Development of Conceptual Models to Understand Patient Experiences with and Attributes of Adherence to HIV Oral Antiretroviral Therapy (OART) and Considerations in Switching to Long-acting OART

P032

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Background

- Daily oral antiretroviral therapy (OART) revolutionized outcomes (viral suppression and significantly improved survival) in patients living with HIV (PLWH)
- Treatment is life-long. Patients may face barriers that impact their ability to remain adherent
- Long-acting OART (LA-OART) agents are being investigated to enable more personalized choice
- Patient-reported outcome (PRO) measures can provide unique insights, from patient perspective, on impact of or on a health state or treatment
- It is important to understand attributes with potential effects on adherence among PLWH

FDA = U.S. Food and Drug Administration

Objectives

- To develop a conceptual understanding of the facilitators and barriers to adherence to daily OART and represent this in a conceptual model (CM)
- To develop a conceptual understanding of the facilitators and barriers to switching to a hypothetical LA-OART and represent this in a CM

Methods

- A targeted literature review (TLR) was conducted on facilitators and barriers to adherence specific to PLWH and OART
  - Conducted in PubMed, EMBASE & PsycINFO
  - Identified qualitative research exploring PLWH experiences with daily OART; focus on attributes defined as facilitators and/or barriers to adherence
- Then, non-interventional, cross-sectional qualitative concept elicitation (CE) interview study in the U.S., following FDA PRO guidance[1]
- One-on-one CE interviews were conducted over telephone by trained qualitative interviewers, following a semi-structured discussion guide
  - Target of 7 physicians experienced in treating PLWH, some in CDC-prioritized areas for HIV[2]
  - Target of 25 to 30 PLWH (waves of 5 participants) to achieve concept saturation[3]
    - Criteria: 18-70 years old, live in U.S., English-speaker, willing to share treatment experiences, have confirmed diagnosis of HIV, currently taking daily OART or on drug-holiday, and not in clinical trial in prior year
    - Aspirational targets by age group, race/ethnicity, and sub-groups[4,5] – men who have sex with men (MSM), heterosexual, people who inject drugs (PWID), and transgender- broadly selected based on epidemiological data of HIV incidence and prevalence in U.S.[6]
- Interviews transcribed verbatim. Researchers coded to framework, ordering by number of patients mentioning concept and by number who prioritized concept. Patient verbatims assembled to provide insight into language patients used
- Review of existing PRO measures related to HIV and/or to adherence; attributes from review mapped to both CMs to assess coverage gaps

Limitations

- May include insufficient representation of diverse PLWH subgroups due in part to recruitment challenges
- Participants reside in the U.S. and speak English
- Telephone interviews may introduce bias compared to face-to-face interviews. While the discussion guide was developed with attempt to build rapport, it may not develop between some participants and moderators, potentially resulting in reduced disclosure of sensitive information about living with HIV

Results

Figure 1. Conceptual Model Development

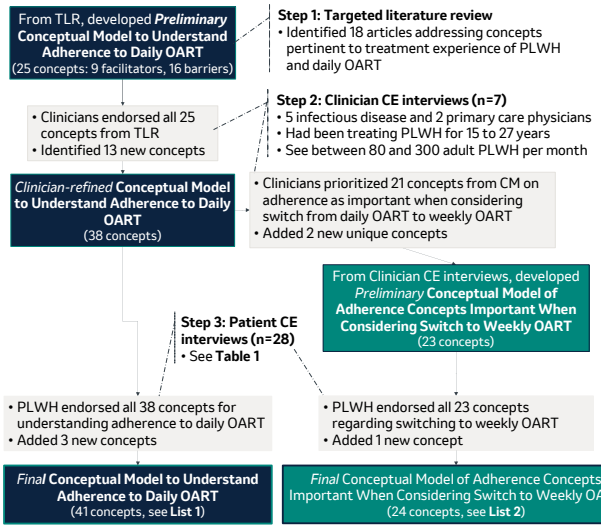

Table 1. Selected PLWH Demographics

Demographic	Total n=28 (aspirational target*)	Demographic	Total n=28 (aspirational target*)
Age Group		**Treatment Experience on Daily OART**	
18-29 years	5 (5)	< 5 years	2
30-49 years	9 (9)	5 – 10 years	10
50-70 years	14 (11)	> 10 years	16
Sub-group		**Geography**	
MSM	18 (13)	CDC prioritized area	19 (17)
Heterosexual men or women	8 (6)	**Current Living…**	
PWID	3 (3)	Alone	13
Transgender persons	1 (3)	With someone	14
Race/Ethnicity		Other, e.g., nursing facility	1
Caucasian or White	6 (5)	**Treatment history with daily OART**	
African American, African, or Black	15 (10)	On 1st daily OART	3
Hispanic, Latinx, Central or Spanish origin	3 (5)	On 2nd daily OART	4
Other	4 (5)	On ≥ 3rd daily OART	20

*Aspirational targets were not set for all characteristics

CDC = U.S. Center for Disease Control. MSM = men who have sex with men. OART = oral antiretroviral therapy. PLWH = patients living with HIV. PWID = people who inject drugs.

List 1. Barriers and Facilitators of Adherence to Daily OART: Final Conceptual Model

Facilitators to Adherence (16 concepts)

- Belief in treatment efficacy
- Perception that treatment improves physical health
- Use of medication to reduce risk of transmission
- ⊕ Patient buy-in during regimen selection
- ⊕ Access to behavioural health services
- Fear of drug resistance from poor adherence
- HIV support groups
- ⊕ Supportive family, partners, friends, people in the household
- 👤 HIV activism/leadership
- 👤 HIV+ partner
- Dosing regimen that fits routine (convenience)
- Small pill size
- ⊕ Use of a regimen-taking reminder system
- Low-frequency dosing regimen
- Treatment regimen facilitating infrequent clinic attendance
- 👤 Case management and/or care coordination

Either Facilitator or Barrier to Adherence (3 concepts)

- Relationship with treating healthcare team
- ⊕ Socioeconomic status
- Access to HCP/ART

Barriers to Adherence (22 concepts)

- Medication side effects (e.g., weight gain)
- ⊕ Failure to perceive the consequences of regimen non-adherence
- ⊕ Perception that medication is no longer needed (drug holiday)
- Perceived good health of those not on HIV medication
- Regimen serving as reminder of HIV status§
- ⊕ Medical mistrust (barrier)
- ⊕ Mental health issues / emotional difficulties
- Fear of disclosure of HIV status
- Shame from HIV status
- ⊕ Stigma associated with HIV status
- Time needed to come to terms with diagnosis
- Substance misuse
- Housing issues
- Unemployment
- High pill burden
- Transportation to HIV clinic or pharmacy
- Out-of-pocket costs (co-pays)
- ⊕ Lapse in or loss of insurance coverage or medication coverage
- Accidental non-adherence (forgetting to take)
- ⊕ Regimen with a food requirement
- Lack of access to food/water
- ⊕ Difficulty swallowing pills (of any size)

Legend
- Identified from TLR
- ⊕ Identified in clinician CE
- 👤 Identified in patient CE

List 2. Barriers and Facilitators of Adherence Following a Hypothetical Switch from Daily to LA-OART: Final Conceptual Model

Facilitators to Adherence (8 concepts)

- Belief in treatment efficacy
- Patient buy-in during regimen selection
- Use of medication to reduce risk of transmission
- Fear of drug resistance from poor adherence
- Dosing regimen that fits routine
- Small pill size
- Use of regimen-taking reminder system
- 👤 Reduced preoccupation w/regimen-taking

Either Facilitator or Barrier to Adherence (3 concepts)

- Low-frequency dosing regimen
- Access to HCP/ART
- Relationship with treating healthcare team

Barriers to Adherence (13 concepts)

- Medication side effects (e.g., weight gain)
- ⊕ Fear of switching to a new regimen from an efficacious regimen and routine that have been working well
- ⊕ Doubt over new regimen efficacy
- Accidental non-adherence (forgetting to take)
- High pill burden
- Out-of-pocket costs (co-pays)
- Regimen with a food requirement
- Difficulty swallowing pills (of any size)
- Regimen serving as reminder of HIV status
- Mental health issues / emotional difficulties
- Fear of disclosure of HIV status
- Shame from HIV status
- Stigma associated with HIV status

Legend
- Identified from TLR
- ⊕ Identified in clinician CE
- 👤 Identified in patient CE

- No single or collection of existing PROs, among the 56 reviewed, capture all the concepts in either the CM to understand adherence to daily OART nor the CM to understand adherence considerations when switching to a LA-OART

Conclusions

- The adherence CM and switch CM provide a structured framework to understand
  - Experience of PLWH with adherence to OART,
  - Facilitators and barriers to OART adherence, and
  - Possible facilitators and barriers influencing switch to LA-OART
- The CMs will inform the development of new PRO measures to address gaps in existing PROs and for use in appropriate clinical research for PLWH

References

1. U.S. Food and Drug Administration. https://www.fda.gov/media/116277/download 2. Centers for Disease Control and Prevention. www.cdc.gov/endhiv/priorities.html 3. U.S. Food and Drug Administration. Federal Register https://www.federalregister.gov/documents/2020/06/17/2020-13046/patient-focused-drug-development-collecting-comprehensive-and-representative-input-guidance-for 4. Centers for Disease Control and Prevention. https://www.cdc.gov/hiv/statistics/systems/nhbs/index.html 5. World Health Organization. https://apps.who.int/iris/handle/10665/258967 6. Centers for Disease Control and Prevention. extension://elhekieabhbkpmcefcoobjddigjcaadp/https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/hiv-incidence-fact-sheet_508.pdf

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