

## Viewpoint

# Hypothetical questionnaires may overestimate willingness to participate in HIV cure research: Comparison of a cross-sectional survey to actual willingness to participate in an HIV cure study in the Netherlands



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## ABSTRACT

**Objective:** Little is known about willingness among people living with HIV (PLHIV) to participate in HIV cure research in the Netherlands. We compared results of a cross-sectional questionnaire assessing hypothetical willingness to actual willingness among PLHIV to take part in a clinical HIV cure trial.

**Methods:** Between March and June 2018, PLHIV visiting the outpatient clinic of a university hospital in the Netherlands were asked to complete a questionnaire about HIV cure research. Results were compared to the number of PLHIV willing to take part in an actual HIV cure study at the same center during an overlapping time period.

**Results:** In total, 165 participants, predominantly male (80%) from Western European countries (61%) completed the questionnaire. The majority would participate in cure research ( $n = 111$ , 67%). Separately, actual willingness among PLHIV to participate in an HIV cure study was addressed in 312 cases. Apart from gender (96% male), baseline characteristics were comparable. Less than half expressed actual willingness to participate in the study ( $n = 135$ , 43%).

**Conclusions:** Hypothetical willingness to participate in cure-related research was high among PLHIV who completed the questionnaire. Actual willingness among eligible PLHIV to take part in an HIV cure study was much lower. Our findings show that questionnaires may overestimate willingness to participate in HIV cure trials and indicate that reasons for refusal in actual research should be further explored.

## Introduction

Currently, little is known about willingness among people living with HIV (PLHIV) to participate in cure-related research in the Netherlands [1]. Since most of the studies in the field of HIV cure are either preclinical or early phase clinical trials [2], PLHIV who participate in HIV cure research cannot expect an immediate clinical benefit at this stage. Therefore, assessing the view of PLHIV is important, and indeed was defined as one of the key recommendations of the International AIDS Society global scientific strategy [3]. Such information is crucial to determine acceptability of HIV cure research and trial participation, and helps guide (future) HIV cure research [4]. Previous studies showed that PLHIV consider participation in HIV cure research mainly for altruistic reasons [5–8]. Some participants indicated that they would need more information and education about the potential risks before taking part in HIV research [5, 8]. Furthermore, three

online questionnaires completed by a large group of PLHIV in the Netherlands, United Kingdom and USA showed that HIV cure research is highly acceptable, and that many PLHIV who are willing to participate in HIV cure research would accept risks, including antiretroviral therapy (ART) interruption [1, 9, 10]. However, since online questionnaires often rely on self-selection, the results should be interpreted with caution. Here, we compare the results from a questionnaire about hypothetical willingness to take part in HIV cure research to actual willingness to participate in an HIV cure study among PLHIV visiting the same outpatient clinic in the Netherlands during an overlapping period of time.

## Methods

We conducted two separate studies. First, a quantitative, cross-sectional questionnaire in the Dutch and English language containing

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18 questions was developed based on literature focusing on attitudes towards HIV cure research [6, 9, 10]. It was adjusted with the help of healthcare professionals from the Erasmus University Medical Center (MC), Rotterdam who are involved in research questionnaires as well as HIV care and HIV cure research (AV, CR, HP, SB) (appendix). After approval of the Medical Ethics Review Committee, PLHIV visiting the HIV outpatient clinic of the Erasmus MC between March and June 2018 were asked to fill out the questionnaire. Inclusion criteria for the study were age  $\geq 18$  years and understanding of the spoken Dutch or English language. After providing written informed consent, participants completed the questionnaire in the presence of the investigator. One question could be answered by “yes”, “no”, or “maybe”. The others included a 5-point Likert scale ranging from 1 = “very important” or “very likely” to 5 = “totally not important” or “totally not likely”. The investigator, a medical student, was present when participants filled out the questionnaire, and provided an explanation if a question was not understood or if the participant was illiterate (n = 4). All demographic characteristics of the PLHIV who completed the questionnaire (n = 165) were retrieved from electronic patient records.

Separately, PLHIV visiting the outpatient clinic of the Erasmus MC between January and December 2018 were screened for eligibility to take part in a randomized controlled clinical trial involving latency reversing agents (LUNA).[11] Eligible PLHIV were informed by their treating physician about a trial involving two weeks of study medication and ten study visits with phlebotomies. PLHIV were informed that their ART would not be interrupted and that participation would not lead to cure. If PLHIV expressed willingness to participate they were referred to the HIV clinical trial unit for additional screening. Demographic characteristics were retrieved from Stichting HIV Monitoring Netherlands [12] for all the 312 eligible PLHIV with whom participation in the HIV cure study was discussed.

## Results

### Hypothetical willingness to participate in HIV cure research

A total of 165 PLHIV completed the questionnaire, 80% (n = 132) were men with a median age of 50 years (interquartile range (IQR): 41–58). The majority (n = 100, 61%) were born in Western Europe, followed by the Caribbean (n = 27, 16%) and Sub Saharan Africa (n = 25, 15%). The main mode of transmission was male to male sexual contact (n = 93, 56%) or heterosexual transmission (n = 66, 40%). Most participants were currently on ART (n = 162, 98%) with an undetectable plasma viral load of  $<20$  copies/mL (n = 148, 90%). These patient characteristics are representative for the general outpatient at the Erasmus MC (data not shown).

Almost all participants (n = 163, 99%) indicated that HIV cure research was “very important”. Over two-thirds (n = 111, 67%) responded “yes” to the question whether they would participate in HIV cure research for altruistic reasons, while 7% (n = 11) answered “maybe”. Fig. 1A shows the perceived importance of six potential disadvantages or risks of HIV cure research. A higher HIV transmission risk, having to interrupt ART, and viral rebound were considered ‘very important’ by 82% (n = 136), 58% (n = 96) and 68% (n = 112) respectively. Responses to the questions regarding undergoing extra invasive procedures such as phlebotomies and additional hospital visits were more diverse; 18% (n = 30) and 22% (n = 36) stated that these disadvantages were “very important”, while respectively 45% (n = 74) and 38% (n = 63) answered “totally not important” to these questions. The most important potential advantages according to the majority of the participants (n = 152, 92%) were not being able to transmit HIV after a cure and, depending on the cure approach, not being able to become re-infected with HIV after cure. Furthermore, 69% (n = 114) answered that losing HIV stigma was “very important”, while 9% (n = 15) indicated that this was “totally not important” (Fig. 1B). Having fewer HIV-related health problems and contributing to scientific knowledge was “very important” to respectively 74% (n = 122) and 84% (n = 138).

### Actual willingness to participate in an HIV cure trial

During 2018, 2036 PLHIV visiting the outpatient clinic of the Erasmus MC were screened for eligibility for a clinical HIV cure study (11). In total, 594 PLHIV were eligible and physicians treating 312 candidates addressed participation during the consultation. Since females in the reproductive age were excluded from the trial, most of the 312 eligible PLHIV were male (n = 299, 96%). The majority (n = 235, 75%) originated from Western Europe, followed by Sub Saharan Africa or the Caribbean (n = 35, 11%), and 9% (n = 29) from Eastern Europe or Asia. Median age was 50 years (IQR: 42–58). Main mode of HIV transmission was male to male sexual contact (n = 225, 72%).

Of the 312 cases in which participation was addressed, 43% (n = 135) indicated willingness while 57% (n = 177) refused, either at their own discretion (n = 131, 74%) or because the treating physician judged that they were not suited for inclusion at that moment (n = 46, 26%). PLHIV who refused most commonly gave no reason (n = 53, 40%) or considered participation not logistically feasible (n = 50, 38%). Others indicated not to be interested (n = 16, 12%) or gave different reasons (n = 12, 9%).

## Discussion

For this questionnaire, PLHIV attending a large HIV outpatient clinic in Western Europe were approached without preselection. Of the PLHIV

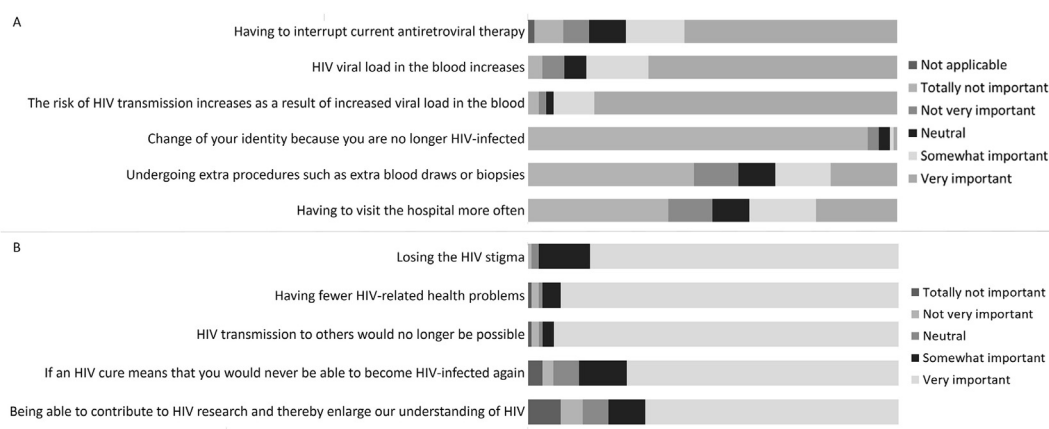


Fig. 1. Selected number of questions from the questionnaire (appendix). 1A. Importance of potential disadvantages and risks of HIV cure research. 1B. Importance of potential advantages of HIV cure research. Bars in the chart columns are based on percentages (not shown).

who completed it, the majority expressed high willingness to take part in HIV cure studies in a hypothetical scenario. Participation rates predicted by the questionnaires are in line with previous online surveys that indicate that at least 50% of the participants would participate in HIV cure studies without personal benefits (9, 10). Separately, but during an overlapping period of time at the same medical center, a larger, pre-screened number of PLHIV was approached to take part in an HIV cure study. Here, actual willingness among PLHIV to take part in HIV cure research was considerably lower. A reason for refusal to participate that was commonly given was that participation was logistically unfeasible. These findings might partly reflect the need expressed by PLHIV for more information and education about the potential risks and logistical implications of participating in HIV cure research (5, 8). However, given the personal, behavioral, ethical and social implications of participating in HIV cure research, the reasons for refusal are likely to extend beyond logistic impracticalities. To comprehend such motives, and why refusal rates are higher when faced with the actual opportunity to participate in HIV cure research, it is important to understand of the meaning of HIV cure to PLHIV, and what they deem acceptable risks (3, 4). It would also be interesting to further explore the reasons why treating physicians judged some eligible PLHIV as unsuitable for inclusion in a clinical HIV cure study.

To our knowledge, this is the first time a questionnaire assessing hypothetical willingness to participate in HIV cure research is compared to the actual willingness of PLHIV to take part in an HIV cure study during an overlapping period of time at the same medical center. In this case, the questionnaire overestimated hypothetical willingness when compared to actual willingness to take part in a specific HIV cure study. A possible explanation for this observation is that logistical feasibility is a less influential factor in a hypothetical context. However, the reasons why PLHIV decline to participate in HIV cure research likely extend beyond logistic impracticalities.

### Limitations

The cross-sectional questionnaire has a number of potential limitations. There is no missing data since the investigator was present while participants filled out the questionnaire. However, this might have introduced some social desirability bias. Moreover, participants who did not understand the Dutch or English language could not be included, and permission to take part in the questionnaire was asked by the treating physician, possibly introducing selection or referral bias. With regard to the HIV cure trial, PLHIV were pre-screened for eligibility while PLHIV approached to fill out the questionnaire were not. Comparison between the two distinct groups should be made with caution, and further studies are needed to explore these findings. Permission to take part in the HIV cure study was also asked by the treating physician and could also have led to referral bias. To avoid such biases in the future, assistance of an HIV specialized nurse could prove helpful in ascertaining that all PLHIV who visit the outpatient clinic are systematically asked to take part in a study. Finally, the questionnaire assessed willingness to take part in HIV cure research in general whereas the HIV cure study that PLHIV were asked to take part in was a randomized controlled trial involving latency reversing agents. Another type of HIV cure study may have resulted in a different level of willingness to participate.

### Conclusion

In conclusion, while participation in cure studies is altruistic and may involve individual health-related risks, our findings indicate a high level

of willingness to participate in hypothetical HIV cure research among PLHIV. Actual willingness among a larger pre-screened population to take part in an HIV cure study was much lower. These findings indicate that questionnaires may overestimate hypothetical willingness to participate in HIV cure studies. However, further studies comparing hypothetical willingness to actual willingness to take part in different types HIV cure trials are needed. Although information about logistic implications is key, reasons for refusal to take part in HIV cure research are likely to extend beyond impracticalities. Therefore, understanding how PLHIV perceive HIV cure and clear communication about the implications of participation in HIV cure research is vital.

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### Declaration of competing interest

There are no conflicts of interest.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jve.2020.100014>.

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