

# Exploring metabolic outcomes in African adults living with HIV switching to injectable antiretroviral therapy

Fellow: Dr Jonathan Kitonsa<sup>1</sup>

Supervisors: Dr Fiona Cresswell<sup>1,2,3</sup>, Dr Robert Kalyesubula<sup>4</sup>, Jaime Vera<sup>2</sup>, Eugene Ruzagira<sup>1</sup>.

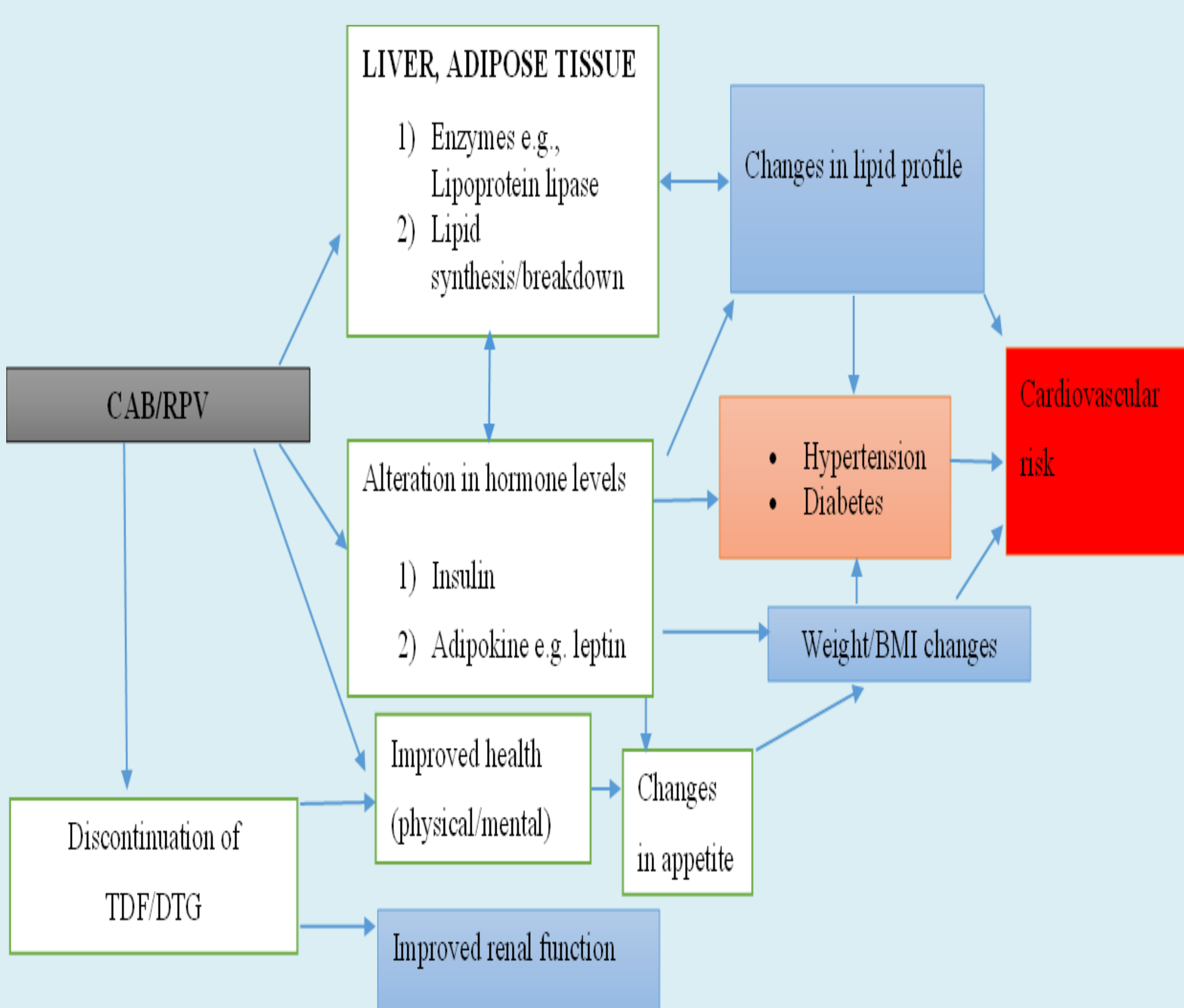
Affiliations: 1 MRC/UVRI & LSHTM Uganda Research Unit; 2 Brighton and Sussex Medical School; 3 LSHTM; 4 Makerere University Kampala

## Introduction

- The assortment of HIV antiretroviral therapy (ART) options has diversified over time with newer drugs offering better viral control and reduced toxicity, among other benefits.
- Focus has now turned to the use of injectable long-acting (LA) ART to relieve burden of daily dosing.
- Currently available LA drugs in high income settings include cabotegravir (INSTI) and rilpivirine (NNRTI), which are given 2-monthly by intramuscular injection.
- Unfortunately, LA ART has not been adequately investigated in sub-Saharan African adults living with HIV.
- I will aim to describe the metabolic outcomes of adults living with HIV who are switched from first-line oral dolutegravir-based ART to LA injectable cabotegravir and rilpivirine over a 2-year period.



## Conceptual framework



## Objectives

- To compare changes in weight and BMI, lipid profiles, blood pressure, over 2-years among patients receiving 2-monthly LA cabotegravir and rilpivirine and compare this with those remaining on oral ART, and determine factors associated with observed changes.
- To describe the baseline glycaemic status of an African population with a history of suboptimal HIV control, and the change in HbA1c, and rate of incident diabetes mellitus whilst on LA cabotegravir and rilpivirine compared with patients remaining on oral DTG-based ART through 2 years of follow-up.
- To compare change in 10-year cardiovascular risk among patients on LA cabotegravir and rilpivirine with those remaining on oral DTG-based ART.
- To quantify the impact of TDF cessation on eGFR.
- To compare serum leptin and fasting insulin levels during follow-up in a subset of participants with significant weight gain and a sample of similar participants without weight gain at 24 months.

## Methods

- This study will utilise data from an open-label phase III randomised clinical trial entitled 'Improving HIV control in Africa with Long-acting Antiretrovirals (IMPALA, NCT5546242). In the trial, 540 virologically suppressed adults with a history of sub-optimal HIV control from Uganda, Kenya and South Africa are randomised 1:1 to receive 2-monthly injectable cabotegravir and rilpivirine or remain on oral ART.



## Methods

- Initially, a search strategy will be developed followed by a literature review of existing publications, open-source datasets or exploration of availability of data from other studies to understand the current knowledge base around metabolic outcomes on injectable ART.
- For objectives 1-4, data collected in the IMPALA trial will be used; for objective 5, a matched case control study in 50:50 cases/controls will be conducted using stored samples.

## Analysis

- Demographics of the study population will be described by study arm.
- For objectives 1 to 4:**
  - The median or mean, change from baseline to 24 months and 95% confidence intervals for different outcomes will be described for the LA ART and the oral ART groups and compared.
  - Generalised linear regression will be used to compare change in metabolic parameters between groups.
  - Linear mixed models will be used to determine factors associated with different metabolic outcomes.
- For objective 5** a linear mixed-effects model will be used to account for repeated measures of leptin and insulin, assessing their longitudinal associations with weight gain while adjusting for ART regimen, baseline BMI, and any other variables.

## Acknowledgements

- The Impala study teams and participants in Uganda, Kenya, and South Africa
- The CREATE Program
- Welcome Trust

