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## Plan Overview

*A Data Management Plan created using DMPTool*

**Title:** Observational Cohort study

**Creator:** Bourgi, Kassem - **ORCID:** [0000-0001-9734-7489](https://orcid.org/0000-0001-9734-7489)

**Affiliation:** Indiana University (iu.edu)

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**Template:** Mock Template, Generic

### Project abstract:

Integrase Inhibitors, including dolutegravir (DTG), are now a commonly used and critical component of antiretroviral therapy (ART). Recently a large-scale rollout of DTG been expanded to low- and middle-income countries (LMIC) including Kenya. Data from our recent studies in North America (NA) suggest that treatment naïve persons living with HIV (PLWH) receiving DTG are at risk for greater enhanced weight gain. Additionally, substantial weight gain has been reported in treatment-experienced PLWH switching from non-nucleoside reverse transcriptase inhibitor (NNRTI) - to DTG- based regimens. However, there is a paucity of evidence describing the outcomes of patients receiving DTG in LMIC. While ART associated weight gain has been linked to increased multimorbidity among PLWH with higher BMI, such weight gain is associated with improved immunologic recovery and survival in persons with advanced HIV disease. Compared to PLWH in NA, PLWH in Kenya are predominantly women, have higher rates of coinfection with Tuberculosis (TB) as well as lower CD4 T-cell count and body mass index (BMI) at time of treatment initiation. Therefore, while the increased weight gain with DTG- is likely associated with deleterious metabolic perturbations in NA, similar weight gain among PLWH in Kenya could be associated with improved outcomes. In this proposal, we aim to assess the change in weight over time among PLWH receiving DTG in the Academic Model Providing Access to Healthcare (AMPATH) program. Weight gain will be assessed in both treatment experienced patients with  $\geq 1$  year sustained viral suppression on an NNRTI-containing regimen switching to a DTG-containing regimen, as well as in treatment naïve patients starting DTG containing regimens. We also aim to compare the incidence of diabetes and CD4 T-cell count recovery among AMPATH patients receiving DTG- vs. NNRTI- based ART. Data will be obtained from the peer navigator – patient symptom screen form and retrospective analysis of the patient’s medical records within AMPATH open medical records system. A multivariate linear mixed effects model will be built to generate adjusted marginal predictions of weights over time. These results will define the relative benefits vs. risks of DTG-associated weight changes in LMIC.

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# Observational Cohort study

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## Data Collection

### Sample question for mock plan

The current proposal will leverage the AMPATH and the East Africa International epidemiologic Databases to Evaluate AIDS (IeDEA) consortium funded by the National Institutes of Health, to assess the impact of starting or switching to a DTG-containing ART regimen on weight gain and CD4 T-cell recovery in a study population from a low-income east African country with high prevalence of HIV and HIV/TB co-infection. We will carry out the assessment at the Moi Teaching and Referral Hospital (MTRH) AMPATH clinic. AMPATH is a partnership between MTRH, Moi University College of Health Sciences, and a consortium of North American universities and academic medical centers. AMPATH's research network supports and sustains high-quality translational and implementation research. The network has received 112 million dollars in sponsor support and produced more than 550 peer-reviewed journal articles.

### Study Population

In treatment experienced patients: PLWH on an NNRTI-based regimen: any 2 Nucleoside Reverse Transcriptase Inhibitors (NRTIs) + 1 NNRTI for  $\geq 2$  years with  $\geq 12$  months sustained viral suppression (viral load  $< 1000$  copies/mL) switching to a DTG-based regimen: any 2 NRTIs + DTG. Controls: PLWH on an NNRTI-based regimen for  $\geq 2$  years with  $\geq 12$  months sustained viral suppression who remain on that NNRTI. In treatment naïve patients: PLWH starting a first treatment regimen containing DTG + any 2 NRTIs. Controls: PLWH starting first treatment regimen containing NNRTI + any 2 NRTIs. For both groups, we will exclude patients who are pregnant at time of ART initiation (or switch). Additionally, patients who become pregnant, at any time during the study period, will be censored.

### Time Period

We plan to use the IeDEA database to extract data from patients starting ART after 01/01/2013. Treatment experienced patients: PLWH starting ART after 01/01/2013 and switching to DTG-based regimen between 10/01/2017 – 09/30/2018; Follow-up weights until 12/31/2019 (range of follow-up duration after switching: 15 – 27 months). Treatment naïve patients: PLWH starting NNRTI-based regimen after 01/01/2013 compared to those starting DTG-based regimen between 10/01/2017 – 09/30/2018; Follow-up weights until 12/31/2019 (range of follow-up for PLWH starting DTG: 15 – 27 months).

### Data Collection

A combination of data collected through the peer navigator – patient symptom screen form and retrospective analysis of the patient's medical records within AMPATH open medical records system will be used. Data collection will include BMI, age at ART initiation, sex, duration from diagnosis of HIV infection to treatment, year of ART initiation/switch, treatment regimen as well as pre- and post-ART initiation/switch longitudinal data on weights, available CD4 T-cell lymphocyte count and available plasma HIV-1 RNA measurements. Body weight nearest to ART initiation/switch within the period from 90 days before to 30 days after treatment start will be used to calculate baseline weight and baseline BMI. Similarly, CD4 T-cell count and plasma HIV-1 RNA measurements nearest to ART initiation/switch will be used to define baseline CD4 T-cell count and baseline plasma HIV-1 RNA count. Additional clinical variables that will be collected include: TB-specific (co-infection, treatment regimen, initiation date, and treatment outcome).