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

Medicines Patient Pool 2024; WHO 2024; Heestermans et al, BMJ GH 2016; US DHHS Guidelines 2024; Stellbrink et al, AIDS 2013

Background: Population Effectiveness of <u>D</u>olutegravir <u>I</u>mplementation in <u>S</u>ub-Saharan Africa—A Prospective <u>Co</u>hort 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** ($\geq$50 cp/mL) at 48 weeks

McCluskey et al, *J Inf Dis* 2024; McCluskey et al, HIV Drug Resistance Workshop 2023

Objective

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
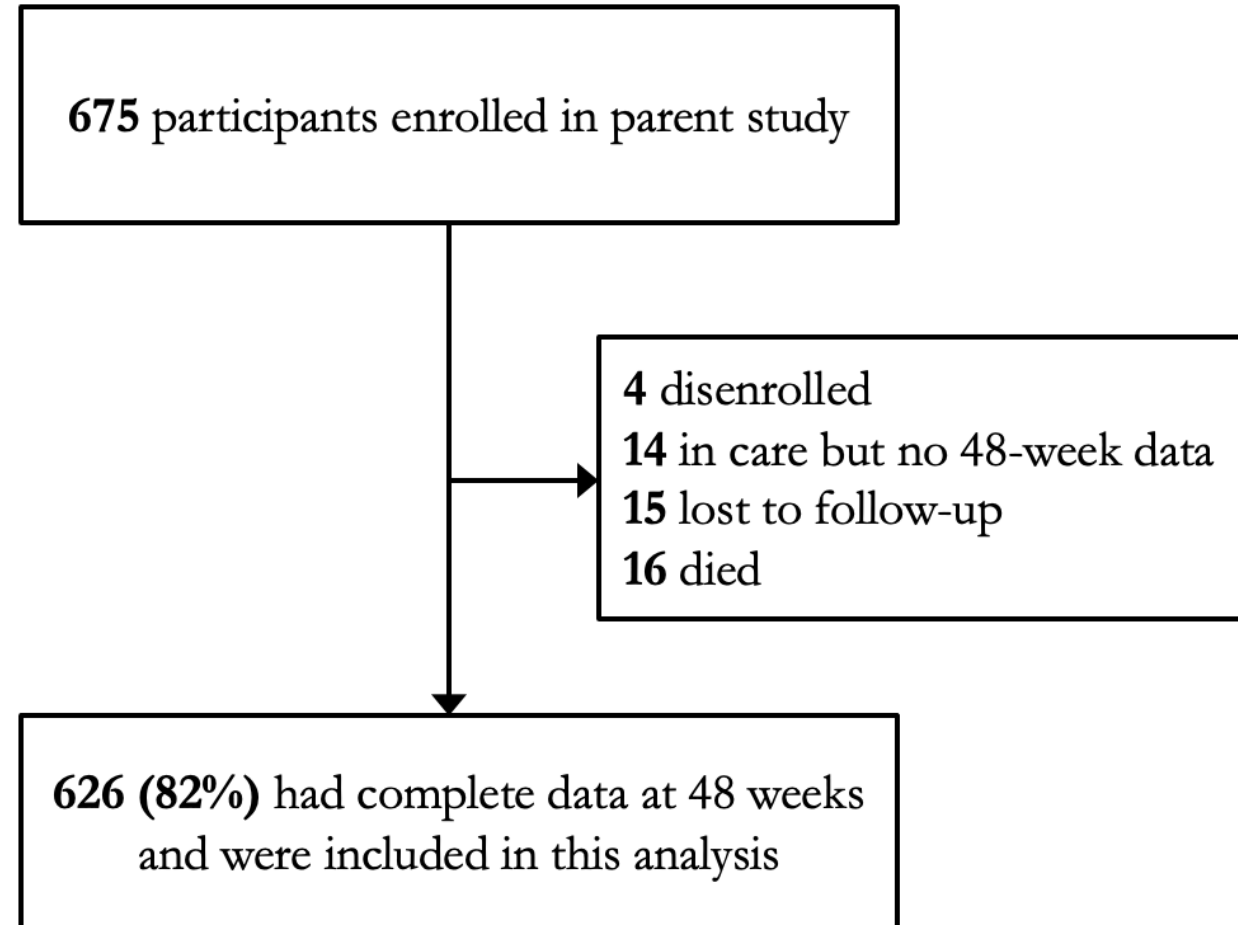
Berg et al, *AIDS Behav* 2012

Methods: Statistical Techniques

Multivariate logistic regression
- Univariate logistic regression screen for p-value ≥0.25 among covariates of interest
- Complete case analysis
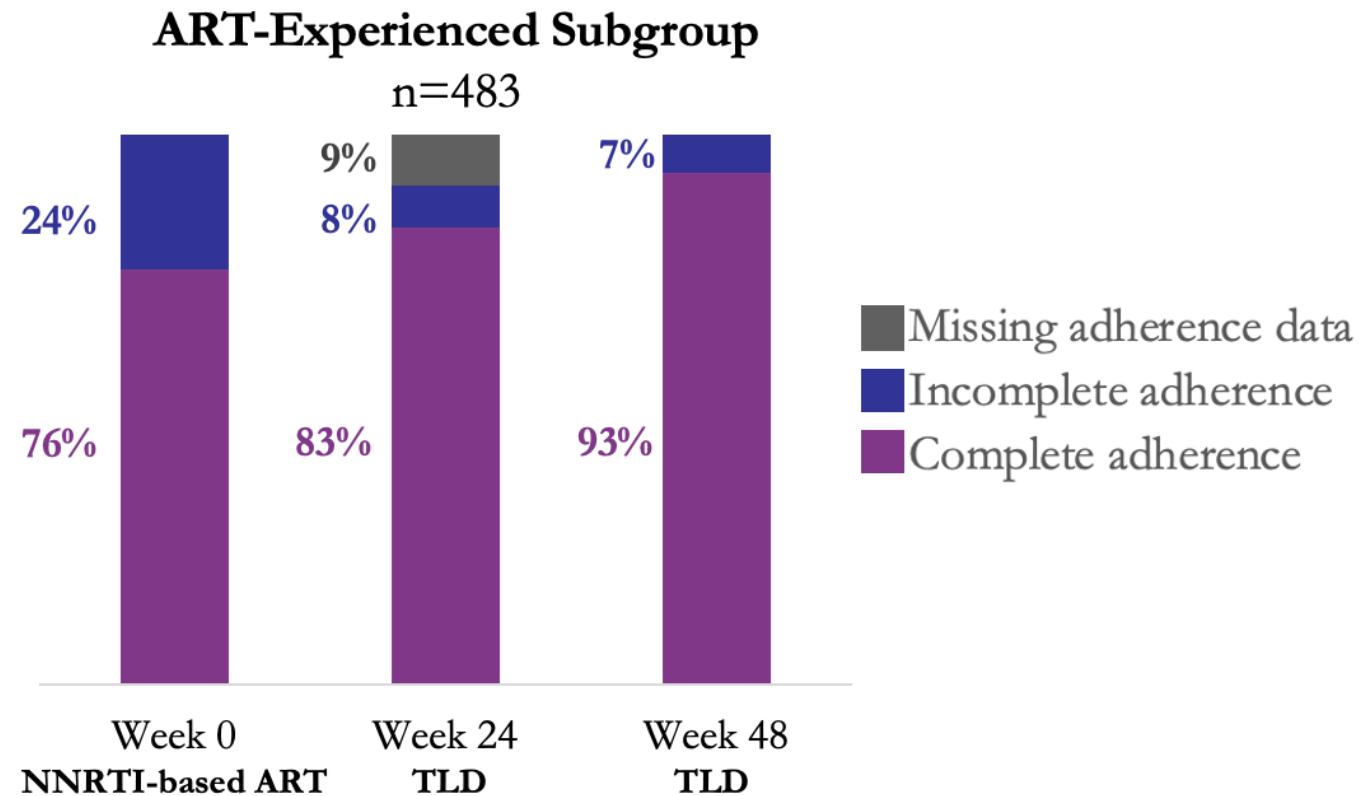
Results: Study Population Characteristics

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┌─────────────────────────────────────────────────┐
│  675 participants enrolled in parent study       │
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                        │
                        │        ┌──────────────────────────────────────┐
                        │───────▶│  4 disenrolled                       │
                        │        │  14 in care but no 48-week data      │
                        │        │  15 lost to follow-up                │
                        │        │  16 died                             │
                        │        └──────────────────────────────────────┘
                        ▼
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│  626 (82%) had complete data at 48 weeks          │
│     and were included in this analysis            │
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Results: Study Population Characteristics

Characteristics	ART-Experienced Cohort (enrolled 2019)	ART-Naïve Cohort (enrolled 2020-21)
	n = 483	n = 143
Age in years, *median (IQR)*	47 (40-53)	32 (26-39)
Female	42%	60%
Married or in domestic partnership	66%	73%
No schooling or primary education only	62%	39%
Years on ART, *median (IQR)*	9 (6-12)	-
ART prior to TLD, *n (%)*		
3TC/TDF/EFV	44%	-
3TC/AZT/NVP	39%	-
Other	17%	-

Results: Self-Reported Adherence to TLD Through 48 Weeks

ART-Experienced Subgroup
n=483

Week 0 — NNRTI-based ART: 76% Complete adherence, 24% Incomplete adherence
Week 24 — TLD: 83% Complete adherence, 8% Incomplete adherence, 9% Missing adherence data
Week 48 — TLD: 93% Complete adherence, 7% Incomplete adherence

Legend:
- Missing adherence data
- Incomplete adherence
- Complete adherence

Among ART-experienced participants, self-reported incomplete adherence to NNRTI-based ART before transition **did not predict** adherence to TLD

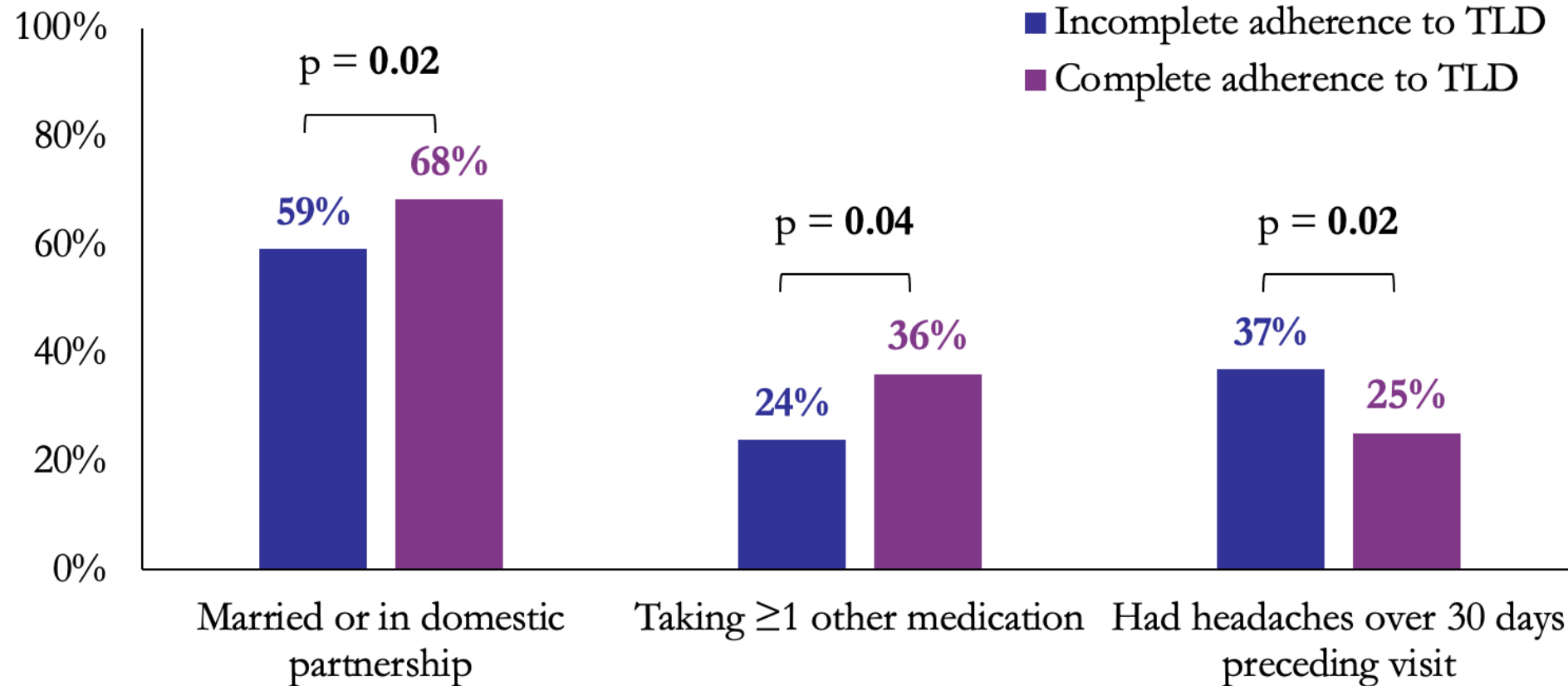# Results: Self-Reported Adherence to TLD Through 48 Weeks

ART-Naïve Subgroup
n=143

Week 0 — Not on ART
Week 24 — TLD: 78%, 16%, 6%
Week 48 — TLD: 85%, 15%

■ Missing adherence data
■ Incomplete adherence
■ Complete adherence
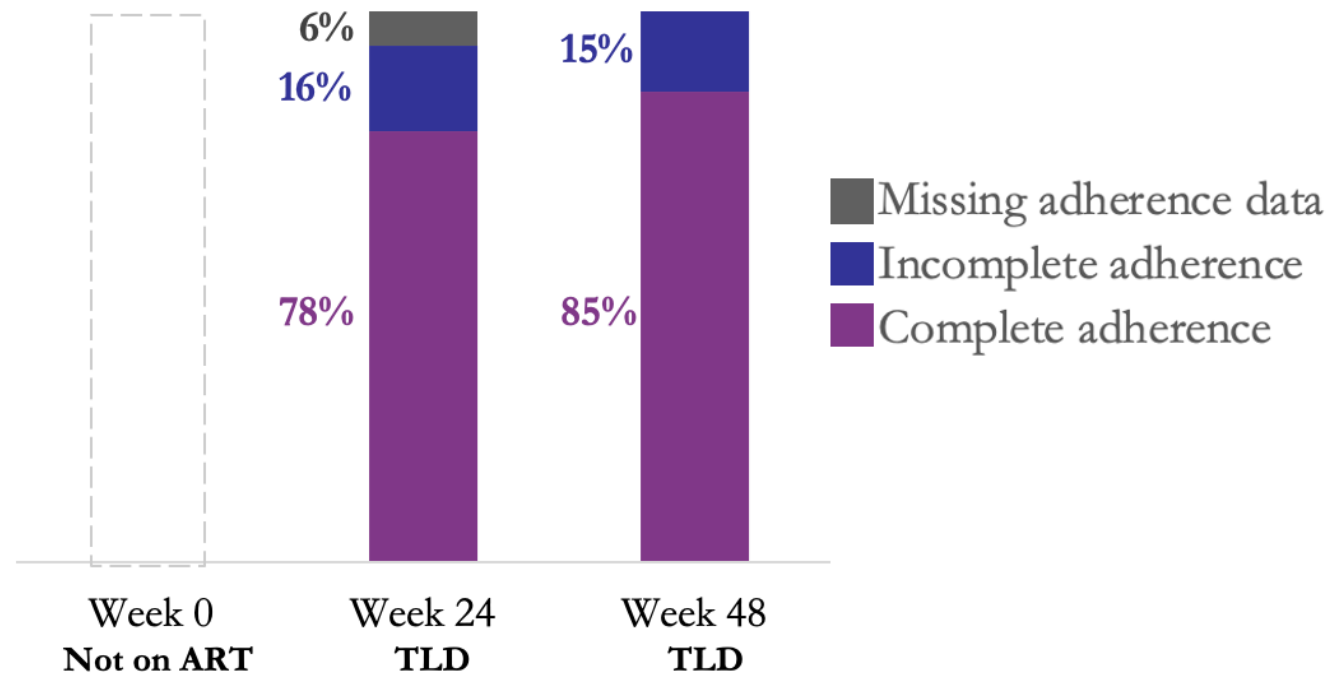
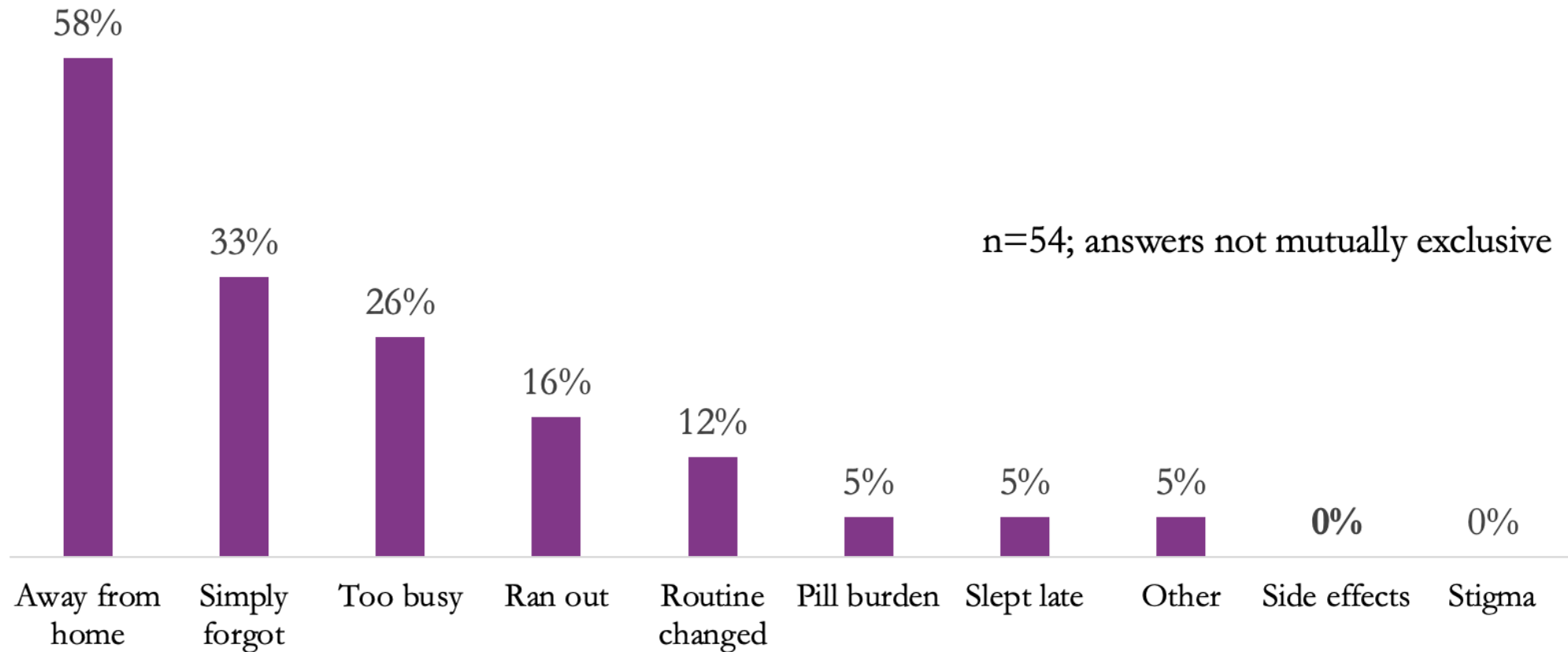# Results: Predictors of Incomplete Adherence to TLD Through 48 Weeks

Results: Covariates That Did <u>Not</u> 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

n=54; answers not mutually exclusive

Away from home	Simply forgot	Too busy	Ran out	Routine changed	Pill burden	Slept late	Other	Side effects	Stigma
58%	33%	26%	16%	12%	5%	5%	5%	0%	0%

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

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