Tools to Predict and Measure HIV Medication Readiness and Adherence

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Adherence in HIV Care

- Defining Adherence
- Importance of Adherence
- Challenges to Adherence (Why is this so hard?)
- How to Measure Medication Adherence
- Predictors of Adherence (e.g., Depression, Readiness)
- Validating and Translating tools to predict medication adherence
What is Adherence?

“Adherence is the degree to which a patient’s behavior coincides with medical advice suggested by a health care provider.”

(Meichenbaum & Turk, 1987)
**Importance of Adherence in HIV care**

- Expected levels of adherence for most chronic illnesses (e.g., hypertension, diabetes) is **50-80%**

- For HIV medications, the goal of adherence is **95-100%**.

- HAART regimens are very **unforgiving**
Importance of Adherence to HAART

HIV non-adherence ⇔ sub-optimal drug levels

HIV non-adherence ⇔ drug failure (stops working)

HIV non-adherence ⇔ HIV viral load rebound

HIV non-adherence ⇔ HIV drug resistance

HIV non-adherence ⇔ cross-resistance to drugs in the same class/family of drugs

HIV non-adherence ⇔ transmission of drug resistant strains of the virus
Importance of Adherence to HAART

After 3 months on HIV medications:

<table>
<thead>
<tr>
<th>% Adherence</th>
<th>HIV Viral Load</th>
<th>Undetectable</th>
</tr>
</thead>
<tbody>
<tr>
<td>95%</td>
<td>81%</td>
<td></td>
</tr>
<tr>
<td>90-95%</td>
<td>64%</td>
<td></td>
</tr>
<tr>
<td>80-90%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>70-80%</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>&lt; 70%</td>
<td>6%</td>
<td></td>
</tr>
</tbody>
</table>

(Paterson et al., 1999)
Adherence to HIV medications

Adherence is most challenging when...

1. The regimen is complex (simple is better)
   - Several doses/day, many pills/day, refrigerate
2. Treatment is long-term (for life vs 10 day antibiotics)
3. Patient is asymptomatic and initial side-effects of treatment are unpleasant (e.g. nausea, diarrhea)
4. Long term side-effects (e.g. lipodystrophy, diabetes)
5. Financial costs of treatment are high
6. The medical condition has negative stigma
Methods of Measuring Adherence

Ideal method for measuring adherence

- Psychometrically strong: reliable and valid
- Practical and uncomplicated to use (easy and fast)
- Low financial cost to patients and clinicians
- Adaptable to changes in treatment care

No Ideal method exists (reality)

- Limitations to each method
- Multi-method is most reliable
Methods of Measuring Adherence

1. Pharmacy refills of HIV medications
   a. Low cost measure of adherence – data on refills
   b. Requires common medication dispensing site
   c. Patients have pills but forget to take them on time

2. Pill counts (at HIV clinic or pharmacy visits)
   a. Low cost and convenient
   b. Patient may empty pill bottle prior to visit
   c. Solution: unannounced pill counts by phone (Kalichman, et al., 2008).
Methods of Measuring Adherence

3. Electronic Pill Cap Monitoring
   a. EDEM or MEMS: assess exact number of and time of day of bottle cap openings
   b. Provides “objective” measure of medication taking patterns
   c. “Gold standard” for RCT
   d. Graphic outputs provide useful feedback to patients about medication taking patterns
   e. Only measures opening of bottle cap not ingestion
   f. Not available as a “pill-box” or “dosette”
   g. Expensive, logistically complex for clinic care
Measuring Patient Adherence

EDEM Graphic Printout

EDEM Cap

![Display results]

**Patient:** 301  
**Fixed Time Regimen**

**Drug:** Drug 1  
**Twice a day**

**Physician:**

**Results:** From 03.07.90 00:00 to 02.08.90 23:59 (1)

- Number of prescribed doses: 64
- Number of doses taken: 61
- Number of monitored days: 32
- Interval (hrs): Longest: 23.7  
  Shortest: 1.9
- % Prescribed doses taken on schedule: 82.5%

**Chronology**

**Timing distribution**

![Timeline chart]
Methods of Measuring Adherence

4. Plasma Drug Levels (Pharmacokinetics (PK))
   a. Accurately indicator of active HIV drug in blood
   b. Assesses only recent adherence (pills ~24hrs)
   c. Adherence tends to be highest prior to medical visit (e.g., brush teeth just before seeing dentist)
   d. Expensive (technology and expertise)

5. HIV Viral Load (VL) in Blood
   a. Accurate as a medical outcome
   b. But only an indirect indicator of adherence (e.g., 100% adherence ≠ undetectable VL if drug resistant strain)
   c. Expensive (technology and expertise)
Methods of Measuring Adherence

7. Directly Observed Therapy (DOT)
   a. Clinical worker watches patient swallow pill (often used in active TB disease)
   b. Accurate measure of adherence
   c. Impractical and expensive for lifelong HIV regimen
   d. Patients often experience DOT as intrusive and paternalistic (not collaborative or empowering)

8. Physician Estimate of Patient Adherence
   a. Low cost and convenient
   b. Inaccurate – overestimate is very common
Methods of Measuring Adherence

9. Patient Self-report Adherence Tools:
   a. Advantages
      i. low financial cost
      ii. ease and speed of administration
      iii. low burden to patient and staff
      iv. flexible in terms of mode of administration and timing
      v. potential to yield info about dose timing and food requirements
      vi. highly correlated with VL (Nieuwkerk & Oort, 2005)
   b. Disadvantages
      i. susceptible to recall bias
      ii. inaccurate memory
      iii. social desirability bias (i.e. overestimate)

** Self-report is most widely used adherence method
Examples of Validated Self-Report Tools

1. AACTG Adherence Scale (Chesney, et al., 2000)
   a. Self-reported HIV adherence in past 3 days

   a. Self-reported adherence in last month (0-100%)
   b. Patients’ estimate the number of correct doses taken in the past month on a scale of 0-100%

3. Swiss HIV Cohort Study (SHCS; Deschamps et al 2008)
   a. “In the past 4 weeks, how often did you miss a dose of your HIV medications” on a 6 point scale from: never (0) to everyday (6) (0=100%) and
   b. Did you forget 2 doses one after the other (yes/no) Yes = not 100%
Examples of Validated Self-Report Tools

4. HIV Adherence Treatment Scale (HATS; Balfour et al., 2006)
   a. Adapted from AACTG *but* with 5 items
   b. Assessed self-reported HIV adherence in past week

5. General Treatment Scale (GTS; DiMatteo et al 1992)
   a. validated across medical populations
   b. 5 item scale, self-reported adherence in past month
Research Evidence on Self-Reports

1. Self-Reported Adherence and Viral Load
   a. tend to correlate .30 to .60 (medium to large effects)
   b. odds ratio and hazard ratios of 2.0 (95% CI excluding 1.0) for VL < 50 copies
   c. with 2 or more self report measures:
      sensitivity = 87.5%, and specificity = 59.6% for VL < 50 copies
Best Practices for Measuring Self Reported HIV Medication Adherence

• Only use validated adherence tools
• Use tools with more than one item (more items = greater reliability)
• Use more than one adherence tool (greater reliability and predictive validity).
  • Patients must indicate at least 95% adherence on each self-reported adherence tool.
Assessing Adherence in HIV Clinics

How We Ask About Adherence is important!

1. Give The Patient Permission to Tell The Truth
   a. Ask in a non-judgmental way:
      i. “How are things going with your medication?”
      ii. “We know that taking these medications is not easy”
      iii. “We want to know what is really happening, not what you think we want to hear”
   b. Do not ask pressure-filled questions
      i. “Have you been good with your pills?”
      ii. “You’ve taken your pills correctly, right?”
Assessing Adherence in HIV Clinics

2. Focus on recent adherence behaviors
   a. Assess pill taking behavior:
      i. During the past week (include weekends)

3. Assess timing of HIV medication doses
   Are HIV medications taken:
   • At the correct time of day? (e.g. twice/day by end of day all pills will have been taken)
   • With meals?
Ready to Start HAART? Predictors of Medication Adherence
When to Start HAART?

HIV treatment guidelines suggest starting HIV medications based on *medical markers*:

- CD4 count (e.g. less than 350)
- High HIV viral load
- Opportunistic infections (e.g. PCP)
Ready to Start HAART?

- HIV treatment guidelines also emphasize the need to carefully assess patients’ medication readiness prior to initiating HAART (www.hivguidelines.org)
- However the guidelines do not indicate how to assess HIV medication readiness
- To address this gap we developed and validated a brief HIV Medication Readiness tool (high readiness predicts high adherence)
- Depression and low HIV treatment knowledge also predict poor adherence (Balfour et al., 2006)
Psychological Predictors of Adherence

1. Depressed Mood → Non-Adherence
   a. Symptoms of depression include:
      i. Sadness and hopelessness,
      ii. Poor concentration and poor memory,
      iii. Low energy/motivation,
      iv. Sleep problems.

• Depression is the most consistent predictor of poor adherence across medical conditions
HIV and Depression?

- HIV Stigma, double stigma
- Disclosure, rejection, isolation
- Identity, shame, future?, work
HIV and Depression

- 40%-60% of people living with HIV experience periods of depression
Predictors of HIV Adherence

Depressed Mood → Non-Adherence
• Sadness and Hopelessness, poor concentration and poor memory, low energy/motivation, sleep problems

HIV tx knowledge gaps → Non-Adherence
• Information, motivations, beliefs about health

Not psych. ready → Non-Adherence
• Anxious about HIV medications and meaning of starting HIV medications
Pre-HAART Assessment Flow-chart

1. **Initiate Baseline Assessment**
   - Assess Medication Readiness
     - Med Readiness score < 26
     - Med Readiness score ≥ 31.5
   - Assess HIV Tx Knowledge
     - Identified knowledge gaps
     - No apparent knowledge gaps
   - Assess Sleep Quality
     - PSQI score ≥ 5
     - PSQI score < 5
   - Assess Depression (CES-D)
     - CES-D score ≥ 22
     - CES-D score < 22 (no depression)

2. **Increase Medication Readiness**
   - Provide HIV Tx Education
     - Psychotherapy or Medication for Depression
   - Provide Sleep Interventions

3. **Start HAART**
Feasibility and Evidence

Feasibility of Using Flow-Chart in HIV clinics
• The 4 medication readiness assessment scales can easily be completed by HIV patients in the waiting room in 10 minutes.
• Scoring of scales is fast and easy, and can be done by a nurse or nursing assistant within minutes

Evidence for the validation of the tool
• Study (1) HIV medication readiness scale – validation study
• Study (2) HIV treatment knowledge scale – validation study
Social and Systemic Barriers to Adherence

• Cost of HIV treatment
  • Pill costs
  • Travel costs to attend medical appointments
  • Time off work
  • Cost of child care to attend appointments

• Inconsistent access to HIV treatments
  • Pharmacy runs out of medications
  • Prohibitive costs of newer medications
  • HIV specialists are unavailable

• Distance to medical appointment

• Stigma and Fear of HIV Disclosure
  • Social stigma
  • Self stigma
Validation of the HIV Medication Readiness Scale
Scale Validation = Scale Quality
Methods: Tool Development

An initial pool of 30 items was generated based on:

- an extensive literature review
- theories of psychological readiness
- consultation with HIV experts

Items were:

- simply worded,
- avoided regional language use (colloquialisms)
- at a grade 8 reading level
Methods: Tool Development

Scale Development (Cont.)

• Response format: 0 (Not at all) to 4 (Extremely)
• Higher scores = higher levels of readiness

Example Items: Medication Readiness Scale

How ready are you to:

1. Deal with bringing your HIV pills to social activities (e.g., restaurant, friend’s house).
2. Accept the idea of taking these HIV pills for a very long time (e.g. years).
3. Continue taking your HIV pills even if you experience unpleasant side-effects (e.g. diarrhea, body fat changes)
Methods – Scale Validation

Participants and Procedures

• 142 HIV patients were recruited
  • during their regular HIV outpatient clinic visit at The Ottawa Hospital

• Participants completed questionnaires at:
  1. study baseline – not on HAART
  2. 4-weeks post-baseline
  3. The day patient started HIV medications and
  4. month post-started HIV medications (adherence)
Methods: Measuring Adherence

Adherence Outcome Measure

*General Treatment Scale* (DiMatteo et al., 1992)

- Five-item self-report questionnaire assessing adherence to treatment regimens in the past month

- Total score = 0 to 100 (we categorized pts into 2 groups)
  - $\geq 95$ = “optimally adherent”
  - $< 95$ = “sub-optimally adherent”
Participants – HIV pts ($N=142$)

<table>
<thead>
<tr>
<th>Baseline Info</th>
<th>MEAN ($SD$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>40.5 (8.8)</td>
</tr>
<tr>
<td>CD4 cell count</td>
<td>330.3 (200.0)</td>
</tr>
<tr>
<td>HIV viral load</td>
<td>74238.2 (115667.4)</td>
</tr>
<tr>
<td>Years since HIV Dx</td>
<td>4.7 (5.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex:</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>123</td>
</tr>
<tr>
<td>Women</td>
<td>19</td>
</tr>
<tr>
<td>Depressed:</td>
<td>65</td>
</tr>
</tbody>
</table>
Readiness Tool Validation

Step 1) Item Analysis of readiness scale:

- 10 of 30 items were excellent items.
  - statistically normally distributed
  - no ceiling or floor effects.

- These 10 items were retained and comprised the final version of the HIV Medication Readiness Scale
Construct Validity

What is it?
• The extent to which a new scale relates to other variables and constructs in theoretically meaningful and predictable ways

How is it tested?
• By comparing the Medication Readiness Scale scores between: Sample 1 (pts beginning HIV medications immediately) and Sample 2 (pts not starting HIV medications for several months)
**Results: Construct Validity**

- Patients starting HAART immediately had higher Readiness scores than patients starting HAART later.

<table>
<thead>
<tr>
<th></th>
<th>Sample 1</th>
<th></th>
<th>Sample 2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Beginning HAART immediately</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=58)</td>
<td></td>
<td></td>
<td>(n=84)</td>
<td></td>
</tr>
<tr>
<td>Mean ((SD))</td>
<td>(27.9 (8.0)^*)</td>
<td></td>
<td>(21.8 (9.7)^*)</td>
<td></td>
</tr>
<tr>
<td>HIV Medication Readiness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(t(140) = 3.99, p<.001\). Possible Range of scores = 0 to 40.
Readiness Tool Validation

Step 3) Predictive Validity

What is it?
• The ability of a new scale (e.g. readiness scale) to predict a meaningful criterion (e.g., medication adherence)

How is it tested?
• By comparing “optimally adherent” versus “sub-optimally adherent” patients at one month post-HIV medications on their HIV Medication Readiness scores
Results: Predictive Validity

Patients who were optimally adherent had higher Readiness scores than patients who were sub-optimally adherent

<table>
<thead>
<tr>
<th>HIV Medication Readiness</th>
<th>Optimally adherent pts (≥95%) (n=38)</th>
<th>Sub-optimally adherent pts (&lt;95%) (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>------------------------------</td>
<td>--------------------------------------</td>
<td>-----------------------------------------</td>
</tr>
<tr>
<td>31.5 (7.3)*</td>
<td>26.4 (10.1)*</td>
<td></td>
</tr>
</tbody>
</table>

$t(84) = 2.69, \ p<.01$. Range of scores = 0 to 40.
Step 4) Reliability – Internal Consistency

What is it?
• Internal consistency is the degree to which a scale’s items measure an underlying construct.

How is it tested?
• Internal consistency is evaluated using coefficient alpha (minimal acceptable level = .80)

Result
• The HIV Medication Readiness Scale demonstrated excellent internal consistency (alpha = .90).
Readiness Tool Validation

Step 5) Reliability – Test-Retest Stability

What is it?

• Test-retest reliability (stability) measures whether a scale is stable between two different time points.

How is it tested?

• Test-retest reliability is typically measured by correlating the total scale scores at two time points ($r = .80$ is very good)

Result

• The 4-week test-retest reliability of the HIV Medication Readiness Scale in control pts was high ($r = .83, p<.001$).
Step 6) Sensitivity to Change

**What is it?**
- A scale’s ability to assess change as a function of a treatment or intervention

**How is it tested?**
- Evaluated by administering the scale pre- and post- treatment
- In this study, the proposed scale was administered before and after the 4-week STAART psycho-educational intervention
Results: Predictive Validity

Readiness increased following a 4-Week Psycho-educational adherence readiness intervention

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>((n=29))</td>
<td>((n=31))</td>
</tr>
<tr>
<td>Mean ((SD))</td>
<td>21.4 (10.2)</td>
<td>22.9 (10.0)</td>
</tr>
<tr>
<td>Baseline Readiness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-week Readiness</td>
<td>26.2 (6.9)*</td>
<td>24.0 (9.1)*</td>
</tr>
</tbody>
</table>

ANCOVA. \(^*\) \(p<.05\). Range of scores = 0 to 40.
Readiness Tool: Conclusions

• The HIV Medication Readiness Scale is a novel, easy to use, psychometrically sound instrument
• It demonstrating high levels of validity, reliability, and sensitivity to change
• It can be used in HIV clinics to help identify HIV patients who may not be psychological ready to Start HAART and are at risk of sub-optimal adherence
• Identified patients could be helped to increase their medication readiness and ability to succeed on HAART
Translation/Cross-Cultural Validation

• The goal is to have both a linguistic and cultural equivalence of the original scale so that the meaning is accurately reflected

5 dimensions of cross-cultural validation/translation

1. Content Equivalence (e.g., bazuca, ganja instead of ecstasy)
Translation/Cross-Cultural Validation

5 dimensions of cross-cultural validation/translation

2. Semantic Equivalence
   a. meaning has to stay the same
   b. use “standard Spanish” not “local dialects”
   c. need independent back-translations with bi-cultural, high quality translators
   d. pilot test the translated items to check that a similar meaning is understand by target subjects
Translation/Cross-Cultural Validation

5 dimensions of cross-cultural validation/translation

3. Technical Equivalence
   a. method needs to be comparable; self-report vs verbal tradition

4. Criterion Equivalence
   a. the interpretation of the measurement is the same across cultures
      (e.g. Rich vs Poor in USA vs Cuba ?)

5. Conceptual Equivalence
   a. Does the same concept exist in each culture ?
      (e.g. Canada, homosexuality – MSM vs in India, no word exists for homosexuality, closest term is “men who have fun with men”)
Conclusions

• HIV medication adherence can be assessed by validated tools

• Important predictors of non-adherence include:
  a) Psychological readiness
  b) Depression
  c) Gaps in HIV treatment knowledge

• Tools can be translated and cross-culturally validated in Colombia

• These issues can be addressed to improve HIV medication adherence
Thank You! Gracias!

- HIV study patients
- Study Co-investigators
- Funding partners (e.g. AIDS Bureau, OHTN, CTN, and CIHR)
- Dr. Martinez, Dr. Galindo, CorpoSIDA,
- XV Cali Conference organizers/participants
- Thank you for your interest and attention
Strength in Multidisciplinary Team Work

Strength in International Collaborations