Cardiometabolic risks and the transition to integrase inhibitors in aging people living with HIV in South Africa

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BACKGROUND

Dolutegravir (DTG) is recommended globally for first and second-line HIV treatment, leading to a change to **integrase inhibitor-based regimens** for South Africans on ART. While there are many benefits of DTG, clinical cohorts have demonstrated its association with weight gain and risk of high blood pressure and high total cholesterol. Some studies have demonstrated higher weight gains among women.

AIM

To evaluate the population-level impact of the roll-out of dolutegravir on cardiometabolic risk factors for HIV-positive older adults living in rural South Africa.

STUDY SETTING

HAALSA: *Health and Ageing in Africa: Longitudinal Studies in South Africa*

- Nested within the Agincourt Health and Demographic Surveillance System in Mpumalanga Province, South Africa
- Population-based longitudinal cohort study of adults aged 40+ years, with 5,059 initially enrolled in 2013-2014
- Household-based surveys collect data on health and socioeconomic factors, anthropometrics, blood pressure
- Dried Blood Spots (DBS) tested for HIV Ag/Ab showing a 23% HIV prevalence
- DBS tested for antiretrovirals to define a participant's regimen: DTG, EFV, LPV, 3TC, FTC

METHODS

- Longitudinal follow-up of the cohort from **Wave 2** to **Wave 3** to evaluate **changes** in: BMI, Waist circumference, Waist-to-hip ratio, Blood pressure
- Comparing the following **groups**:
  (1) HIV+, switched to DTG
  (2) HIV+, no switch to DTG
  (3) HIV+, not on ART
  (4) HIV-
- **Linear regression** models
  - For the full population and sex-stratified
  - Controlling for age, sex, education, wealth index

This study demonstrates that switching to **dolutegravir among adults aging with HIV is associated with cardiometabolic risk factors** in a real-world setting:
Weight gain and increased blood pressure, including higher diastolic blood pressure for women

HAALSA HIV-positive population, survey Waves 1-3:

Wave 1: 2014-2015
HIV+: 1048
64% on ART

Wave 2: 2018-2019
HIV+: 888
84% on ART:
EFV regimen: 89%
Other regimen: 11%

DTG roll-out
December 2019

Wave 3: 2021-2022
HIV+: 809
88% on ART:
EFV regimen: 34%
DTG regimen: 49%
Other regimen: 17%

Table. Linear regression results for change from Wave 2 to Wave 3 for each outcome.

Women

Group	N	BMI (kg/m2)	Waist circumference (cm)	Waist-to-hip ratio	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
HIV-	1002	(ref)	(ref)	(ref)	(ref)	(ref)
HIV+/ART/No DTG	101	0.27 (-1.04, 1.59)	-1.43 (-4.78, 1.91)	-0.018 (-0.044, 0.008)	-0.41 (-4.59, 3.78)	1.67 (-0.81, 4.14)
HIV+/ART/DTG	143	**2.11 (0.97, 3.25)****	**2.66 (-0.24, 5.56)***	-0.001 (-0.024, 0.021)	2.11 (-1.53, 5.76)	**2.49 (0.33, 4.64)****
HIV+/no ART	19	-1.37 (-4.26, 1.52)	**-8.62 (-16.22, -1.02)****	-0.042 (-0.100, 0.017)	**8.24 (-0.94, 17.42)***	1.97 (-3.45, 7.40)

Men

Group	N	BMI (kg/m2)	Waist circumference (cm)	Waist-to-hip ratio	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
HIV-	726	(ref)	(ref)	(ref)	(ref)	(ref)
HIV+/ART/No DTG	72	-0.52 (-1.91, 0.87)	2.61 (-2.13, 7.35)	0.011 (-0.023, 0.044)	-0.89 (-6.29, 4.51)	-0.13 (-3.24, 2.98)
HIV+/ART/DTG	76	0.10 (-1.25, 1.45)	3.11 (-1.47, 7.68)	-0.005 (-0.037, 0.027)	3.82 (-1.43, 9.07)	-0.67 (-3.69, 2.34)
HIV+/no ART	13	**-3.47 (-7.00, 0.06)***	-3.08 (-14.83, 8.67)	-0.030 (-0.112, 0.053)	-4.52 (-16.75, 7.70)	-2.72 (-9.75, 4.31)

*Notes: Linear regression models adjusted for age, sex, education level, wealth asset index. ** p < 0.05; *p < 0.10*

WHY STUDY HAALSA?

- Population-based cohort provides an HIV-negative comparison group
- Longer time horizon compared to some clinical studies
- Focus on middle-age and older adults who may be at higher risk for cardiometabolic diseases

RESULTS

Compared to the HIV- group over the 3 year time period:

- Among the full population:
  - People on ART who switched to DTG had greater increases in BMI (1.38 kg/m^2, 95% CI: 0.51, 2.25), waist circumference (2.87 cm, 95% CI: 0.40, 5.35), and slightly higher systolic blood pressure (2.62 mmHg, 95% CI: -0.38, 5.62).
  - People on ART without switch to DTG had no differences for these outcomes.
  - People who were HIV+ and not on ART had relatively large decreases in weight.
- Among women:
  - People on ART who switched to DTG had greater diastolic blood pressure (Table).

CONCLUSIONS

There are cardiometabolic risks at the population-level associated with the change to integrase inhibitor-based regimens, in particular an increase in diastolic blood pressure among women, which is a risk factor for heart disease and stroke. Investments in care to offset these risks in people with treated HIV are essential for healthy aging with HIV.

ADDITIONAL RESOURCES

For more information and public datasets please visit: ***haalsi.org***



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