1. Introduction

The HIV epidemic is a public health challenge of unprecedented dimensions. Sub-Saharan Africa is at the epicentre of the epidemic and continues to carry the greater burden of its health and socioeconomic impact. In 2011, an estimated 23.5 million adults and children were living with HIV in the region and 1.2 million died, representing three-quarters of the global HIV mortality[1]. The scale-up of antiretroviral treatment (ART) programmes across Africa has made great progress over the last decade and early pessimism about delivery and effectiveness of ART has largely proven unfounded. It has been possible to deliver treatment through existing health systems and meta-analyses have found that the levels of treatment adherence, virological suppression and immune recovery are similar to high-income countries[2,3]. However, despite the progress, data from the region has shown that the mortality rate of patients in the first months of ART is several folds higher among patients in low- than high-income countries, even after adjusting for differences in immunodeficiency[2]. A comparative study found that the risk of death within the first year of treatment was 6-21% in a patient in Africa, in contrast to 2-4% in a patient with similar demographic and clinical characteristics in Europe or North America[4]. Reviewers have consistently shown that the main predictors of early mortality are low CD4, advanced HIV stage, anaemia and poor nutritional status at initiation of ART[4–6].

International agencies have called for interventions to address malnutrition of patients[7] and nutritional support services are becoming an integrated part of HIV care in many countries. Reviews of 2008 data from ART facilities across sub-Saharan Africa, showed that nearly all sites provided nutritional counselling and 17-18% of sites offered some type of food rations for patients[8,9]. Supplements are typically given in the form of fortified blended foods (FBF) or the more energy-dense, and more costly, lipid-based nutrient supplements (LNS).

Meanwhile, there is very little knowledge on the effects of nutritional supplementation for HIV patients. In fact, nutritional supplementation in various forms is becoming standard care without an evidence base. The reasons for the paucity of strong data include ethical constraints for conducting randomised controlled trials in settings with high prevalence of food insecurity and malnutrition. Another reason may be a tendency of regarding nutritional supplementation as beneficial by definition, although it in fact might be ineffective or even harmful during certain disease processes[10–12]. Information is urgently needed to guide supplementation programmes on the optimal composition, timing and duration of supplementation as well as identification of individuals most likely to benefit.

The present PhD thesis is based on data from the ARTfood study, in which the effects of supplementation with LNS on general and HIV specific outcomes were investigated among patients commencing ART. The thesis reports the study's findings on weight gain, body composition, functional outcomes, viral load and immune recovery. Potential benefits of whey protein in nutritional supplements for HIV patients were assessed by comparing whey- and soy-containing LNS. In addition, the thesis presents differences in effects of supplementation when provided either concurrently with ART initiation or after a three months delay. The thesis also includes a description of the levels and predictors of patients' physical activity and capacity at baseline and a qualitative assessment of their perspectives of supplementation.

1.1 Objectives of PhD thesis

The overall objective of this thesis is to assess the effects and feasibility of providing HIV patients with LNS for three months after ART initiation.

Specific objectives include:

- To describe physical activity and capacity in HIV patients eligible for ART and assess the impact of malnutrition and HIV severity on these outcomes (Paper I)
- To explore the use, perceptions and acceptability of nutritional supplementation among HIV patients (Paper II)
- To assess the effects of nutritional supplementation on weight, lean body mass, grip strength, physical activity, viral load and immune recovery, including a comparison of whey- and soy-containing LNS and a comparison of early and delayed timing of supplementation (Paper III[i])

[i] Data on viral load and immune recovery is presented here, but the results will be further elaborated in a thesis by Alemseged Abdissa who has shared first-authorship of Paper III.