Development and Validation of an Electronic Medical Record Based Alert for Risk of ART Failure in a Low-Resource Setting

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Background

- Rapid scale-up of ART in Haiti since 2004
- Viral load testing and second-line ART regimens are still expensive and not widely available
- High ART adherence is necessary for HIV viral suppression, but no perfect measures of ART adherence exist


Photo: I-TECH
Aim: Develop and validate an alert for risk of ART failure using information on ART adherence and other patient characteristics.
Study Methods

Step 1 • Identify best-performing adherence measure

Step 2 • Identify other predictors

Step 3 • Validate risk score algorithm

Step 4 • Test performance of risk score for long-term prediction of ART failure
Primary: 12-month outcome

2,510 patients ever started on lifelong multi-drug ART regimen

2,506 patients

4 patients started ART on second-line regimen

2,117 patients

389 patients no baseline CD4 measure

1,983 patients

134 patients initiated ART within 182 days of study close

1,978 patients

5 patients lost to follow up within first 182 days

1,055 patients no follow-up CD4 from 6-12 months

923 patients with 12-month outcome

Secondary: 42-month outcome

2,510 patients ever started on lifelong multi-drug ART regimen

2,506 patients

4 patients started ART on second-line regimen

2,117 patients

389 patients no baseline CD4 measure

1,983 patients

295 patients initiated ART within 365 days of study close

1,822 patients

283 patients lost to follow up within first 365 days

1,539 patients

237 patients no follow-up CD4 from 6-42 months

1,302 patients with 42-month outcome
ART Adherence Measures

**Pharmacy-based measures**
- MPR = Medication possession ratio; sample size: n=2,458
- PDC = Proportion of days covered; sample size: n=2,458
- TVR = Timely visit ratio; sample size: n=2,242

**Self-reported adherence measures**
- VAS = Visual analogue scale; sample size: n=1,496
- %NoMD = Proportion of visits with no missed dose reported; sample size: n=1,505.

**Comparison groups**
- No ART failure (n=727) and ART failure (n=196) groups refer to patients in the primary analysis. Excluded group refers to patients excluded from the primary analysis (n=1,587). Overall group refers to the full population of adult ART patients (n=2,510).
Risk Score

Associated factors:
- Lower PDC
- Higher baseline CD4
- Shorter pre-ART duration
- Male sex

\[
\text{Risk Score} = 7.7(pdc \leq 0.80) + 9.6(cd4 \geq 250) + 8.9(duration \leq 160) + 6.3(male \text{ sex})
\]

Area under receiver operating curve (AUC)
- 0.67 (95% CI 0.61 – 0.73)
ART Failure by Risk Groups

ART Failure (Kaplan-Meier curves)

Proportion without ART failure outcome

Analysis time (6-month periods)

- 95% CI
- Low risk
- Medium risk
- High risk
## Applying Risk Categories in Practice

<table>
<thead>
<tr>
<th>Test classification characteristics</th>
<th>All groups have positive “risk test” (no test)</th>
<th>Medium + high groups have positive “risk test”</th>
<th>High group has positive “risk test”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>100.0%</td>
<td>89.6%</td>
<td>70.8%</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.0%</td>
<td>24.4%</td>
<td>53.7%</td>
</tr>
<tr>
<td>PPV</td>
<td>20.8%</td>
<td>23.8%</td>
<td>28.7%</td>
</tr>
<tr>
<td>NPV</td>
<td>NA</td>
<td>89.9%</td>
<td>87.5%</td>
</tr>
<tr>
<td>Correctly classified</td>
<td>20.8%</td>
<td>38.0%</td>
<td>57.3%</td>
</tr>
</tbody>
</table>

**Hypothetical population of 1,000 with unlimited resources for targeting**

<table>
<thead>
<tr>
<th></th>
<th>Total targeted</th>
<th>Cases of failure among targeted</th>
<th>Cases of non-failure among targeted</th>
<th>Cases of failure missed</th>
</tr>
</thead>
<tbody>
<tr>
<td>All groups have positive “risk test” (no test)</td>
<td>1000</td>
<td>208</td>
<td>792</td>
<td>0</td>
</tr>
<tr>
<td>Medium + high groups have positive “risk test”</td>
<td>785</td>
<td>186</td>
<td>599</td>
<td>22</td>
</tr>
<tr>
<td>High group has positive “risk test”</td>
<td>514</td>
<td>147</td>
<td>367</td>
<td>61</td>
</tr>
</tbody>
</table>

**Hypothetical population of 1,000 but with resources to target only 500**

<table>
<thead>
<tr>
<th></th>
<th>Total targeted</th>
<th>Cases of failure among targeted</th>
<th>Cases of non-failure among targeted</th>
<th>Cases of failure missed</th>
</tr>
</thead>
<tbody>
<tr>
<td>All groups have positive “risk test” (no test)</td>
<td>500</td>
<td>104</td>
<td>396</td>
<td>104</td>
</tr>
<tr>
<td>Medium + high groups have positive “risk test”</td>
<td>500</td>
<td>119</td>
<td>381</td>
<td>89</td>
</tr>
<tr>
<td>High group has positive “risk test”</td>
<td>500</td>
<td>143</td>
<td>357</td>
<td>65</td>
</tr>
</tbody>
</table>
Implications

• PDC measure performed best in alert

• Automated re-use of pharmacy data is efficient

• Drop routine data collection of self-reported adherence measures

• Re-direct personnel toward targeted follow-up, counseling and support

Photos: I-TECH
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Questions
Thank you!