Systematic review and pairwise meta-analysis comparing the predictive performance of treatment adherence measures for virologic failure detection in people living with HIV

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BACKGROUND AND OBJECTIVES

- A critical feature of an adherence assessment tool is its ability to predict virologic failure in people living with HIV (PLHIV)
- We therefore aim to compare the predictive performance of commonly used adherence measures

METHODS

- Systematic search: MEDLINE, EMBASE and LILACS up to February 2018
- Inclusion criteria:
  - People living with HIV on ART
  - Adherence measures
  - Virologic failure (as defined by each study)
- Quantitative observational studies
- Data collection: individual patient-level data → for each adherence measure, we collected the number of virologic failures within non-adherent participants
- Analysis: two or more studies comparing the same pair of adherence measures → Pairwise meta-analyses with random effects

RESULTS

- Significant heterogeneity within studies in some of the pairwise meta-analysis was explained by either sensitivity analyses or subgroup analyses (data not shown)
- In subgroup analysis, physician assessment had higher odds of predicting virologic failure than did either self-report (OR: 2.63, 95%CI: 1.37-5.26, p<0.01) or pharmacy refill (OR: 3.57, 95%CI: 1.69-7.34, p<0.001)
- Self-report was a better predictor of virologic failure than pill count when the recall period was within one week (Figure 2)
- The combination of multiple measures did not increase the predictive value when compared to any of the measures alone (Table 1)
- Different cut-offs points for virologic failure and non-adherence did not result in significant group differences or any change in magnitude effects across any of the comparisons (data not shown)

DISCUSSION

- Self-report outperforms pill count only when the self-report instrument refers to a shorter recall time frame
- Self-report measures are prone to recall bias, so a shorter time frame would increase accuracy
- Clinician assessment has been reported as the least reliable adherence measure among all.

Low-cost and simple adherence measures such as self-report predict virologic failure better than or equally well as objective measures.

Our findings favoring physician-estimated non-adherence may be explained by the fact that physicians are likely to rely on the available clinical information when they are unsure about patient adherence or do not trust the patient’s report
- There is still no consensus on how best to combine measures, which measures to combine, or how many time points to include

This heterogeneity could explain the lack of association we found between multiple vs. single measures

CONCLUSION

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References:


Figure 1. Flow diagram for study inclusion

Table 1. Summary of main findings of pairwise meta-analyses comparing the effects of adherence measures on virologic failure

<table>
<thead>
<tr>
<th>Comparison</th>
<th>No of studies</th>
<th>Sample size</th>
<th>Pooled OR (95% CI)</th>
<th>p-value</th>
<th>OR (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-report vs. pharmacy refill</td>
<td>24</td>
<td>11248</td>
<td>1.04 (0.82-1.33)</td>
<td>0.72</td>
<td>4.9% (0.005)</td>
</tr>
<tr>
<td>Self-report vs. electronic monitoring</td>
<td>7</td>
<td>345</td>
<td>1.34 (0.75-2.38)</td>
<td>0.33</td>
<td>0% (0.74)</td>
</tr>
<tr>
<td>Self-report vs. pill count</td>
<td>7</td>
<td>494</td>
<td>1.44 (0.84-2.48)</td>
<td>0.18</td>
<td>20% (0.28)</td>
</tr>
<tr>
<td>Self-report vs. physician assessment</td>
<td>5</td>
<td>1295</td>
<td>1.00 (0.49-2.02)</td>
<td>1.00</td>
<td>80% (0.003)</td>
</tr>
<tr>
<td>Pharmacy refill vs. pill count</td>
<td>2</td>
<td>299</td>
<td>1.13 (0.61-2.10)</td>
<td>0.70</td>
<td>40% (0.20)</td>
</tr>
<tr>
<td>Pharmacy refill vs. physician assessment</td>
<td>4</td>
<td>1683</td>
<td>0.48 (0.25-0.93)</td>
<td>0.03</td>
<td>62% (0.05)</td>
</tr>
<tr>
<td>Electronic monitoring vs. pill count</td>
<td>2</td>
<td>69</td>
<td>1.10 (0.33-3.71)</td>
<td>0.88</td>
<td>0% (0.52)</td>
</tr>
<tr>
<td>Self-report + pharmacy refill vs. self-report</td>
<td>3</td>
<td>215</td>
<td>1.04 (0.56-1.92)</td>
<td>0.91</td>
<td>0% (0.67)</td>
</tr>
<tr>
<td>Self-report + pharmacy refill vs. pharmacy refill</td>
<td>3</td>
<td>282</td>
<td>0.98 (0.59-1.64)</td>
<td>0.94</td>
<td>0% (0.91)</td>
</tr>
</tbody>
</table>

* p-value for heterogeneity; OR: Odds ratio (95% confidence interval)

Figure 2. Forest plot of subgroup analysis (self-report vs. pill count)