Development of Two Versions of a Patient Reported Outcome Measure to Evaluate Participant Experience and Satisfaction During the Intervention and Analytical Treatment Interruption Periods of Cure-Related and Other HIV Trials

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Conclusions

- Content validation through cognitive debriefing indicated that both versions of the Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV were valid patient-reported outcome measures to assess the experiences and satisfaction of people with HIV regarding HIV cure–related research interventions and analytical treatment interruptions
- **Overall, people with HIV interpreted the questionnaires as intended, but several revisions to questionnaire items were identified to improve interpretability and clarity**
- Two versions of the questionnaire, specific to either the intervention or analytical treatment interruption period, will be psychometrically validated during cure-related and other HIV trials

Plain Language Summary

- Studies focused on an HIV cure or antiretroviral treatment–free control might include a planned break from HIV medicine, known as an "analytical treatment interruption"
- While analytical treatment interruptions are important to assess HIV cure–related research interventions, they may also lead to increased levels of HIV in participants, which can increase the chance of transmission, as well as have psychosocial impacts
- The Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV is being developed to better understand the experiences and satisfaction of people with HIV during HIV clinical studies and during periods when HIV medicines are stopped, as well as the potential psychosocial impacts of HIV cure–related research interventions
- This study looked at whether people with HIV found the questions and instructions easy to understand and whether they interpreted them as intended
- Most people thought the questions and instructions were clear and made sense, and feedback was provided to help improve the questionnaire before testing it further

Introduction

- Clinical trials that incorporate analytical treatment interruptions (ATIs) are important for assessing potential HIV cure regimens in people with HIV (PWH) but can pose risks, such as viral rebound and psychosocial impacts, that may deter PWH from participating in the clinical trials[1,2]
- Upon review of the literature and existing patient-reported outcome measures (PROMs), a need was identified for a PROM that captures the experiences and satisfaction of PWH during both the intervention and ATI phases of HIV clinical trials
- To address this gap, 2 versions of the Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV (QUEST-HIV) were developed; the QUEST-HIV-I evaluates the HIV cure–related research intervention period, and the QUEST-HIV-ATI evaluates the ATI period (**Table 1**)
- The development and content validation of the 2 versions of the QUEST-HIV are reported here, with further assessment and validation planned

Table 1. QUEST-HIV at a Glance[a]

QUEST-HIV-I	QUEST-HIV-ATI
Objective: intended to be completed by PWH during an **active intervention period**	**Objective:** intended to be completed by PWH during an **ATI period**
Recall: 7 days	**Recall:** 7 days
Number of items: 22	**Number of items: 24**
Response options: 5-point verbal descriptor scales (not at all–extremely, very satisfied–very dissatisfied)	**Response options:** 5-point verbal descriptor scales (not at all–extremely, **completely–not at all**, very satisfied–very dissatisfied)
Item topics (n)	**Item topics (n)**
Experience with **study intervention period (8)**	Experience with **ATI observational period (14)**
Satisfaction with **study intervention period (8)**	Satisfaction with **ATI observational period (4)**
Experience with site, study logistics, and staff (3)	Experience with site, study logistics, and staff (3)
Overall satisfaction (3)	Overall satisfaction (3)

[a]Bolding denotes differences between the QUEST-HIV-I and the QUEST-HIV-ATI.
ATI, analytical treatment interruption; PWH, people with HIV; QUEST-HIV-ATI, Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV (Analytical Treatment Interruption); QUEST-HIV-I, Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV (Intervention).

Objective

- To develop and content validate the 2 versions of the QUEST-HIV to assess the experiences and satisfaction of PWH during the intervention (QUEST-HIV-I) and ATI (QUEST-HIV-ATI) phases of clinical trials

Methods

- To guide the development of the QUEST-HIV, we reviewed the literature and existing PROMs assessing patient experiences and satisfaction
- The QUEST-HIV-I included questions related to experiences and satisfaction with the HIV cure–related research intervention, whereas the QUEST-HIV-ATI included questions related to experiences and satisfaction with not receiving any HIV medications during an ATI (**Table 1**)
  - Both versions of the QUEST-HIV had a 7-day recall period, with each item assessed on a 5-point verbal descriptor scale
- A PWH advocate and 3 external disease experts reviewed the original drafts of both versions of the questionnaire
  - Based on their feedback, we refined the drafts by adding items to assess the impact of the intervention or ATI on partners of PWH and to capture the satisfaction of PWH with how they are monitored during an ATI
- We then evaluated the refined questionnaire to confirm content validity, clarity, and appropriateness through structured, 90-minute cognitive debriefing interviews conducted virtually with 14 PWH in the United States between March and June of 2025
  - PWH were recruited to ensure diversity in age, sex, gender, race/ethnicity, education, and treatment experience; PWH were ≥18 years of age and currently on antiretroviral therapy
- Interviewers used a conversational, think-aloud method, in which they encouraged PWH to verbalise their thoughts while completing the QUEST-HIV to assess comprehensibility and clarity, as well as whether the recall period and response options were appropriate
- We analysed transcripts of completed interviews using MAXQDA (v22.6.0 or higher) to identify potential issues with the content, language, structure, and format of the QUEST-HIV

Results

Study Population

- Characteristics of PWH who participated in the cognitive debriefing interviews are summarised in **Table 2**

Overview of Cognitive Debriefing Results

- Among the 19 PWH who participated in the interviews, 14 cognitively debriefed the QUEST-HIV-I and 10 cognitively debriefed the QUEST-HIV-ATI

▶ All instructions and most items from both versions of the QUEST-HIV were interpreted as intended and clear (**Table 3** and **Figure 1**)

  - Item 10 from the QUEST-HIV-I was reported as unclear by 4 of 13 PWH (31%) with evaluable data due to the use of "modes," with suggestions to revise to "types" or "doses" or to specify the modes of medication (**Figure 2**)
  - Item 9 from the QUEST-HIV-ATI was misinterpreted by 2 of 10 PWH (20%) with evaluable data due to issues with understanding what the central concept of "feeling closer to how one did pre–HIV diagnosis" meant (**Figure 3**)
  - Items 11 and 12 from the QUEST-HIV-ATI were reported as unclear by 2 of 10 PWH (20%) with evaluable data due to the broadness of the concept of "feeling happy" and the use of "partner," with suggestions to use the term "HIV-negative person" instead (**Figure 3**)
- Proposed revisions based on feedback from PWH are summarised in **Figures 2** and **3**
  - Revisions included reordering items to help with interpretation and rephrasing items to clarify the meaning of central concepts

Table 2. Characteristics of PWH

Characteristic, n (%)	Recruitment Goal (%)	PWH (N = 19)[a]	
Sex assigned at birth			
Male	≥50	14 (73.7)	✓
Female	≥25	5 (26.3)	✓
Gender			
Nonbinary/transgender	≥10	1 (5.3)	⚐
Age, y			
18-24	≥10	1 (5.3)	⚐
25-34	≥30	5 (26.3)	⚐
35-44	≥20	3 (15.8)	⚐
≥45	≥20	10 (52.6)	✓
Race			
African American	≥40	8 (42.1)	✓
White	≥30	10 (52.6)	✓
Ethnicity			
Hispanic/Latino(a)	≥15	6 (31.6)	✓
Highest education level			
High school diploma or less	≥20	6 (31.6)	✓
Treatment burden[b]			
VS on a single-tablet regimen	≥33	12 (63.2)	✓
VSTE on a complex regimen	≥10	2 (10.5)	✓
HTE	≥6.7	2 (10.5)	✓

Key: ✓, goal met; ⚐, goal partially met.
[a]Due to time constraints,14 PWH completed the cognitive debriefing interview for the QUEST-HIV-I and 10 PWH completed the cognitive debriefing interview for the QUEST-HIV-ATI.
[b]Treatment burden categories VSTE and HTE were defined by criteria provided by Gilead Sciences, Inc.; participants could be counted in multiple treatment burden categories.
HTE, heavily treatment experienced; PWH, people with HIV; QUEST-HIV-ATI, Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV (Analytical Treatment Interruption); QUEST-HIV-I, Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV (Intervention); VS, virally suppressed; VSTE, virally suppressed treatment experienced.

Table 3. Interpretation and Clarity of the QUEST-HIV-I and QUEST-HIV-ATI

Instructions/Item	QUEST-HIV-I		QUEST-HIV-ATI	
	Interpretation	Clarity	Interpretation	Clarity
Instructions (overall experience)	✓	✓	✓	✓
Item 1 (concern about viral load)	✓	✓	✓	✓
Item 2 (concern about side effects)	✓	✓	–	–
Item 2 (concern about lingering side effects)	–	–	✓	✓
Item 3 (preoccupied with HIV status)	✓	✓	✓	✓
Item 4 (concern about keeping up with the study intervention)	✓	✓	–	–
Item 4 (concern about keeping up with the clinical study)	–	–	✓	✓
Item 5 (emotional instability)	✓	✓	✓	✓
Item 6 (worry about viral rebound)	✓	✓	✓	✓
Item 7 (worried about HIV status disclosure due to medication)	✓	✓	–	–
Item 7 (worried about HIV status disclosure due to clinical study)	–	–	✓	✓
Item 8 (worried about transmission)	✓	✓	✓	✓
Instructions (satisfaction with study intervention period)	✓	✓	–	–
Item 9 (convenience)	✓	✓	–	–
Item 9 (feel closer to before diagnosis)	–	–	⚐	✓
Item 10 (frequency of multiple modes of medication)	✓	✗	–	–
Item 10 (improve self-esteem)	–	–	✓	✓
Item 11 (multiple modes of medicines)	✓	✓	–	–
Item 11 (feel happy)	–	–	✓	⚐
Item 12 (study intervention injections)	✓	✓	–	–
Item 12 (improve communication with partner)	–	–	✓	⚐
Item 13 (study IV infusions)	✓	✓	–	–
Item 13 (positively impact relationship status)	–	–	✓	✓
Item 14 (study pills)	✓	✓	–	–
Item 14 (positively impact sex life)	–	–	✓	✓
Item 15 (amount of pain or discomfort)	✓	✓	–	–
Item 15 (daily HIV medicines)	–	–	✓	✓
Item 16 (number of medicines)	✓	✓	–	–
Item 16 (remain undetectable)	–	–	✓	✓
Instructions (experience with site, study logistics, and staff)	✓	✓	–	–
Item 17 (communication with site staff)	✓	✓	–	–
Item 17 (frequency of monitoring)	–	–	✓	✓
Item 18 (amount of time required)	✓	✓	–	–
Item 18 (satisfaction with monitoring process)	–	–	✓	✓
Item 19 (logistics)	✓	✓	✓	✓
Item 20 (overall satisfaction with study intervention)	✓	✓	–	–
Item 21 (impact of study intervention on relationship)	✓	✓	✓	✓
Item 22 (overall satisfaction with ATI period)	–	–	✓	✓
Item 23 (satisfaction on relationships)	–	–	✓	✓
Item 22/24 (overall satisfaction with clinical study)	✓	✓	✓	✓

Key: ✓, misinterpreted or reported as unclear by <20% of PWH who provided evaluable data; ⚐, misinterpreted or reported as unclear by 20% to 30% of PWH who provided evaluable data; ✗, misinterpreted or reported as unclear by >30% of PWH who provided evaluable data.
ATI, analytical treatment interruption; IV, intravenous; PWH, people with HIV; QUEST-HIV-ATI, Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV (Analytical Treatment Interruption); QUEST-HIV-I, Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV (Intervention).

Figure 1. Representative Feedback Confirming the Content Validity of the QUEST-HIV (Both Versions)

PRO item	PWH feedback
Item 1 (concern about viral load) *Over the past 7 days, how concerned were you about your viral load?*	14 of 14 PWH (100%) with evaluable data interpreted as intended, and 13 of 14 (93%) reported as clear
Item 8 (worried about transmission) *Over the past 7 days, how worried were you about transmitting HIV to intimate partners?*	13 of 13 PWH (100%) with evaluable data interpreted as intended, and 12 of 13 (92%) reported as clear

Representative PWH quotations

*"It is asking, over the past 7 days, **if I've been worried about if my viral load was undetectable** or not or **if the numbers have fallen**."*

*"It's **clear** to me."*

*"It's just asking if you have **any worries about transmitting the disease** to someone else, if you thought about it **during a sexual encounter** or just if you worried about passing it on to the next person."*

*"It's **clear**. It is something that I agree and **it should be in there**."*

PRO, patient-reported outcome; PWH, people with HIV; QUEST-HIV, Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV.

Figure 2. Summary of Feedback on and Revisions to the QUEST-HIV-I

PRO item	PWH feedback
Item 10 (frequency of multiple modes of medication) *Over the past 7 days, how satisfied were you with how often you take multiple modes of medicines?*	4 of 13 PWH (31%) with evaluable data reported clarity issues with the term "modes"; suggestions included revising "modes" to "types" (n = 1), specifying the modes of medication (n = 1), and revising "modes" to "doses" (n = 2)

Proposed revision

Repeat the explanation of modes listed in Item 11 (ie, "pills, injections, intravenous [IV] infusions"), which was interpreted as intended and clear, in Item 10, which appears first in the questionnaire.
Revised item:
Over the past 7 days, how satisfied were you with how often you take multiple modes of medicines (for example, pills, injections, intravenous [IV] infusions)?

Representative PWH quotations

*"I would say… **I would look at it as how often you take multiple types of medicine**, I guess, would be something that I could put, because modes of, honestly, I've never heard of it that way, so it might bring questions to other people."*

*"A **little bit too hard** to even determine, that it says multiple modes, so all I say is maybe if you wanted to say **how often you—are you taking pills as opposed to getting an injection or an IV?**"*

*"I feel like it's **a little unclear**… So I would say over the past 7 days, how satisfied were you with **how often you take multiple doses of medicines**."*

IV, intravenous; PRO, patient-reported outcome; PWH, people with HIV; QUEST-HIV-I, Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV (Intervention).

Figure 3. Summary of Feedback on and Revisions to the QUEST-HIV-ATI

PRO item	PWH feedback	Proposed revision	Representative PWH quotations
Item 9 (feel closer to before diagnosis) *Over the past 7 days, how much did being off all HIV medicines make you feel closer to how you felt before you were diagnosed with HIV?*	2 of 10 PWH (20%) with evaluable data reported issues understanding the concept of feeling closer to how one did pre–HIV diagnosis	Based on review of feedback from PWH who interpreted the item as intended, revise to "In the past 7 days, how much did being off all HIV medicines remind you of how you felt before you were diagnosed with HIV?"	*"I guess **that one just needs to be a little more explained or more details into that, what they mean by before**."*
Item 11 (feel happy) *Over the past 7 days, how much did being off all HIV medicine make you feel happy?*	2 of 10 PWH (20%) with evaluable data reported clarity issues with the broadness of the concept of feeling "happy"	No proposed action given the majority of PWH interpreted the item as intended and reported it to be clear	*"Maybe it's **unclear**. Happy is so **broad**."*
Item 12 (improve communication with partner) *Over the past 7 days, how much did being off all HIV medicine improve your ability to communicate openly with your partner or potential partner?*	2 of 10 PWH (20%) with evaluable data reported clarity issues; suggestions included using the term "HIV-negative person" instead of partner (n = 1)	Based on feedback from PWH who interpreted the item as intended, revise to "Over the past 7 days, how much did being off all HIV medicine improve your ability to communicate openly about your HIV status with your partner or potential partner?"	*"I don't know what else to say except I think **it's more appropriate to use the HIV-negative person**."*

PRO, patient-reported outcome; PWH, people with HIV; QUEST-HIV-ATI, Questionnaire to Understand the Experiences and Satisfaction in a Trial in HIV (Analytical Treatment Interruption).

References: 1. Julg B, et al. *Lancet HIV*. 2019;6:e259-68. **2.** Dubé K, et al. Presented at: International Society for Pharmacoeconomics and Outcomes Research (ISPOR); 13-16 May 2025; Montreal, QC, Canada. Poster PCR126.

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