Development of a Patient Preference Questionnaire Appropriate for Use With Potential Regimens for HIV Cure

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Conclusions

- Our research suggests there is a gap in available patient-reported outcome (PRO) tools to assess the preferences of people with HIV (PWH) undergoing clinical trials of potential HIV cure regimens involving an analytical treatment interruption (ATI)
- We developed a de novo preference questionnaire—the HIV Treatment Preference Questionnaire (HIV-TPQ)—and evaluated it for content, clarity, and relevance with physicians, PWH advocates, and PWH
- Overall, the interviewees interpreted the questionnaire as intended, but several revisions to the questionnaire instructions and questions were identified and incorporated into a revised draft that will be further validated

Plain Language Summary

- An important global initiative is to identify new combinations of drugs or vaccines that may result in a cure for HIV
- To test these new combinations, PWH are invited to join clinical trials in which they may be asked to stop taking their current HIV medications for a time to see the effect of such combinations on their HIV levels
- We are developing a new questionnaire to use in potential clinical trials which can measure the preferences of PWH on new vs previous regimens
- We tested the questionnaire with disease experts and advocates for PWH, as well as PWH themselves, and amended the survey according to their feedback

References: **1.** Lau JSY, et al. *J Infect Dis*. 2022;226:236-45. **2.** Gold DT, et al. *Value Health*. 2011;14:1109-16. **3.** Rummel M, et al. *Ann Oncol*. 2017;28:836-42.

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Abbreviations: **ART**, antiretroviral therapy; **ATI**, analytical treatment interruption; **CD4**, cluster of differentiation 4; **HIV-TPQ**, HIV Treatment Preference Questionnaire; **NNRTI/non-nukes**, non-nucleoside reverse transcriptase inhibitor; **NRTI**, nucleoside/nucleotide reverse transcriptase inhibitor; **PWH**, people with HIV; **PRO**, patient-reported outcome.

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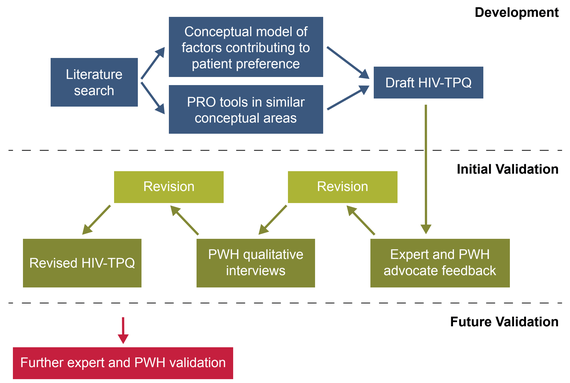
Introduction

- ATIs are important in the evaluation of potential regimens for HIV cure in clinical trials. However, ATIs are not risk free,[1] and clinical trial participants may experience viral rebound and/or psychosocial consequences of being off treatment, thereby limiting who may wish to participate in these studies
- We conducted an informal literature review of existing HIV clinical outcome assessments, and identified a gap in PRO measurement tools to capture PWH perspectives of long-lasting and/or cure interventions in clinical trials
- Our aim was to develop a de novo patient preference questionnaire (the HIV-TPQ) to address this need
- Here, we report the development and initial content validation of the draft HIV-TPQ. Further assessment and validation is planned

Methods

- A literature review contributed to the development of a conceptual model that described aspects of PWH treatment experience (**Supplement – see QR code**)
- Items included in the draft 11-item HIV-TPQ were developed based on the conceptual model and review of identified PRO tools in similar conceptual areas[2,3]
- Items compare participant preferences for various aspects of their regimen before the study vs the study regimen
- The draft questionnaire was evaluated in the United States by disease experts, PWH advocates, and PWH, as outlined in **Figure 1**
- The instructions on how to complete the questionnaire and the questions and response options themselves, including readability, were assessed as well as an additional set of instructions that incorporated a graphical depiction of preference (an arrow depicting direction of preference)

Figure 1. Development and Initial Content Validation of HIV-TPQ



HIV-TPQ, HIV Treatment Preference Questionnaire; PWH, people with HIV; PRO, patient-reported outcome.

Part 1 – Expert Feedback

- Written feedback on the draft HIV-TPQ was elicited from 2 disease experts and 1 PWH advocate through an online survey

Part 2 – PWH Feedback

- The draft questionnaire was then evaluated for content, relevance, and clarity through structured 90-minute interviews conducted virtually via HIPAA-compliant Zoom calls with PWH taking antiretroviral therapy
- PWH were provided copies of the questionnaire to complete during the interview using a cognitive debriefing approach
- Instructions, items, or response options for which issues emerged during the cognitive debriefing were further evaluated to determine if revisions to the HIV-TPQ were warranted
- We report results from the initial validation in 13 PWH (**Table 1**); after revision to the draft questionnaire, a second cohort of PWH will be enrolled for further validation

Results

Table 1. Characteristics of PWH Participating in the HIV-TPQ Cognitive Debriefing

Demographics (N = 13)	
1. Age Range, 18-68 years Mean, 43.4 (SD, 14.4)	**7. Education** Some high school (no degree), 1 High school graduate (or equivalent), 2 Some college (no degree), 3 Bachelor's degree, 3 Master's degree, 3 Doctoral degree, 1
2. Gender Male, 7 Female, 5 Transgender, 1	**8. Work status, mark all that apply** Part time, 5 Full time, 4 On disability, 3 Homemaker, 1 Retired, 1 Unemployed, 1
3. Sex Male, 8 Female, 5	**9. Health status** Excellent, 3 Very good, 3 Good, 7 Fair, 0 Poor, 0
4. Sexual orientation Gay or lesbian, 6 Heterosexual, 6 I don't know, 1	
5. Ethnicity Not Hispanic or Latino, 11 Hispanic or Latino, 2	
6. Race, mark all that apply Black or African American, 7 White, 6 Asian, 1	
Clinical Characteristics (N = 13)	
1. Time since HIV diagnosis Range, 2.8-37.4 years Mean, 14.2 (SD, 11.5)	**6. Past ART regimen[a]** Complete regimens, 11 NRTIs, 3 NNRTIs or non-nukes, 4 Protease inhibitors, 2 Integrase inhibitors, 2
2. ART regimen[a] Complete regimens, 12 NRTIs, 2 Protease inhibitors, 2 Integrase inhibitors, 4	**7. Virally suppressed** HIV undetectable, 13
3. No. of pills per day 1 pill, 10 > 1 pill, 3	**8. CD4 count** 0-50 copies/mL, 2 350-500 copies/mL, 2 > 500 to 3000 copies/mL, 6 I don't know, 3
4. Time since participant started current ART regimen Range, 0.4-20.2 years Mean, 5.8 (SD, 5.0)	**9. Most recent blood draw to measure CD4 count and/or viral load** Within the past 6 months, 13
5. Time since participant started taking any ART Range, 2.7-34.8 years Mean, 12.6 (SD, 8.8)	

Data presented as n except as noted.
[a]Participants could be counted in multiple regimens.
ART, antiretroviral therapy; CD4, cluster of differentiation 4; HIV-TPQ, HIV Treatment Preference Questionnaire; NNRTI/non-nukes, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor.

Part 1 – Expert Feedback

- Neither the disease experts nor PWH advocates reported any questions that were inappropriate to ask, but suggested simplifying some of the language and explaining some terms
- Accordingly, the instructions were modified for plain language, additional detail was added to instructions for clarity, and a definition of "treatment plan" was included

Part 2 – PWH Feedback

- Fifteen PWH were enrolled in the interview process matching the desired level of diversity, of whom 13 underwent the cognitive debrief (**Table 1**). Four of 13 did not fully complete the debrief process for reasons of time
- Most interview participants interpreted the HIV-TPQ as intended. Minor clarity and interpretation issues informed modifications to 4 items and PWH feedback supported inclusion of the additional instructions (**Table 2**)
- Current revisions to the questionnaire are summarized in **Table 3**

Table 2. PWH Cognitive Debriefing Feedback

	Interpretation	Clarity
Instructions	✓	✓
Item 1: overall preference	✓	✓
Item 2a: fit with lifestyle	✓	✓
Item 2b: convenience	✓	✓
Item 2c: ease of following treatment plan	✓	✓
Item 2d: ease of accessing treatment plan	✓	✓
Item 2e: ease of continuing treatment plan	✓	⚑
Item 2f: mental impact of managing treatment plan	⚑	⚑
Item 2g: emotional impact of treatment plan	✓	✓
Item 2h: physical impact of treatment plan	✓	✓
Item 2i: mode of administration	⚑	✓
Item 2j: confidence regimen is working	✓	⚑
Additional instructions	✓	✓

✓ denotes overwhelmingly interpreted as intended (ie, not misinterpreted) and clear; only misinterpreted by or unclear to ≤ 10.0% of participants providing evaluable data.
⚑ denotes misinterpreted by or reported as unclear by 10.0%-20.0% of participants providing evaluable data.

- PWH also reported minor interpretation issues with some response options
- Investigators felt that the included response options were necessary to maximize sensitivity of the measure and would likely be clearer to PWH when participating in clinical trials; therefore, no revisions were made at this stage
- Interpretation and clarity of response options will continue to be monitored in subsequent validations

Table 3. Summary of Feedback and Revisions to the HIV-TPQ

	Feedback	Revisions
Instructions	Include additional instructions (eg, arrow indicating direction of preference)	Incorporate
Item 2b: convenience	"Convenience" misinterpreted as adherence (n = 1)	Revise to emphasize convenience/shorten given examples
Item 2e: ease of continuing treatment plan	"Ease of continuing" confusing (n = 1)	Revise to specify not forgetting/adhering
Item 2f: mental impact of managing treatment plan	"Mental impact" unclear or confusing (n = 3)	Revise to improve clarity and emphasize the impact as mental load/mental burden of managing plan
Item 2i: mode of administration	"Mode of administration" not understood (n = 1)	Revise language related to mode of administration to improve clarity

Limitations

- The draft HIV-TPQ has only been evaluated by 13 PWH, and only in US residents
- Respondents had not participated in a clinical trial involving an ATI and the current evaluation of the questionnaire by PWH is therefore hypothetical; consideration will be given to collecting information from participants with such experience in the next stage of qualitative and psychometric evaluation