Weight gain among people living with HIV in Zambia transitioning to dolutegravir-based antiretroviral regimens by tenofovir formulation

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Background

Dolutegravir (DTG) as first-line antiretroviral therapy (ART)[1]

- Superiority over efavirenz-based regimens:
  - Shorter time to viral suppression
  - Higher CD4 cell count recovery
  - Lower risk of treatment discontinuation
- Higher viral suppression on DTG compared to protease inhibitors (PI)

Global evidence of weight gain on DTG

- Greater weight gain on DTG compared to other ART regimens[2]
- Greater weight gain on DTG with tenofovir alafenamide (TAF) than tenofovir disoproxil fumarate (TDF)[3]

Transition to DTG in Zambia

- DTG-based regimens adopted as first-line ART in 2018 Zambia Consolidated Guidelines for Prevention and Treatment of HIV Infection
- Now, over 80% of PLHIV on ART in Zambia receive a DTG-based regimen

We compared weight changes among PLHIV who switched to a DTG-based regimen with TAF or TDF using data from electronic health records (EHR) in Zambia.

Methods

Study design and participants

- Retrospective cohort study of EHR data
- Inclusion criteria (fig. 1):
  - Received ART between 2017 and 2022
  - Aged ≥20 years at ART initiation
  - Transitioned from a PI- or NNRTI-based regimen to DTG-based with TAF or TDF and XTC (PLHIV initiated on DTG were excluded due to lack of pre-DTG weights)
  - ≥2 weights before and after switch (minimum 4 weights recorded in EHR)

Statistical analysis

- Chi-squared tests to detect differences by DTG-based regimen at time of transition
- Linear mixed effects regression model
  - Fixed effects: sex, age group, previous ART regimen, DTG-based regimen, viral load status, and body mass index (BMI) at time of regimen switch
  - Participant as random intercept
  - Linear splines with knots at time of switch and 12-months post-switch
- Model predictions to estimate weight changes before DTG exposure, within 12 months of switch, and ≥12 months since DTG transition

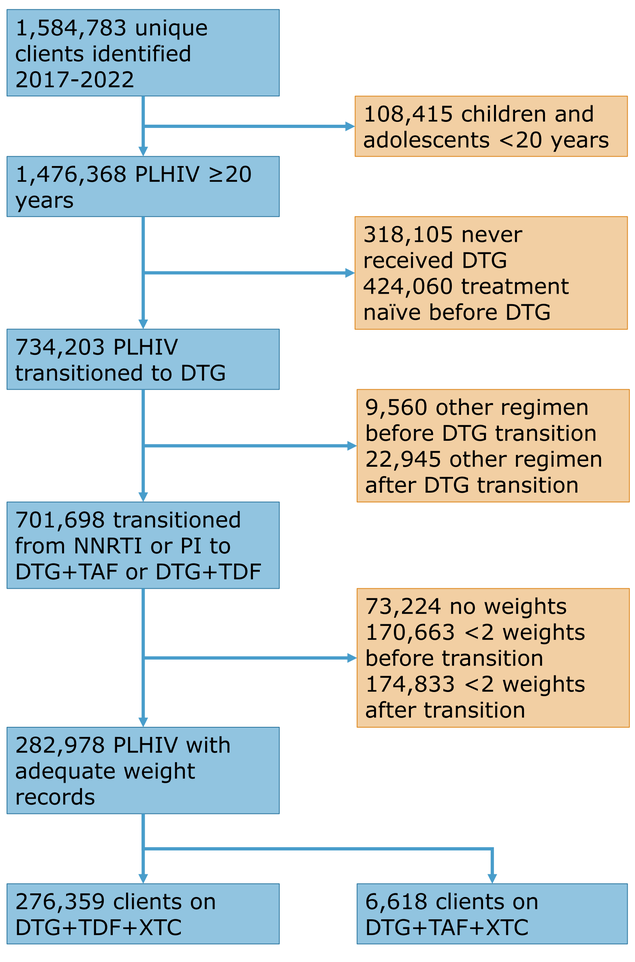

Figure 1. Participant cascade of people living with HIV in Zambia transitioned to DTG-based ART (with TAF or TDF) from a PI- or NNRTI-based regimen and captured in the electronic health record system.

PLHIV gained more weight on DTG+TAF than DTG+TDF, but weight gain reduced in both groups after the first year

Results

- 282,978 records analyzed of PLHIV on ART in Zambia, 2017-2022 (fig. 1)
- 97.7% transitioned to DTG+TDF+XTC; 2.3% transitioned to DTG+TAF+XTC
- PLHIV on DTG+TAF weighed 3.8kg (95% CI: 3.4-4.1) more, on average, and a greater proportion were overweight or obese (36.6% vs 26.6%) at the time of transitioning to DTG compared to PLHIV on DTG+TDF (table 1)
- PLHIV transitioned to DTG+TDF gained an average of 0.4kg/year before transitioning to DTG, 1.3kg in the year following the transition, and 0.3kg/year in the second year and beyond (fig. 2)
- PLHIV on DTG+TAF gained significantly more weight during all three time periods (p<0.001) with an average of 0.5kg/year before the transition, 2.4kg in the year after the transition, and 0.6kg/year thereafter

Table 1. Characteristics of PLHIV at time of transition to DTG (N=282,978)

	DTG+TDF N=276,359 n (%)	DTG+TAF N=6,618 n (%)	p-value
Sex			
Female	181,230 (65.6)	4,382 (66.2)	0.288
Male	95,129 (34.4)	2,236 (33.8)	
Age group, years			<0.001
20-29	34,134 (12.4)	212 (3.2)	
30-39	83,300 (30.1)	640 (9.7)	
40-49	97,096 (35.1)	2,132 (32.2)	
50-59	45,955 (16.6)	2,294 (34.7)	
60+	15,874 (5.7)	1,340 (20.2)	
Previous ART regimen backbone			<0.001
NNRTI	271,553 (98.3)	6,166 (93.2)	
PI	4,806 (1.7)	452 (6.8)	
Viral load status			0.002
Suppressed	244,705 (88.5)	6,092 (92.1)	
Unsuppressed	8,683 (3.1)	264 (4.0)	
Missing	22,971 (8.3)	262 (4.0)	
Body mass index category			<0.001
Underweight (<18.5 kg/m²)	34,434 (12.5)	765 (11.6)	
Normal (18.5 - <25 kg/m²)	163,301 (59.1)	3,345 (50.5)	
Overweight (25 - <30 kg/m²)	48,902 (17.7)	1,513 (22.9)	
Obese (≥30 kg/m²)	23,525 (8.5)	907 (13.7)	
Missing	6,197 (2.2)	88 (1.3)	

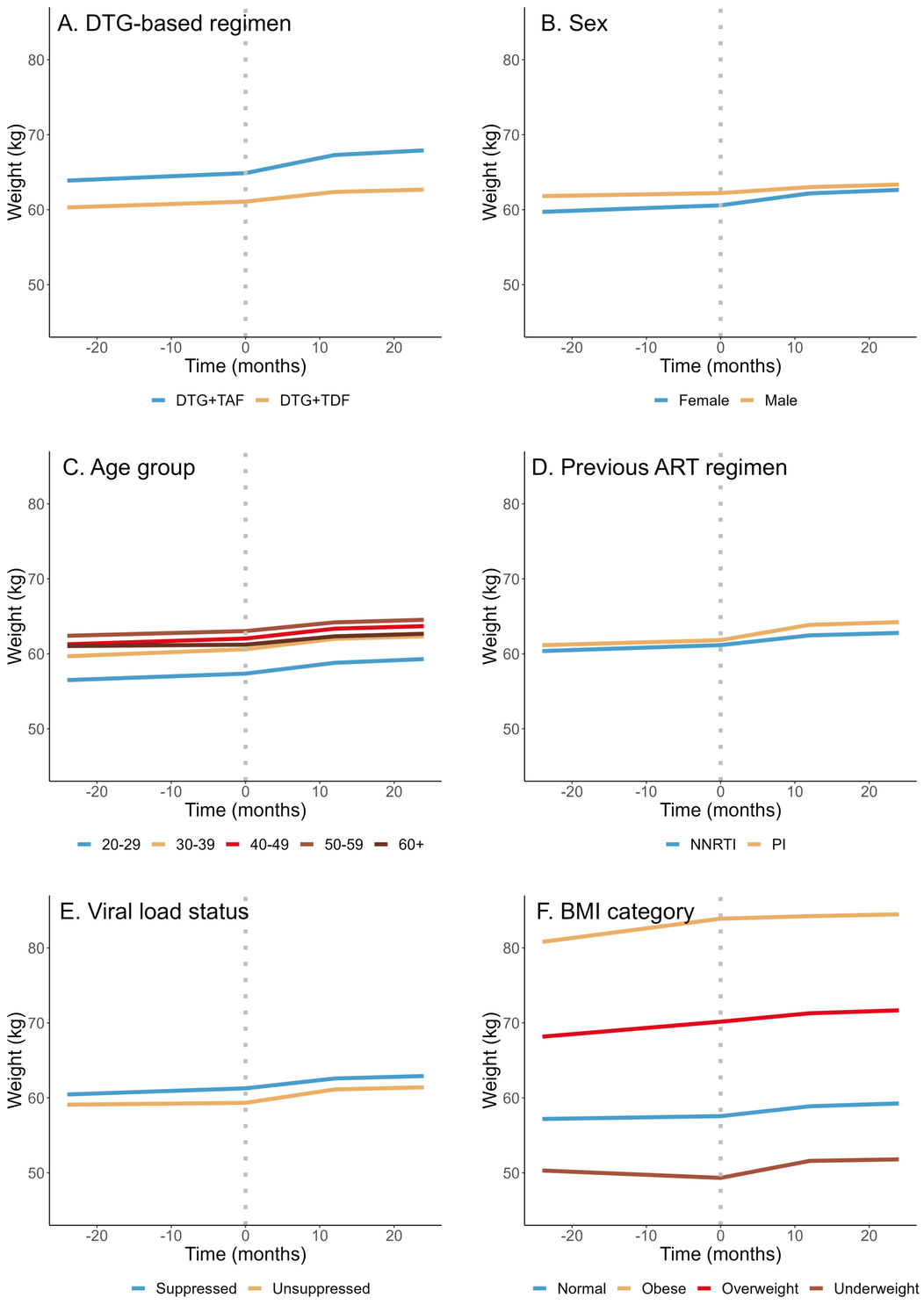

Figure 2. Model predictions by DTG-based ART regimen and participant characteristics at time of regimen switch. Vertical dotted line represents transition to DTG-based regimen.

Results, Continued

- PLHIV with an overweight or obese BMI increased among PLHIV on DTG+TDF from 26.8% at the time of transition to 32.1% at the most recent interaction and from 37.0% to 46.1% among PLHIV on DTG+TAF (fig. 3)
- Incidence of obesity was 46/1,000 person-years among PLHIV on DTG+TDF and 69/1,000 person-years among PLHIV on DTG+TAF

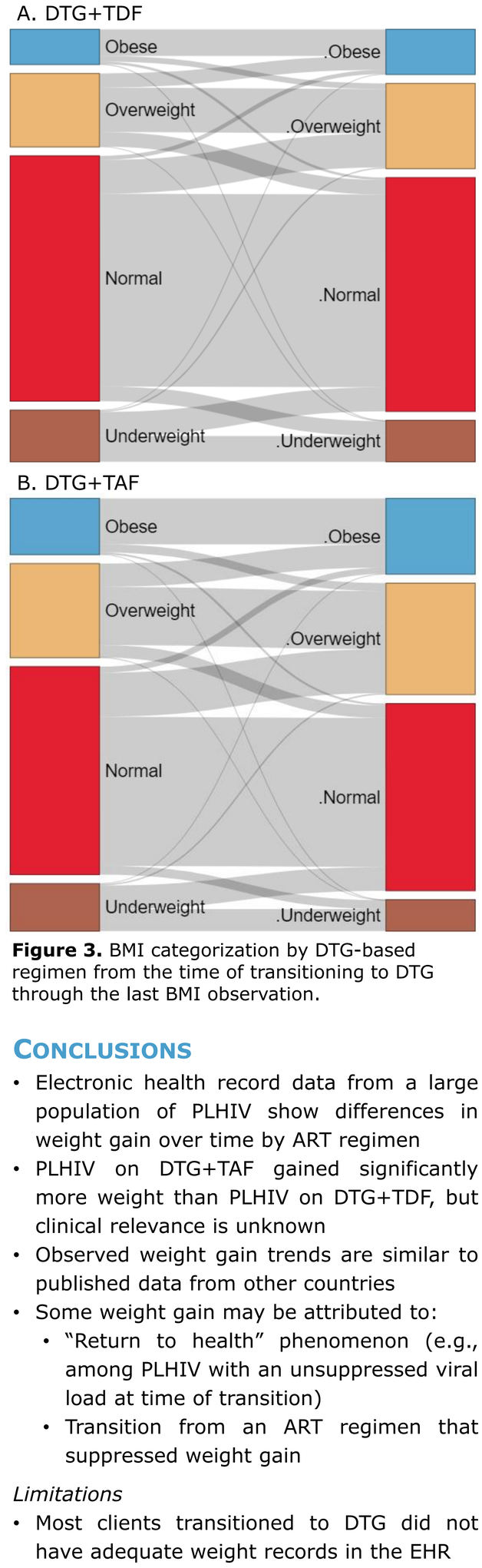

Figure 3. BMI categorization by DTG-based regimen from the time of transitioning to DTG through the last BMI observation.

Conclusions

- Electronic health record data from a large population of PLHIV show differences in weight gain over time by ART regimen
- PLHIV on DTG+TAF gained significantly more weight than PLHIV on DTG+TDF, but clinical relevance is unknown
- Observed weight gain trends are similar to published data from other countries
- Some weight gain may be attributed to:
  - "Return to health" phenomenon (e.g., among PLHIV with an unsuppressed viral load at time of transition)
  - Transition from an ART regimen that suppressed weight gain

Limitations

- Most clients transitioned to DTG did not have adequate weight records in the EHR
- Clinical data on possible impacts of weight gain (e.g., blood pressure, blood sugar, cholesterol) were not available

Recommendations

- Ensure weights are measured and recorded in the EHR at every clinical encounter
- Tailored weight management counseling
- Screening of overweight and obese PLHIV for metabolic syndrome
- Integration of noncommunicable disease management into routine HIV care

References

1. WHO. Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV: interim guidelines. Dec 2018.
2. Lake JE, et al. Risk factors for weight gain following switch to integrase inhibitor-based antiretroviral therapy. *Clin Infect Dis* 2020; 71(9):e471-7.
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