Predictors of Incomplete Adherence to Dolutegravir-Based ART in Southwestern Uganda Through 48 Weeks of Follow-Up

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Background: A New Era in Global HIV Treatment

- ≥24 million people are now prescribed TLD for HIV treatment
- Extensive literature on barriers to and facilitators of adherence to older ART regimens in Africa, but limited regimen-specific data on TLD
- Potential barriers to TLD adherence may include dolutegravir-specific adverse effects such as weight gain, headaches, and insomnia
  - Abdominal fat gain associated with worse adherence in the era of first-line protease inhibitor-based ART

Tenofovir disoproxil fumarate
Lamivudine
Dolutegravir

Background: Population Effectiveness of Dolutegravir Implementation in Sub-Saharan Africa—A Prospective Cohort Study (DISCO)

- **Design:** longitudinal cohort study
- **Setting:** two public sector HIV clinics in Mbarara, Uganda
- **Study population** (followed from 2019-2023):
  - 500 suppressed ART-experienced adults transitioned from NNRTI-based ART to TLD
  - 171 ART-naïve adults newly initiated on TLD
- **Study procedures:** visits at enrollment, week 24, week 48
  - Data collected via interviews, chart reviews, anthropomorphic measurements
- Self-reported incomplete adherence to TLD predicted viral non-suppression (≥50 cp/mL) at 48 weeks

McCluskey et al, *J Inf Dis* 2024; McCluskey et al, HIV Drug Resistance Workshop 2023
To evaluate any **dolutegravir-specific** predictors of incomplete adherence to TLD in Uganda
Methods: Predictors of Interest and Outcome

Predictors of Interest:
- Demographics
  - Age, sex, education, marital status, clinic
- Clinical history:
  - Prior ART experience
  - Anthropomorphic data
  - Tuberculosis co-infection
  - Other medication use
  - Traditional healer use
- 41-item ACTG symptom inventory:
  - Weight gain
  - Headaches
  - Insomnia
  - Depression
  - Myalgias

Outcome of Interest:
- Composite measure of self-reported incomplete adherence to TLD over 30 days preceding 48-week visit
  - Percentage ≤80%, or
  - Frequency “a good bit of the time” or lower, or
  - Ability to take as directed “good” or lower
Methods: Statistical Techniques

**Multivariate logistic regression**

- Univariate logistic regression screen for \( p \)-value \( \geq 0.25 \) among covariates of interest
- Complete case analysis
Results: Study Population Characteristics

675 participants enrolled in parent study

- 4 disenrolled
- 14 in care but no 48-week data
- 15 lost to follow-up
- 16 died

626 (82%) had complete data at 48 weeks and were included in this analysis
### Results: Study Population Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ART-Experienced Cohort (enrolled 2019)</th>
<th>ART-Naïve Cohort (enrolled 2020-21)</th>
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<tbody>
<tr>
<td></td>
<td>n = 483</td>
<td>n = 143</td>
</tr>
<tr>
<td>Age in years, median (IQR)</td>
<td>47 (40-53)</td>
<td>32 (26-39)</td>
</tr>
<tr>
<td>Female</td>
<td>42%</td>
<td>60%</td>
</tr>
<tr>
<td>Married or in domestic partnership</td>
<td>66%</td>
<td>73%</td>
</tr>
<tr>
<td>No schooling or primary education only</td>
<td>62%</td>
<td>39%</td>
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<tr>
<td>Years on ART, median (IQR)</td>
<td>9 (6-12)</td>
<td>-</td>
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<tr>
<td>ART prior to TLD, n (%)</td>
<td></td>
<td></td>
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<tr>
<td>3TC/TDF/EFV</td>
<td>44%</td>
<td>-</td>
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<tr>
<td>3TC/AZT/NVP</td>
<td>39%</td>
<td>-</td>
</tr>
<tr>
<td>Other</td>
<td>17%</td>
<td>-</td>
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</tbody>
</table>
Results: Self-Reported Adherence to TLD Through 48 Weeks

Among ART-experienced participants, self-reported incomplete adherence to NNRTI-based ART before transition did not predict adherence to TLD.
Results: Self-Reported Adherence to TLD Through 48 Weeks

ART-Naïve Subgroup
n=143

Week 0 Not on ART
6% Missing adherence data
16% Incomplete adherence
78% Complete adherence

Week 24 TLD
15% Missing adherence data
16% Incomplete adherence
85% Complete adherence

Week 48 TLD
15% Missing adherence data
16% Incomplete adherence
85% Complete adherence
Results: Predictors of Incomplete Adherence to TLD Through 48 Weeks

- Married or in domestic partnership: 59% Incomplete adherence, 68% Complete adherence, p = 0.02
- Taking ≥1 other medication: 24% Incomplete adherence, 36% Complete adherence, p = 0.04
- Had headaches over 30 days preceding visit: 37% Incomplete adherence, 25% Complete adherence, p = 0.02
Results: Covariates That Did Not Predict Adherence to TLD Through 48 Weeks

- Prior ART experience (77% of cohort)
- Myalgias (25%)
- Insomnia (13%)
- Measured weight gain ≥10% from weeks 0-48 (13%)
- Self-perceived weight gain (10%)
- Depression (5%)
- Recent use of traditional medicines (6%)
- Tuberculosis co-infection (3%)
- Age, sex, level of education, or clinic site
Results: Self-Reported Reasons for Most Recent Missed Dose of TLD Among Participants Reporting Incomplete Adherence at 48-Week Visit

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<tr>
<th>Reason</th>
<th>Percentage</th>
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<tr>
<td>Away from home</td>
<td>58%</td>
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<tr>
<td>Simply forgot</td>
<td>33%</td>
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<tr>
<td>Too busy</td>
<td>26%</td>
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<tr>
<td>Ran out</td>
<td>16%</td>
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<tr>
<td>Routine changed</td>
<td>12%</td>
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<tr>
<td>Pill burden</td>
<td>5%</td>
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<tr>
<td>Slept late</td>
<td>5%</td>
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<tr>
<td>Other</td>
<td>5%</td>
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<tr>
<td>Side effects</td>
<td>0%</td>
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<tr>
<td>Stigma</td>
<td>0%</td>
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n=54; answers not mutually exclusive
Limitations

• Reliance on self-report
  ○ Expanded analysis underway using pharmacologic measures

• Some previously characterized psychosocial and structural predictors of adherence not assessed in parent study survey instruments
  ○ Planning qualitative study of perspectives on treatment failure

• Lack of 48-week adherence data for participants who died or were lost to follow-up

• Moderate missingness for measured weight data at 48-week visit due to COVID-19 “lockdowns” requiring some visits to be conducted virtually
Conclusions

- Excellent overall adherence to TLD at public-sector clinics in Uganda through 48 weeks; lower in previously ART-naïve group
- Prior adherence to NNRTI-based ART did not predict adherence to TLD
- Use of other medications and social support associated with better adherence to TLD
- Incident headaches associated with incomplete adherence to TLD
- Measured and self-perceived weight gain not associated with incomplete adherence to TLD
# Acknowledgements

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