A Self-Reported Adherence Measure to Screen for Elevated HIV Viral Load in Pregnant and Postpartum Women on Antiretroviral Therapy


11th International Conference on HIV Treatment and Prevention Adherence
Conflict of interest disclosure

The authors have no real or apparent conflicts of interest to report.
Background

• There has been rapid global implementation of universal antiretroviral therapy (ART) for all pregnant and breastfeeding women

• Maternal ART adherence is a concern with implications for vertical transmission and maternal health

• Measuring and monitoring ART adherence is very challenging
  • Viral load (VL) invaluable for treatment monitoring - does not directly measure adherence, expensive and often infrequent
  • Scepticism about self-report measures but often one of the few if not only practical methods in low resource settings

• There is need for adherence measures which can be conducted frequently with limited resources, both in clinical and research settings
Study aims

• To investigate the association between a new three-item self-reported adherence measure and elevated HIV VL in HIV-infected pregnant and postpartum women

• To assess differences in reported adherence across sociodemographic subgroups
Setting

• Gugulethu, Cape Town
• High levels of poverty and unemployment
• Large primary care clinic with integrated antenatal ART services
• Antenatal HIV prevalence 33% in 2014 (Myer et al, 2015)
Background – three-item scale

• Developed and field tested in the US (Wilson et al, 2014)
  • Literature review of all commonly used self-report items used
  • Four rounds of cognitive testing to identify which items were most consistently understood
  • Narrowed down to three items which had excellent internal consistency in field testing ($\alpha=0.86$)

• Performed well in validation against electronic drug monitoring in the US (Wilson et al, 2016)

• Scale has never been assessed outside of the US
Three-item scale

1. Days missed the last 30 days: On how many days did you miss at least one dose of any of your HIV medicines? (0–30 days)
2. Frequency: In the last 30 days, how often did you take your HIV medicines in the way you were supposed to? (never/rarely/sometimes/usually/almost always/always)
3. Rating: In the last 30 days, how good a job did you do at taking your HIV medicines in the way you were supposed to? (very poor/poor/fair/good/very good/excellent)

Aggregate scale score:
- Item 1 reverse coded into “days taken”
- Each item linearly transformed to a 0-100 scale with 0 being the worst and 100 representing the best adherence
- The mean of the three scores taken to get an equally weighted aggregate scale score
Methods

• Participants enrolled into the MCH-ART study from April 2013 - June 2014

• MCH-ART eligibility:
  • Aged 18 and older
  • Newly initiating ART in pregnancy

• Initiated a fixed dose combination of EFV+FTC/3TC+TDF

• Questionnaires translated into isiXhosa

• Up to three study visits from ART initiation to six weeks postpartum

• At each visit
  • In person study visits with questionnaires administered isiXhosa
    • Demographics
    • Three-item self-reported adherence scale (Wilson et al, 2014 & 2016)
  • HIV RNA VL (Abbott RealTime HIV-1)
    • VL ≥1000 copies/mL to indicate elevated VL
Methods

• The first study visit with both adherence and VL measure for each woman after 16 weeks on ART was included
  • to ensure all women had the opportunity to reach viral suppression

Analyses

• Internal consistency
  • Cronbach’s alpha

• Association between VL and adherence assessed
  • Logistic regression
  • Receiver Operating Characteristics (ROC) curve analysis
Results

• 628 women enrolled in MCHART
  • 176 were excluded (169 insufficient time on ART, 7 missed essential measures)
  • Women excluded were more likely to present later for antenatal care
  • No other differences at baseline between women included or excluded

• 452 women included
Description of 452 women included

<table>
<thead>
<tr>
<th>At the time of booking for antenatal care</th>
<th>Median (IQR) or N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years of age</td>
<td>28(25-32)</td>
</tr>
<tr>
<td>Completed secondary school</td>
<td>117(26)</td>
</tr>
<tr>
<td>Married/ Cohabiting</td>
<td>187(41)</td>
</tr>
<tr>
<td>Diagnosed in this pregnancy</td>
<td>241(53)</td>
</tr>
<tr>
<td>Primigravida</td>
<td>80(18)</td>
</tr>
<tr>
<td>Pre-ART HIV VL ≥1000 copies/mL</td>
<td>382(85)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>At the time of adherence assessment</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Pregnant at time of sampling</td>
<td>147(33)</td>
</tr>
<tr>
<td>Weeks on ART</td>
<td>19(18-21)</td>
</tr>
<tr>
<td>VL &lt;1000 copies/mL at the time of assessment</td>
<td>404(92)</td>
</tr>
<tr>
<td>Aggregate three-item scale score</td>
<td>89 (78-94)</td>
</tr>
</tbody>
</table>
Histogram showing distribution of individual items and the combined three-item scale score

- **Item 1:** Missed doses
- **Item 2:** Frequency
- **Item 3:** Rating

- All items and scale left-skewed
- Prominent ceiling effect in missed dose item
- Ceiling effect reduced on aggregate scale
  - Only 12% reaching perfect score on all items compared to 80% when only considering missed doses

Aggregate scale score

Cronbach’s α=0.79
Distribution of scale responses by participant subgroups
Presented as median (IQR) of aggregate score and AUC predicting VL≥1000

<table>
<thead>
<tr>
<th></th>
<th>Median three-item scale score (IQR)</th>
<th>ROC analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VL&lt;1000 (n=414)</td>
<td>VL≥1000 (n=38)</td>
</tr>
<tr>
<td>All women</td>
<td>89(78-94)</td>
<td>81.1(76-89)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completed</td>
<td>92(83-94)</td>
<td>88.9(81-89)</td>
</tr>
<tr>
<td>did not complete</td>
<td>89(78-94)</td>
<td>78.9(76-94)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnant</td>
<td>89(78-94)</td>
<td>81(78-89)</td>
</tr>
<tr>
<td>Postpartum</td>
<td>89(81-94)</td>
<td>78(71-89)</td>
</tr>
<tr>
<td>ART duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-20 weeks</td>
<td>89(78-94)</td>
<td>81(76-94)</td>
</tr>
<tr>
<td>20.1-24 weeks</td>
<td>89(79-94)</td>
<td>82(79-89)</td>
</tr>
<tr>
<td>&gt;24 weeks</td>
<td>93(81-94)</td>
<td>78(11-89)</td>
</tr>
</tbody>
</table>

- Elevated VL consistently associated with lower adherence scores
- AUC was 0.656 using a VL cut-off of ≥1000 copies/mL
- No difference by subgroups other than education (p<0.001)
Sensitivity, specificity and predictive values for three-item scale scores to predict VL≥1000 copies/mL

<table>
<thead>
<tr>
<th>Three-item scale score</th>
<th>Viral load</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥1000</td>
<td>&lt;1000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-adherent (&lt;80)</td>
<td>17</td>
<td>108</td>
<td>45%</td>
<td>74%</td>
<td>14%</td>
</tr>
<tr>
<td>Adherent (≥80)</td>
<td>21</td>
<td>306</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-adherent (&lt;90)</td>
<td>29</td>
<td>253</td>
<td>76%</td>
<td>39%</td>
<td>10%</td>
</tr>
<tr>
<td>Adherent (≥90)</td>
<td>9</td>
<td>161</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-adherent (&lt;100)</td>
<td>37</td>
<td>360</td>
<td>97%</td>
<td>13%</td>
<td>9%</td>
</tr>
<tr>
<td>Adherent (100)</td>
<td>1</td>
<td>54</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Using any non-perfect score (<100) detected 97% of women with VL≥1000
- Very high negative predictive values - those scoring above threshold on the scale had a very low probability of have a raised VL
Discussion

• First use of this new three-item scale in a non-English speaking setting
  • Performed well after translation

• Simple self-report adherence scale showed reduced ceiling effect

• Potential as a first-stage ART adherence screener in HIV-infected pregnant and postpartum women
Limitations & further research

• Very adherent population
  • limited our ability to show relationships between adherence scale scores and VL

• All women newly initiated and persisted on treatment to the time of assessment
  • Performance in treatment experienced populations and repeatedly over time requires further investigation

• Administered by trained research interviewers outside of routine care
  • Reduced social desirability bias
  • Generalizability to routine care setting not known

• Not able to compare to other adherence measures used in routine care
  • Shows promise compared to missed doses alone
  • Further research needed to compare to measures such as pharmacy refill and pill counts commonly used in routine care
Conclusion

• In the era of universal ART, critical need to focus attention on maternal adherence monitoring in low resource settings

• Simple self-report adherence scale showed potential as a first-stage adherence screener in HIV-infected pregnant and postpartum women

• With further validation within routine care, this simple scale may add value to adherence monitoring, both for this vulnerable group and more generally in ART programmes
Acknowledgements

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