Participants’ perceived barriers to adherence vs. empirically-based barriers to adherence: Do they agree?

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Conflict of Interest Disclosure

John A. Saucedo, PhD, MSc

Has no real or apparent conflicts of interest to report.
Update on ART Adherence

There is exhaustive literature on barriers to ART adherence.

What are the most important barriers to adherence?
Figure 2. Barriers Reported in Developed Countries

Mills et al., 2006 – Systematic Review
Background

Assumption: We accept that the “most important” barrier is the one that is most commonly self-reported.

- “Simply forgot” is most common barrier reported.

Inconsistencies: Do the facilitators of adherence coincide with the barriers to adherence?

- Common facilitators are high self-worth & prioritizing ART over substance use.
Objective

Two primary hypotheses:

1) Rankings between participants and our empirical test will be different.

2) Empirical test would rank the psychosocial barriers as more important, compared to the participant rankings.

Outcome: Self-reported treatment interruption (non-adherence).
Method

Procedures and Recruitment:
1. U.S-based online survey advertised on social media
2. Survey to explore mobile technologies and social media among PLWH.
3. Informed by HIV community advisory boards in S.F. Bay Area.

Inclusion Criteria:
1. 18 years or older
2. HIV-positive
3. Living in U.S.

Checks:
1. One Internet Protocol (IP) address allowed
2. No monetary incentives were provided
3. Placement of medically-relevant facts and trivia-related questions/information

UCSF IRB approved study:
• 87% who answered first question completed all questions.

Method

Measures (Self-Report)

1. Basic demographic and ART information
2. VL as “undetectable” (0) or “detectable” (1) at most recent clinic visit

1. Outcome - Non-adherence to ART as treatment interruptions.

Rationale: Adherence and VL is increasing.

- **ART is simpler** - less pill burden, regimen complexity.
- **ART is more potent** - forgiving to minor lapses, i.e., what does less than 100 or 80% mean, a missed dose, % of days covered anymore
- **ART is tolerable** – toxicity concerns.
- Self-reported measures must account for this shift in new treatments.
- ...one 4-day period where zero ART doses were taken in past 3 months (0 = no interruption, 1 = at least one interruption).

(Saberi P, ... Johnson MO. (2013). A Pilot Study to Engage and Counsel HIV-Positive African American Youth via Telehealth Technology. AIDS Patient Care and STDs.)
Method

Measures (Self-Report)

4. ACTG Adherence Barrier Questionnaire (ABQ; 14 items)

- Item: have you missed taking your medications because you…
  1) “were away from home”; 2) “busy with other things”; & 3) “simply forgot.”

- **Added six barriers:**
  - 15) “had problems with your pharmacy”;
  - 16) “had problems with your insurance company”;
  - 17) “were drinking alcohol”;
  - 18) “were using illicit drugs”;
  - 19) “were reminded of having HIV”
  - 20) “other reasons.”

- 20 barriers reduced to 9 “intervenable” barriers (i.e., less than 2% response).
  - e.g., <1% or 7 of 1217 reported “felt good” as a barrier to ART adherence.
  - 7 of 9 total barriers were original ABQ items.

(Saberi P, ... Johnson MO. (2013). A Pilot Study to Engage and Counsel HIV-Positive African American Youth via Telehealth Technology. AIDS Patient Care and STDs.)
9 barriers were ranked on importance using 2 approaches

<table>
<thead>
<tr>
<th>Participant rankings</th>
<th>Dominance Analysis Rankings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approach</strong>: “Traditional” Method</td>
<td><strong>Approach</strong>: Empirical Approach</td>
</tr>
<tr>
<td><strong>Definition</strong>: Rankings reflect percent of sample that checked “yes” to a barrier (e.g., simply forgot).</td>
<td><strong>Definition</strong>: Rankings are based on all possible regression subsets w/Tx interruptions as the outcome (i.e., each barrier vs. every other barrier)</td>
</tr>
<tr>
<td><strong>Interpretation</strong>: The most-to-least important barriers to adherence are based on percentages, irrespective of how those barriers are actually related to adherence.</td>
<td><strong>Interpretation</strong>: Yields an effect size/dominance weights. The most-to-least important barriers based on effect size of the association of each barrier with adherence.</td>
</tr>
</tbody>
</table>
1. Dominance analysis is a class of Relative Important Analysis
   • Identify the “most important predictor(s) from a set of predictors.”

2. Problems with traditional regression approaches (short list)
   A. Adherence barriers are correlated
   B. Std. regression objective of “impact on Y per change in X” not ideal for “importance.”
   C. $R^2$ is influenced by order, other factors and model dependent

3. Advantage of dominance analysis
   A. General pair-wise regression approach tests *all possible* barriers against one another.
   B. Weight = average squared semi-partial correlation – i.e., each barrier in relation to the outcome of ART non-adherence.
1. Does one barrier consistency outperform other barriers in predicting ART non-adherence?

Based on every possible comparison

<table>
<thead>
<tr>
<th>General (Least dominant)</th>
<th>Conditional (Somewhat dominant)</th>
<th>Complete (Most dominant)</th>
</tr>
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<tbody>
<tr>
<td>Average variance contributed by one barrier is greater than the average variance contributed by another barrier</td>
<td>Average variance contributed by one barrier is greater in size than any one contribution of another barrier</td>
<td>Amount of additional variance one barrier has singularly contributed is greater than any amount of variance contributed by any other barrier</td>
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Demographics

• Sample Characteristics
  • Mean age was 46.7 (SD = 10.9, Median = 48)
  • 44% reported a college-level education
  • 57% reported annual income of less than $40,000
  • 76.3% self-identified as non-Latino White

HIV and ART Adherence-related Information
• 13% reported a detectable VL
• 69.8% reported once-daily dosed ART
• 28.8% twice-daily dosed ART
• 14% reported at least one, 4-day Tx interruption in past 3 months
Results: Comparing Two Sets of Rankings
## Comparison of Rankings – Five most important barriers

<table>
<thead>
<tr>
<th>Total Sample Percentage (n)</th>
<th>Participant ranking of adherence barriers</th>
<th>Dominance analysis rankings of adherence barriers</th>
<th>Standardized dominance weights</th>
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<tr>
<td>33.7% (n=410)</td>
<td>#1 Simply forgot</td>
<td>#1 Fell asleep/slept through dose</td>
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<td>27.6% (n=336)</td>
<td>#2 Day-to-day life</td>
<td>#2 Felt depressed/overwhelmed</td>
<td>.313</td>
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<td>#3 Alcohol or using illicit drugs</td>
<td>#3 Day-to-day life</td>
<td>.116</td>
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<td>9.5 (n=116)</td>
<td>#4 Felt depressed/overwhelmed</td>
<td>#4 Wanted to avoid side-effects</td>
<td>.110</td>
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<td>6.6% (n=80)</td>
<td>#5 Ran out of pills</td>
<td>#5 Alcohol or using illicit drugs</td>
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### Comparison of Rankings (N=1217)

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<td>#6 Asleep/slept through dose time</td>
<td>#6 Simply forgot</td>
<td>.035</td>
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<tr>
<td>4.5% (n=55)</td>
<td>#7 Problems w/pharmacy and insurance</td>
<td>#7 Ran out of pills</td>
<td>.028</td>
</tr>
<tr>
<td>4.1% (n=50)</td>
<td>#8 Avoid side-effects</td>
<td>#8 Felt sick or ill</td>
<td>.026</td>
</tr>
<tr>
<td>3.0% (n=36)</td>
<td>#9 Felt sick or ill</td>
<td>#9 Problems w/pharmacy and insurance</td>
<td>.003</td>
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Path Model –
Std. dominance weights into ORs

ART Four-Day Treatment Interruption

#1 Slept
OR=1.45*

#2Depress
OR=2.60**

#3 Day-to Day
OR=1.34**

#4 Side-Effects
OR=.75, ns

#5Alcohol Drugs
OR=1.46**

Viral Load Status

OR=1.16*

Covariate
Discussion

1. The “importance” of “Simply forgot” as a barrier to adherence was overestimated by participants.
2. “Fell asleep/slept through dose” barrier was underestimated; yielded the largest dominance weight.
   – “Completely” dominated all other barriers except #2 ranked barrier.
3. “Feeling depressed” barrier was 2nd most important predictor of ART non-adherence.
   – “Completely” dominated all barriers except #1 and #3 ranked barriers.
4. Unexpectedly, “alcohol and drug” barrier effect size was small but 3rd most common barrier.

Implications

1. Barriers most frequently reported were not those most strongly associated with non-adherence.
   - Interventions should prioritize those barriers with largest impact on adherence and clinical outcomes to generate largest benefit.

1. “Simply forgot” may be a proxy for disclosing other, more sensitive reasons for missing medications.
   - Probe beyond “simply forgetting.”
   - Mental health and illicit drug use stigma.
   - Communication about lifelong ART adherence
   - Consequences of missed doses in combination with strategies for dealing with lapses in adherence

2. Two most important barriers to adherence (sleeping through doses & feelings of depression) are clinical features of depression, specifically hypersomnia and insomnia.
4. “Fell asleep” barrier - Robust literature on sleep quality and adherence.
   – Quick implementable strategy for detecting problems of adherence could be to inquire about sleep habits.

5. Re-iterate the need of interventions to consider antecedents or co-occurring problems linked to (e.g., depressive disorders or drug abuse) non-adherence, in conjunction with strategies to routinize pill-taking behavior.

6. Certain barriers to adherence may no longer be applicable in the modern era of ART treatment (e.g., pill burden, toxicity concerns, but not side-effects).

7. Moving forward – New markers of adherence (e.g., hair samples) and assessment of barriers to support these findings.

4. Non-adherence as treatment interruptions given new ART is simpler, more potent, and tolerable (but predicated on drug type).
Limitations

1. All data were self-reported.
   - No incentives to participate were provided & the direction of the effect of interest was predicting non-adherence.

2. A replication study is needed to support the stability of weights.
   - Statistical power is not directly related to dominance analysis because it is not a null hypothesis significance test.

3. Total sample consisted of mostly college educated and gay-identified men with access to online social media.

4. We could not determine conclusively the chronological order of effect for a treatment interruption on an HIV VL outcome.
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