources were rarely written in plain language.

> ''I like learning about the new procedures they're trying because trying to read on the internet, there is so much coming at you, I wouldn't even know what was real and what wasn't. So, it's nice to have the actual knowledge that this is what they're trying.''

The research team was seen as an excellent learning resource for participants who wanted to learn more about HIV research and treatments, as they were able to answer questions and describe the science in a way participants understood.

A good candidate for research. Several participants felt they would be good candidates for the trial because they were in good health at the time of enrollment. Indicators of good health were described as a lack of side effects from HIV medication, a high CD4 count, and an undetectable viral load.

> ''Occasionally I do studies for [University], just to help them with research, I guess because I'm in pretty good health. I'm a good subject for them that they can do studies with. So, I figure if it helps to move [research] along, then I don't mind doing it.''

No participant shared that being a good candidate for research was their primary motivation for enrollment.

Compensation. Participants felt that it was important to be compensated for the time and effort they put into the trial, but payments were not the primary or sole motivation for study participation for any participant. One participant described payments as a signal from the research team that they understood and valued the effort put forth by participants, which they appreciated.

> ''Once they gave me the opportunity to do it, I was all in, despite the money. I probably would have done it for free with just some carfare and lunch money, but compensation helps because it says that the science and the people involved with this study consider people's time and their efforts.''

Several participants shared that the payments they received for participation were greatly appreciated, as they were able to use them to ease financial stressors.

Enrollment and understanding of research study

Enrollment decision process. Participants heard about the trial through a variety of sources, including study staff, Craigslist, and, most commonly, their primary HIV care provider. Before giving their consent to participate in the trial, most discussed the study with a combination of HIV providers, family members, friends, and sexual partners. All participants discussed the study with their primary HIV care team, many describing a long-standing relationship that they could lean on for trusted advice. A few participants also mentioned that their primary HIV provider received regular study updates that gave them comfort with some of the riskier aspects of the study.

> ''[My doctor has] always let me direct my healthcare and he just gives me information I need to make better decisions. And if he thought there was [a study] I shouldn't do, he would contact me and say, 'Hey, I don't think you should be in the study.' But he has never done that.''

Participants shared study participation with family, friends, and sexual partners for practical and emotional purposes. Practical reasons included organizing transportation to the study site, having someone check up on them in case something went wrong, or planning partner protection for the ATI phase of the trial. Several participants reported that they had talked through the study details with loved ones to assure them that it would be safe to participate. A few participants did not share their participation with loved ones, citing a belief that study participation was a private matter.

Understanding of research process. When asked how they would describe the trial to a friend or family member, all participants were able to summarize the study objectives, though each had their own way of doing so. Some centered their descriptions around the science involved in study interventions, others explained the study in terms of expectations, and summarized their understanding in lay terms.

Many had participated in research in the past, including clinical trials for previous HIV treatments. Participants understood the procedure for the clinical trial study in which they were enrolled in addition to the research process as a whole.

> ''So how do you think that you get to take a Tylenol? That was a study at one point. It wasn't always, you know, FDA approved. Just because I'm doing [the trial] doesn't make me wrong or stupid, my eyes are wide open to what I'm doing.''

Though all participants had knowledge of the science behind the trial, few thought they would ever see the results, or understand them if they did get to see them. Those who had participated in projects in the past were not accustomed to receiving the study results and did not expect to get them from this trial study.

Working with the research team. All participants spoke at length about their relationship with the trial study team,

praising them for their professionalism, communication, and reliability. Participants noted that study team members took the time to get to know them and several indicated that the efforts of the study team helped them to stay engaged and take their participation seriously.

> ''I don't get worried about stuff like that, because I know that I'm working with a team of people who are actually so considerate about my wellbeing and making sure that I'm okay.''
>
> ''They're just on top of it, and they don't make me feel like a number. They don't make me feel like a secret. They make me feel like a valued human being.''

Several stated that it was occasionally challenging to organize study appointments around their work schedule, particularly when the procedures took a long time or required resting afterward. However, those same participants anticipated these challenges when they enrolled in the trial and appreciated that the trial study team worked with them to make participation as convenient as possible.

Expectations

Analytical treatment interruption. At study entry, several participants mentioned feeling nervous about the pause in ART during the trial. Concerns included being unable to return to having an undetectable viral load, having to switch medications, and experiencing more side effects as a result, and altering a long-established medication routine without knowing what would happen. A few participants stated they may halt participation if their viral load became detectable.

> ''If there comes a time in the study that my numbers start going up or I have health problems, then I would probably opt out, but at this point, I'm still okay.''

Not all participants were anxious about the ATI since they had been off their ART in the past without issue. A few were looking forward to the ATI phase of their participation. These participants felt curious to learn how their body would react when they stopped taking ART. Moreover, the structured, supervised nature of the ''pill holiday'' provided a sense of security for some.

A minority of participants stated that they had sexual partners at the time of their interview. Those who had sexual partners said that they had spoken with their partner about how to protect them during the ATI phase and felt confident that their plan would be effective. Several participants felt that not having a regular sexual partner encouraged them to participate in the trial because they would not have to worry about protecting another person.

Participating in research during the COVID-19 pandemic. Few participants expressed concerns with participating in the trial during the COVID-19 pandemic. Participants felt comfortable coming to the study site, noting that there were consistently low patient volumes in waiting rooms and that mask wearing was universal within the study clinic. COVID-19 vaccines were provided to study participants as soon as they were available. One participant added that the pandemic allowed them to work from home, which made it easier to attend study visits. Another appreciated that study visits gave them an excuse to leave the house at a time when they would otherwise be isolated indoors.

> ''If it wasn't for COVID, it would be difficult to just up and leave my desk to go to the [study] appointments. And if you can't do the appointments, then you can't participate in the study.''

Discussion

Our nested qualitative in-depth interview study provided a unique window into the perspectives of trial participants entering the BEAT-HIV-02 HIV cure-directed clinical trial with an ATI. As a CAB-driven project, our study provides insight into the experiences of trial participants and advances social, behavioral, and health research on the topic. We gained insights into motivators of participation, the critical role of HIV care providers in endorsing trial enrollment, and the experiences of study participants in an HIV cure-directed clinical trial. We learned that worries related to anticipating the ATI are a common experience among participants.

The desire to contribute to finding a cure for HIV and contributing to scientific knowledge was a primary motivator to participation for most trial participants. Our findings are consistent with altruistic benefits reported in similar HIV cure-directed clinical research involving ATIs,[15–17] in addition to hypothetical research around willingness to participate in ATIs.[4,18,19] As conceptualized in HIV cure research, altruism supports individual participation in research for the common good.[16,17,20] As described in a recent scoping review on altruism in HIV cure-directed clinical research,[21] more nuanced socio-behavioral research is needed to better understand the types of altruism driving intentions to participate in HIV cure-directed clinical research [*e.g.,* community, political (HIV activism),[22] experiential, moral, existential, psychological, and other factors]. Notably, participants linked their altruism to a deep sense of community among PLWH and a recognition of the efforts of community members before them who participated in clinical trials to advance HIV research.

Our study highlights the important role of primary HIV care providers in referring participants to HIV cure-directed clinical trials. In the context of this trial, providers acted as a trusted source of information when deciding whether to participate. Préau and colleagues, in assessing acceptability of HIV cure trials among French physicians, suggested that HIV cure research participation should occur within the context of trustful doctor–patient relationships.[23] In China, Rich and colleagues recommended enhancing patient–physician communication about ongoing HIV cure trials as a critical component of developing an HIV cure.[24] In studying the social meaning of curing HIV, Chu and colleagues showed how perceptions of HIV cure research participation could not be dissociated from relationships with physicians and health systems.[25] Considering these findings, and as evidenced by our study, we anticipate HIV care teams will remain important resources for recruiting and supporting HIV cure-directed clinical trial participants. The context of the provider-researcher- participant consultation will also have profound effects on a person's decision whether to enter these trials.

That participation in the trial was motivated by racial inclusion is an important finding, particularly considering the limited Black participant representation in HIV cure-directed clinical trials to date.[26,27] To our knowledge, the parent trial

Table 4. Key Findings and Implications for Future HIV Cure-Directed Clinical Research Generated in Collaboration with BEAT-HIV Community Advisory Board

Key findings	*Implications*
Participants are motivated to improve the lives of community members living with HIV	Link with local community groups to recruit trial participants
Participants are interested in increasing diversity of research trial participants	Learn how to acknowledge the history of distrust between the Black community and research community Directly discuss racism and health disparities with participants
HIV care providers represent a resource to participants while they decide whether or not to enroll	Reinforce the importance of the research team being in contact with the HIV care team Create opportunities for regular communication among the research team, HIV care team, and participant Create materials about HIV cure-directed clinical research specific to HIV care providers
Participants view compensation as a sign of respect for their time	Assure that participants are being paid for their time and for the cost of their transportation to the study site Challenge the default idea that compensation leads to coercion in all cases
Participants are unaware of study results and do not expect to see them	Assure that participants are shown the study results in plain language and are allowed to ask questions about them Include dissemination of aggregate results to participants and community partners as a planned and monitored milestone in clinical trials

is one of the first to report predominant enrollment of Black participants in an ATI trial in the United States.[28] This finding is encouraging given the previously reported lower willingness to participate in HIV cure-directed clinical trials reported among racial and ethnic minorities in the United States.[29–31] These findings underscore the critical importance for integrating intersectional and racial equity frameworks to HIV cure-directed clinical trial implementation, and helping participants overcome barriers to research participation.[32]

We gained insight into specific anticipatory concerns around the ATI. Consistent with similar ATI participant-centered reports, at trial entry, participants were concerned about becoming detectable for HIV, having to change their HIV medication, and altering medication routine.[16,17,20] ATI-related worries were counter-balanced by the close clinical monitoring received as part of the trial. Participants with prior experience being off ART for personal reasons were less worried, consistent with a prior report around hypothetical motivations to participate in ATIs.[4] A deep sense of trust in the study team helped to allay concerns about the ATI. Moreover, the compensation that participants received from the study team was interpreted as a sign of appreciation for their effort.

We find it concerning that participants with prior study experiences did not expect to learn about study results. Congruent with the philosophy that study participants are partners in the research, the parent study will provide feedback about the results. We argue that providing participants with a lay summary of trial outcomes communicates a mutual sense of trust and respect that is key in studies that require significant physical and emotional investment.

Notably, the BEAT-HIV-02 trial occurred during the COVID-19 pandemic. Because all in-person study contacts took place in a health care setting, strict safety measures were in place beginning in March 2020 and few participants reported direct concerns around participation in the clinical trial during this time. While the intensity of the trial may have placed participants at increased risk of COVID-19 by increasing the number of possible exposure events, these risks were mitigated by the close clinical monitoring of trial participants, vaccinations, masking, and social measures.[8] Participants attributed their comfort with regard to COVID-19 risks to the belief that the study team and their primary HIV providers were acutely concerned for their safety and taking necessary precautions to reduce risk.

Limitations

One limitation of this study is that we did not capture the perspectives of individuals who declined to participate in the clinical trial, giving us a limited understanding of the barriers to trial participation.

Additionally, this study took place during the COVID-19 pandemic, requiring interviews to be done over the phone. It is possible that more participants would have enrolled in the parent trial had the pandemic not occurred, or that richer data could have been collected from in-person interviews.

Conclusions

CABs are central partners in HIV cure-directed research. CAB leadership motivated all aspects of this study that provided insights that revealed implications for recruitment and retention into future cure-directed clinical trials (Table 4). Principal motivations were overwhelmingly altruistic: wanting to help other members of the HIV community and contributing to the fight for a cure for the disease. In deciding to participate in the study, participants' trusted HIV providers had the most influence over their decision to enroll. Safety measures and study team respect for participants greatly enhanced adherence to protocols and study retention. Although participants described their experience with procedures as positive thus far, they almost uniformly expressed some level of concern about the upcoming ATI phase. Next steps include examining post-trial reflections on the ATI.

Authors' Contributions

Conceptualization: C.R., K.A.R, D.M., K.D., F.K.B. Data curation: R.N., Z.B. Project administration: R.N., Z.B. Formal analysis and investigation: R.N., N.L.J., C.R., K.A.R., Z.B., K.D., F.K.B. Funding acquisition: F.K.B., K.A.R. Supervision: F.K.B., K.A.R. Writing—original draft preparation: R.N., Z.B., N.L.J., K.D. All authors reviewed and edited article drafts including the final draft of the article.

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Author Disclosure Statement

No competing financial interests exist.

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Supplementary Material

Supplementary Appendix A1

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