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Who are the persons living with HIV who might refuse to participate in HIV cure-related clinical trials with treatment interruption?

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Achieving a HIV cure has become a research priority. As any improvement of knowledge, which could help scientists design new HIV cure-related clinical trials (HCRCT) depends on the risks potential participants are willing to accept, it is important to understand who will agree or refuse to participate and in which proportions. By providing insights into factors associated with reluctance toward HCRCT participation, our results may help clinicians in patient recruitment.

Achieving a HIV cure has become a research priority, implying the need for HIV cure-related clinical trials (HCRCT) with analytical antiretroviral treatment interruption (ATI) [1–13]. In the current context of modern, well tolerated, combined antiretroviral therapy (cART), clinical and biological HCRCT-related issues cannot be disconnected from associated ethical questions or from the consequences on the daily lives of persons living with HIV (PLWH) who will participate in HCRCT [14–26]. As any improvement in knowledge regarding future HCRCT depends on the risks that potential participants

are willing to accept, it is important not only to document their preferences for different candidate HCRCT types but also to acquire a greater understanding about which PLWH would be more likely to agree or to refuse to participate, and in which proportions [15,26–29].

The ANRS-APSEC study (Acceptability, expectations and preferences for HCRCT among PLWH with undetectable viral load and caregivers) [27,29,30] produced new knowledge regarding this issue.

Between October 2016 and March 2017, all PLWH who had a scheduled follow-up consultation during a dedicated week meeting HCRCT eligibility criteria (≥ 18 years old, stable ART regimen ≥ 6 months, undetectable viral load ≥ 3 years, and $CD4^+ > 500$ cells/ μ l) were surveyed in 19 French HIV services. One questionnaire (detailed in [26]) section presented PLWH with four viewpoints (elicited elsewhere [27]), from the most motivated to the most reluctant vis-à-vis participation in HCRCT with ATI. PLWH were asked to rate, on a 7-point Likert scale, to what degree each of the four viewpoints reflected their opinion.

To construct the dependent variable, we performed a principal component analysis of their answers, creating a ‘reluctance score’ to represent their level of willingness to participate in HCRCT (from -5.46 very motivated, to $+6.51$ very reluctant). The higher the score, the more reluctant respondents were to participate.

The reluctance score allowed us to infer the proportion of respondents that would be motivated (score < 25 th percentile) or reluctant (> 75 th percentile) to participate and to compare these proportions with those obtained when we used the usual direct question found in the literature ‘If an HCRCT were available, would you participate in it?’ (‘Absolutely not’, ‘Probably not’, ‘Yes, perhaps’, ‘Yes, definitely’).

We performed a multivariable linear regression to determine factors associated with reluctance to participate in HCRCT.

All 195 PLWH presented to the interviewers agreed to participate. Women constituted 23.58% of the sample, median [IQR] age was 53 [45–61] years, and median experience with HIV was 17 [11–25] years.

Intention to participate in HCRCT using the direct question was distributed as follows: 42.56% responded ‘Yes, definitely’, 37.95% ‘Yes, perhaps’, 10.78% ‘Probably not’, and 8.72% ‘Absolutely not’. More nuanced replies were obtained when inferred from the reluctance score (Fig. 1).

On the basis of the reluctance score, a lower percentage of PLWH would be motivated to participate in HCRCT (26.67%) than the 42.56% who answered ‘Yes, definitely’ to the direct question. In contrast, a larger percentage of PLWH would be reluctant to participate (21.03%) than the 8.72% who answered ‘Absolutely not’.

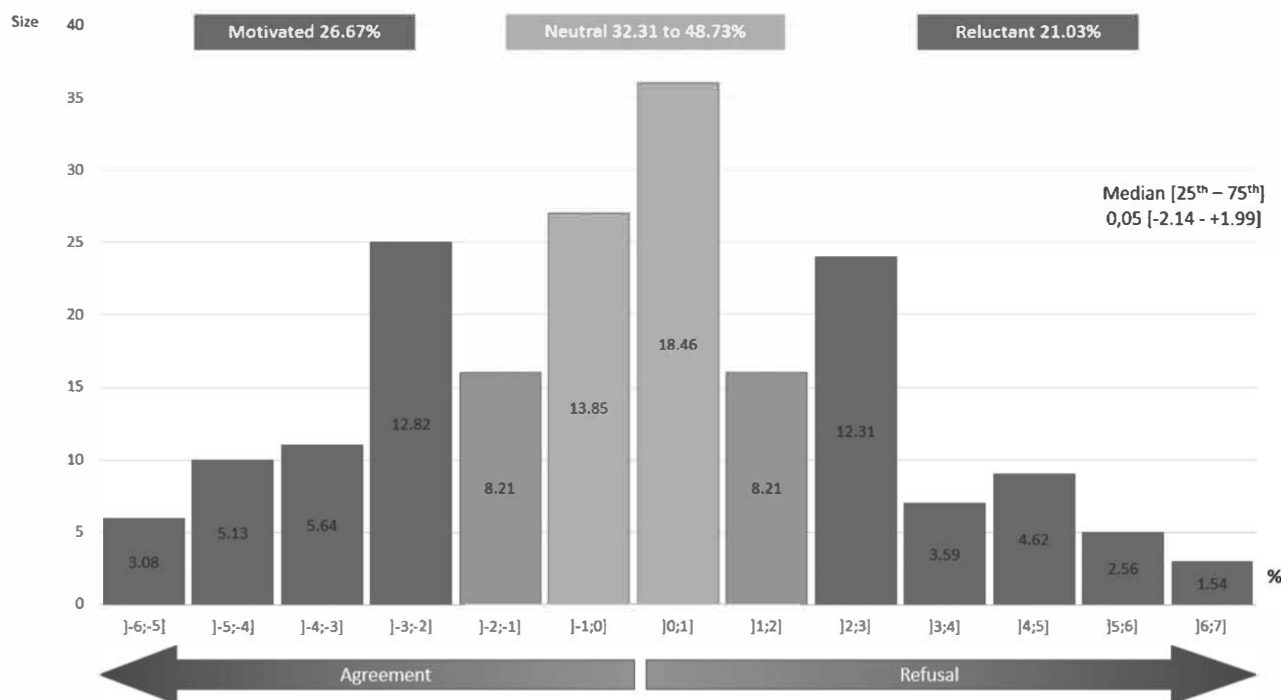


Fig. 1. Distribution of respondents according to the reluctance score ($n = 195$).

The final best-fit model showed that PLWH who reported a precarious financial situation ($\beta=0.863$, $P=0.027$), those with the highest ($\beta=1.220$, $P=0.015$) educational levels, those with the lowest ($\beta=1.399$, $P=0.005$) educational levels, and those who thought that current ART would continue to be effective only in the short/medium term (versus long term) ($\beta=1.548$, $P=0.006$) would all be more reluctant to participate in HCRCT. In contrast, patients who self-identified as belonging to the PLWH community ($\beta=-1.031$, $P=0.014$), and those a little or very concerned about the risk of HIV transmission ($\beta=-0.895$, $P=0.091$; $\beta=-1.231$, $P=0.005$) would be less reluctant, and thus more motivated to participate.

Gender, being a homeowner, professional status, self-perceived health-state, self-identifying as belonging to the LGBT community, being an HIV activist, and feeling proud or self-confident, were no longer significant.

Some of these results deserve special attention. First, financially precarious PLWH may anticipate difficulties regarding hospital visits in terms of time and economic burden. Second, the association between reluctance and both low and high educational levels reflects findings regarding vaccination hesitancy in the general population [31–34]. This result can be explained on the one hand by a lack of information about prevention strategies and on the other hand by misinformation and mistaken beliefs relayed by (social) media [32,35–38]. Third, the association between a lack of confidence in the long-term efficacy of cART and reluctance to participate may seem counter-intuitive, but this factor might have captured a more general lack of confidence in the healthcare system, including HCRCT efficiency [33,39]. Finally, in line with previous surveys underlying that PLWH motivations to participate were more altruistic than individualistic [18,20,26,27,30], the results showed that PLWH concerned about the risk of HIV transmission would be more motivated to participate in HCRCT, hoping they could put an end to transmission.

Using the novel approach of examining PLWH level of agreement with different viewpoints, instead of using the usual direct question, in order to document their willingness to participate in HCRCT, our results, despite being declarative, may better reflect real-world decision-making, and may partly overcome the issue of social desirability bias [40,41]. Declared willingness to participate in HCRCT may have been overestimated in previous quantitative studies [15,22,27,28] as suggested by qualitative surveys [16,42,43,20,29]. Knowing the proportion of PLWH who would agree to participate is important for physicians when designing new HCRCT. Moreover, providing insights into factors associated with reluctance to participate in HCRCT may help clinicians in HCRCT recruitment and inform them of potential

selection bias. Greater attention should be paid to the burden associated with hospital visits for treatment and examinations, particularly during ATI, as well as the need to provide clear information to counter mistaken beliefs about future HCRCT.

Finally, our results emphasize the need to consider not only clinical characteristics, but also social and identity characteristics when implementing HCRCT. They also underline the importance of actively involving PLWH in discussions about the goals of HIV cure research [2,19].

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Conflicts of interest

There are no conflicts of interest.

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