Nutritional status is the major factor affecting grip strength of African HIV patients before and during antiretroviral treatment

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Abstract

Objectives: Low grip strength is a marker of frailty and a risk factor for mortality among HIV patients and other populations. There is limited information about factors associated with grip strength in HIV patients and how it changes during antiretroviral therapy (ART). We investigated factors associated with grip strength in malnourished HIV patients at referral to ART, and at 12 weeks and 2-3 years after starting ART.

Methods: The study involved HIV-infected Zambian and Tanzanian participants recruited to the NUSTART trial when malnourished (body mass index <18.5 kg/m^2) and requiring ART. The relationship of grip strength to nutritional, infectious and demographic factors was assessed by multivariable linear regression at referral for ART (n=1742) and after 12 weeks (n=778) and 2-3 years of ART (n=273).

Results: In analyses controlled only for sex, age and height, most nutrition and infection-related variables were associated with grip strength. However, in multivariable analyses, consistent associations were seen for fat-free mass index, mid-upper arm circumference, haemoglobin and systolic blood pressure, and a variable association with fat mass index in men. C-reactive protein and CD4 count had limited independent effects on grip strength, while receiving tuberculosis treatment was associated with weaker grip strength.

Conclusions: In this population of originally malnourished HIV patients, poor grip strength was more strongly and independently associated with nutritional than with infection and inflammation variables. Programmes to improve health and survival of HIV patients should incorporate nutritional assessment and management and could use grip strength as a functional indicator of improving nutrition.

Introduction

In Africa, where the largest proportion of HIV-infected people reside, the increasing roll out of antiretroviral therapy (ART) means that HIV is becoming a chronic disease, but many African health services are not currently staffed or equipped for the longitudinal management of complex health conditions. There is a need for low cost, clinic-based diagnostic tools to identify and monitor ART-treated HIV patients with declining general health status and function, sometimes referred to as frailty, and at increased risk for mortality. An index of frailty, originally designed to assess older adults, comprising unintentional weight loss, slow walking speed, low grip strength, self-reported exhaustion and low energy expenditure,[1] predicts morbidity and mortality among American and European HIV patients[2-4]. The limited data on frailty and grip strength among HIV-infected persons in sub-Saharan Africa has recently been reviewed [5]. The few prior studies have found that HIV infection is a risk factor for frailty among South Africans[6] and for low grip strength among Ethiopian adults.[7] While in some circumstances the full frailty scale may be useful for HIV-infected African adults,[6] some components might be hard to assess in a busy clinic or not easily applicable to HIV-infected Africans. However, grip strength, measured as the force the hand applies as it pulls on a dynamometer, is objective, easy and cheap to measure, correlates with other physical function tests,[8] and was independently associated with mortality in a multi-country study of HIV-uninfected adults.[9]

The clinical usefulness of grip strength would be improved by greater understanding of how this metric relates to other physiologic parameters and responds to ART or other interventions, which might allow clinicians to intervene as appropriate. In addition to age and sex, two main factors seem to contribute to low grip strength: poor nutritional status and systemic inflammation, associated with either infectious or non-infectious conditions. Low body mass index (BMI) was associated with low grip strength[7] or frailty[6] among HIV patients. Wasting may have longstanding adverse effects on grip strength as seen among HIV-infected American men who had recovered from wasting.[10] It is likely the fat-free mass component of BMI which is important for grip strength[11] and it is notable that both fat-free mass and grip strength increased together following nutritional supplementation of Ethiopian[12] or American[13] HIV patients. However, studies in other patient groups have found that changes in fat-free mass and grip strength were not closely associated in magnitude or time frame, so other factors are clearly involved.[14] Acute inflammation, as assessed by C-reactive protein (CRP), is associated with low grip strength in a variety of non-HIV illnesses.[15] Among HIV patients, low CD4 count is associated with low grip strength[8] or frailty.[6, 16] Few studies have investigated associations of other markers of infection with grip strength of HIV patients but a comprehensive study found stronger associations with grip strength for markers of acute inflammation than for CD4 count.[11] Finally, our observations from the Nutritional Support for African Adults Starting Antiretroviral Therapy (NUSTART) trial suggest that grip strength reflects other unmeasured factors since grip strength was independently associated with mortality in multivariable analyses including sex, age, BMI, fat-free mass, mid-upper arm circumference (MUAC), total CD4 count, CRP, and T cell subsets.[17, 18]

It is important to investigate factors associated with poor grip strength among African HIV patients, and any changes during ART treatment, because grip strength is known to differ between countries[9] and races;[16] because environmental and social risk factors such as infectious disease exposure, nutrition and smoking differ; and because many Africans start ART at advanced HIV stages and are malnourished,[19] which could potentially lead to long term low grip strength.[10] We used

the rich NUSTART databases from both the original trial[19] and a subsequent follow-up of Tanzanian patients[20] to evaluate factors affecting grip strength of malnourished (BMI<18.5kg/m^2) HIV patients (CD4 count<350 cells/µl or WHO stage 3 or 4) at 3 time points: referral for ART, 12 weeks after starting ART, and 2-3 years after starting ART.

Methods

Participants

Participants were from the NUSTART phase III randomized trial which tested the efficacy of vitamins and minerals in a lipid-based nutritional supplement (LNS-VM), compared to a similar supplement without adding micronutrients (LNS), on mortality of malnourished HIV-infected patients starting ART (trial registration: PACTR201106000300631).[19, 21] It was conducted in Lusaka, Zambia and Mwanza, Tanzania between August 2011 and December 2013; 1815 patients were recruited upon referral for ART and followed through 12 weeks of ART. Enrolment criteria were: age at least 18 years, ART-naive (except for standard short-course regimens to prevent maternal-to-child HIV transmission), BMI <18.5 kg/m^2, eligible for ART (CD4 count <350 cells/µl or World Health Organization stage 3 or 4 disease), and willing to undertake stepped-up ART follow-up in the study clinic. Exclusion criteria were participating in another programme with a similar protocol or pregnancy by self-report. Grip strength was obtained from 1742 participants at baseline and 778 participants at 12 weeks after starting ART. In 2015 we were able to follow-up 273 of the Tanzanian patients for a single cross-sectional assessment.

Clinical assessments

Grip strength was measured in kilograms using a digital handgrip dynamometer (Takei TKK 5401, Chasmor, UK); two measurements were taken from each hand and the machine automatically takes the mean of the maximum left- and right-side readings by a standardised protocol. Higher scores indicate better grip strength.

Height, weight, MUAC, and waist and hip circumferences were measured in triplicate using standard methods; the median of the three measurements was used during analysis. Participants underwent bioelectrical impedance analysis (BIA) to estimate fat mass and fat-free mass (Tanita BC418, Tokyo, Japan). Since the internal equations for the BIA machine are not designed for such severely malnourished and ill patients as NUSTART patients were at referral, all values were adjusted using air displacement plethysmography (BodPod) data available for Lusaka patients using regression as used previously for Ethiopian infants.[22] Fat mass index (FMI) and fat-free mass index (FFMI) were calculated in order to control for height in a manner analogous to BMI and quoted in kg/m^2. The BIA machine also provides fat and fat-free mass for trunk and extremities but these showed very similar results to total body fat and lean so are not presented. Hemoglobin (Hb) was measured in fingerprick samples by Hemocue (Angelholm, Sweden) and blood pressure by standard methods.

At the 2-3-year follow-up in Tanzanian patients only,[20] we took similar measurements, although information on Hb and CD4 count was unavailable. We also investigated the presence of diabetes and pre-diabetes according to WHO guidelines.[23]

Laboratory assessments

CD4 count was measured by the local HIV services at both sites. Serum CRP was measured by ELISA (AssayPro, St Charles, MO, USA). Values measured at 6 weeks after starting ART were used for analyses at week 12 ART since CRP results were not available at week 12.

Statistical analyses

For the present analyses we used data available from the original NUSTART trial at referral to ART and 12 weeks after starting ART in both Zambian and Tanzania participants, and from the follow-up

assessment 2-3 years after starting ART in Tanzanians only. Separate linear regression models of factors associated with grip strength were developed for each time point and for the change in grip strength between referral and 12 weeks ART. Analyses were stratified by sex and controlled for age and height since these unmodifiable factors are known to affect grip strength.[9, 24] Other variables investigated were: country, socioeconomic status (SES, indicated by an asset index derived separately for each site and divided into quintiles[25]); treatment group allocation (LNS or LNS-VM); systolic blood pressure (SBP), CD4 count indicating HIV stage, CRP indicating concurrent inflammation, tuberculosis (TB) infection (as indicated by whether the patient was on TB treatment); anthropometric variables (BMI, MUAC, waist and hip circumferences); FMI, FFMI and Hb. Oedema was included at baseline only since very few patients were oedematous at later times; most oedema was in the lower extremities. CD4 was included as its square root transformation in order to normalise data. CRP was used as a categorical variable because its distribution could not be normalised by simple transformation. Other diagnostic and clinical data were not used since diagnoses were found unreliable or variable across sites and virtually all patients (83% at baseline and 100% at later time points) were taking cotrimoxazole as standard of care.

For each time point, multivariable models were run with all available grip strength data, and all available covariates as we had no *a priori* reason to exclude any variables and favoured a causal modelling approach over parsimony. We developed separate models for anthropometric and body composition variables which successfully removed collinearity, identified using variance inflation factors, among the nutritional variables. At baseline and 12 weeks, covariate data were missing for several variables (for details, see table footnotes). We assumed data were missing at random and generated, separately for men and women, ten multiple imputation datasets using chained equations (MICE) as some of the missing data were binary so a joint multivariate normal model was not appropriate. The "mi" suite of commands in Stata 14.1 were used both to impute and analyse the data. Imputation models included in multivariable models the grip strength outcome, and other variables measured at the same time as grip strength. Imputation diagnostics within Stata were used to confirm model fit.[26] At 2-3 years after starting ART there was little missing data among covariates so we conducted complete case analysis. For this time point, models did not adjust for SES, or trial arm because these were measured at referral for ART, country because follow-up was only in Tanzania, and CD4 count which was not collected.

Ethics

Ethical approval for the NUSTART trial was obtained from the ethics committees of the London School of Hygiene and Tropical Medicine, the National Institute for Medical Research (NIMR), Tanzania, and the University of Zambia Biomedical Research Ethics Committee. Approval for the follow-up study was obtained from the Lake Zone Institutional Review Board housed at NIMR, Mwanza, Tanzania. All participants provided written or thumbprint informed consent.

Results

Table 1 describes baseline data from the full cohort of NUSTART participants and for those with available grip strength data at each time point. As a result of trial inclusion criteria, patients were malnourished, had very low FMI, and low CD4 counts at recruitment. Mortality was a major reason for the decreasing sample size with time: 365 of 1815 (20%) of original recruits had died by 12 weeks of ART and in Tanzania an additional 91 of 704 recruits (13%) died between 12 weeks and 2-3 years after starting ART. Therefore, baseline factors associated with missing grip strength data at later times were those associated with mortality: poor initial grip strength, low CD4 count, high CRP, poor nutritional status, and oedema. In addition, a few participants who attended clinic visits did not perform grip strength tests for a variety of reasons.

At baseline and 12 weeks, men had about 6 kg stronger grip than women, and this difference had widened to 12 kg by 2-3 years of ART (t-test p-value <0.001, **Table 2**). However, this likely resulted from the fact that only Tanzanian patients were followed at 2-3 years: although Tanzanian and Zambian women had similar grip strength to each other at baseline (16.5 (SD 5.0) and 16.7 (SD 5.2) kg, respectively) and 12 weeks (20.4 (SD 6.0) and 20.3 (SD 5.1) kg), Tanzanian men had slightly stronger grips than Zambian men at baseline (23.1 (SD 6.8) and 22.7 (SD 6.7) kg, respectively) and 12 weeks (28.4 (SD 7.1) and 25.6 (SD 6.7) kg). Grip strength was highest in participants aged 30-50 years. Height was correlated with grip strength at all times for men and women both separately and together (results not shown). Socioeconomic status quintile and treatment group allocation had no significant associations with grip strength.

At referral for ART, all nutritional and health variables were associated with grip strength in analyses stratified by sex and adjusted for age and height (**Table 3**). In multivariable analyses including body composition (Model 1), FFMI was positively associated with grip strength in both men and women but FMI only in men. In analyses using anthropometric data (Model 2), MUAC had the strongest association with grip strength with additional contribution from calf circumference in both sexes and from hip circumference in men. In both multivariable analyses, Hb was positively associated with grip strength in both sexes and CRP was negatively associated with grip strength in women only. SBP was positively associated with grip strength in all analyses except the anthropometric variables for men. Being on TB treatment or having oedema were generally associated with lower grip strength. CD4 count was not associated with grip strength.

Twelve weeks after starting ART, most nutritional variables remained associated with grip strength in analyses adjusted for height and age; associations appeared stronger among men than among women (**Table 4**). In multivariate analyses, as for baseline, the anthropometric and body composition variables most strongly associated with grip strength were MUAC and FFMI although in men FMI also had an independent association, but in this case negative, with grip strength. Hb was positively associated with grip strength in both sexes and SBP was associated with grip in women only. In multivariable analyses, CRP and CD4 count were not associated with grip strength and being on TB treatment was associated with lower grip strength in men only.

At 2-3 years after starting ART, in analysis adjusted for age and height among women, MUAC, FFMI and SBP were positively associated with grip strength whereas CRP was negatively associated with grip strength (**Table 5**). Among men, in age- and height-adjusted analyses, anthropometric and body composition variables were all positively associated with grip strength. In multivariable analyses in women, FFMI, MUAC and SBP remained positively associated with grip strength and the trend for a negative association with CRP remained, apparently driven mainly by those with very high CRP. In multivariable analysis among men, only MUAC and SBP in the body composition model (model 1) were positive predictors of grip strength. Diabetes or pre-diabetes had no association with grip strength.

We conducted similar models for the change in grip strength between baseline and 12 weeks ART, controlling for baseline grip strength, to identify factors which might inform future interventions to rapidly improve grip strength in patients referred for ART. The results (**Table 6**) added little to the cross-sectional analyses, showing that FFMI generally had the strongest association with change in grip strength. Providing TB treatment strongly benefited women but not men and having oedema at recruitment had larger adverse effects on men than on women. There was a decrease in grip strength over time in men having higher initial CD4 count; this may reflect a greater improvement in health over time with people who were initially sicker.

Discussion

The study confirmed the factors previously shown to be associated with grip strength, notably nutrition, infection/inflammation, sex, age and height in a cohort of malnourished, HIV-infected adults starting ART in sub-Saharan Africa, a population with a high prevalence of frailty and high risk of mortality. In multivariable analyses, nutritional and body composition variables, particularly FFMI, MUAC and Hb, remained strongly associated with grip strength. CD4, our measure of HIV severity, had no independent effects on grip strength in cross-sectional analyses, and CRP, the measure of systemic inflammation, had significant independent effects only among women at baseline and 2-3 years after starting ART. These findings suggest that HIV infection *per se* does not exert adverse effects on grip strength, but rather the effects of untreated HIV and systemic inflammation on accelerated lean mass loss and metabolic derangements likely drive a loss of grip strength as a component of accelerated frailty. Being on TB treatment, our indicator of TB infection at baseline, had a significant negative effect on grip strength in most analyses at baseline and 12 weeks; however, being on TB treatment resulted in more rapid increase in grip strength in women and, in other analyses from the trial, being on TB treatment at baseline was associated with higher 12-week survival.[17, 19]

FMI had variable associations, that is, positive, negative or none, with grip strength in multivariable analyses which also included FFMI. These are difficult to explain biologically and likely reflect the inverse association between FMI and FFMI, even though both increased over time on ART. Hb had an independent effect on grip strength. We previously showed that the LNS-VM intervention, in spite of containing iron and other micronutrients related to Hb, did not increase Hb or other markers of iron status, i.e. ferritin and serum transferrin receptor, likely because of ongoing inflammation, indicated by raised CRP, at 12 weeks ART.[27] It is unclear which factor represented by Hb – status of iron or other micronutrients, inflammation, oxygen transport or some combination of all these – resulted in the association between Hb and grip strength.

SBP was positively associated with grip strength in this population of generally normal SBP. We have previously shown in a small subset of 33 Zambian NUSTART patients that higher serum tumour necrosis factor-α receptor-1 was associated with lower blood pressure and with heart rate variability.[28] It is possible that in the present analysis lower SBP to some extent reflects ongoing inflammation which, through a general loss of cardiovascular autonomic tone, is contributing to frailty. We also have evidence that low SBP in HIV-infected adults may reflect adrenal insufficiency which would be predicted to affect grip strength.[29]

The evolution of grip strength over time on ART is difficult to see in the present analyses since they include different patients at different time points and low grip strength was a risk factor for mortality. Grip strength appeared to increase steadily with time on ART in surviving men although it plateaued after the first 12 weeks of ART in women. Although part of the increase between 12 weeks and 2-3 years in men is an artefact since Zambian men could not be studied at 2-3 years, it seems that, considering Tanzanian men only, there was an increase in grip strength of about 4 kg between 12 weeks and 2-3 years. The reason for the country differences in grip strength trajectories with time on ART in men is unknown but Lusaka is the more urban site with many people employed in office or other sedentary jobs whereas many Tanzanian patients were from rural areas around Mwanza and employed in more physical work such as farming or fishing. The greater grip strength in Tanzanian men may thus reflect improved muscle mass and strength associated with exercise in HIV-infected people.[30]

There was no differential effect on grip strength of allocation to LNS or LNS-VM treatment. However, all patients received at least some nutritional support, from the calories, proteins and fats in the LNS, through the trial design and this may have contributed to the rapid improvements in grip strength as has been shown in a trial in Ethiopia with an unsupplemented control group.[12] The

analysis of factors at baseline affecting the evolution in grip after starting ART did not suggest any additional interventions to improve grip strength; tuberculosis treatment did improve grip strength in women but tuberculosis treatment is already standard of care.

The decreasing sample size over time limits our statistical power, although it is highly relevant since much of the decrease was due to mortality, and that was associated with grip strength. In addition, this was an originally unplanned analysis from a clinical trial so we did not collect data from most patients on some muscle functions, notably heart function, which might be more closely related to mortality than is arm muscle function as measured by grip strength. However, in a large study of grip strength in non-HIV patients, grip predicted both death and disease from cardiovascular causes suggesting it could be used as a proxy.[9]

All NUSTART patients were malnourished at recruitment so it could be argued that the predominance of nutritional factors among associations with grip strength could be an artefact of the trial inclusion criteria. However, these patients also had advanced HIV disease, as indicated by their very low CD4 count at recruitment so, if severe illness itself was the main factor affecting grip strength, analyses from the cohort should have detected this. Furthermore, similar factors were associated with grip strength at all time points, including after 2-3 years of ART when patients were no longer malnourished.

In conclusion, we have documented the large changes in grip strength in the first few years of ART among African patients who were malnourished when referred to ART and were provided with nutritional supplements for the first few weeks. MUAC and FFMI, likely reflecting muscle mass but possibly heart or other lean tissue also, had the strongest associations with grip strength. Our results confirm the importance of monitoring nutritional status as part of HIV care and providing nutritional interventions to patients who are malnourished. Grip strength, which reflects functional lean mass, i.e. muscle, and predicts mortality in HIV patients, could be included in HIV care as a simple tool to monitor nutritional health.

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Table 1. Recruitment characteristics of participants with available grip strength data at each time point and for the full cohort[1]

Variable	Recruitment	12 weeks ART	2-3 years ART	Full cohort
N	1742	778	273	1815
Tanzanian, N (%)	684 (39%)*	282 (36%)	273 (100%)	704 (38%)
Treatment, allocated to LNS-VM, N (%)	884 (51%)	408 (52%)	145 (53%)	914 (50%)
Age (years), mean (SD)	36 (9)	37 (10)*	38.9(9.7) *	36 (9)
Female, N (%)	860 (49.4%)	406 (52%)	178 (65.2)*	900 (49.6%)
Grip strength (kg), mean (SD)	19.8 (7)	20.4 (7)*	20.1 (6.6)	19.8 (7)
Height (m), mean (SD)	164.5 (8.4)	164.2 (8.7)	162.4 (8.1) *	164.5 (8.4)
BMI (kg/m^2), mean (SD)	16.5 (1.3)	16.7 (1.3)*	16.7 (1.2) *	16.5 (1.4)
MUAC (cm), mean (SD)	21.4 (2.1)	21.7 (2.0)*	21.7 (1.9) *	21.4 (2.1)
Waist circumference (cm), mean (SD)	66.4 (4.7)	66.8 (4.7)*	67.6 (4.6) *	66.4 (4.8)
Hip circumference (cm), mean (SD)	79.2 (4.2)	79.9 (4.2)*	80.3 (4.2) *	79.2 (4.2)
Calf circumference (cm), mean (SD)	28.5 (2.2)	28.7 (2.1)*	28.4 (1.9)	28.5 (2.2)
FMI (kg/m^2), mean (SD)	2.6 (0.8)	2.7 (0.8)*	2.9 (0.8) *	2.6 (0.8)
FFMI (kg/m^2), mean (SD)	14.1 (0.9)	14.1 (0.8)*	14.0 (0.9)	14.1 (0.9)
Haemoglobin (g/L), mean (SD)	96 (23)	100 (23)*	93.7 (23.9)	96 (23)
CD4 count (cells/μl), median (IQR)	120 (51, 210)	132 (62, 228)*	100 (37, 199)	120 (51, 211)
C-reactive protein (mg/L), median (IQR)	61 (14, 160)	36 (8, 124)*	46 (0.65, 1748)	61 (14, 160)
TB treatment, N (%)	431 (25%)	223 (29%)*	63 (23.1%)	451 (25%)
Oedema, N (%)	64 (3.6%)	4 (0.7%)*	6 (2.2)	66 (4%)
Systolic blood pressure (mmHg), mean (SD)	97 (13)	97 (13)	101 (15)*	97 (13)

Socioeconomic quintiles, N (%)	Lowest	351 (20%)	126 (16%)*	58 (21%)	364 (20%)
	Low	359 (21%)	162 (21%)	64 (23%)	374 (20%)
	Middle	346 (20%)	168 (22%)	53 (19%)	362 (20%)
	High	343 (20%)	154 (20%)	48 (18%)	355 (20%)
	Highest	343 (20%)	168 (22%)	50 (18%)	360 (20%)

[1] BMI=body mass index, Hb=haemoglobin, FMI=fat mass index; FFMI=fat-free mass index; MUAC=mid-upper arm circumference; IQR=interquartile range; LNS-VM=treatment group given lipid-based nutritional supplement with added vitamins and minerals; SD=standard deviation; TB=tuberculosis.

*different from the full cohort, P<0.05

Table 2. Mean (standard deviation) of grip strength with sociodemographic variables and treatment group at each time point and for change in grip strength[1]

		Recruitment		12 weeks ART		2-3 years ART		Change 12 weeks-recruitment	
Variable		**Mean (SD) kg**	**N**	**Mean (SD) kg**	**N**	**Mean (SD) kg**	**N**	**Mean (SD) kg**	**N**
Site	Zambia	19.9 (6.8)	1058	23.1 (6.6)	496		0	2.7 (6.5)	472
	Tanzania	19.5 (6.8)	684	23.6 (7.5)	282	25 (8.2)	273	3.1 (5.5)	277
Treatment group	LNS	19.5 (6.6)	858	22.8 (7.0)	370	25.1 (8.6)	128	2.6 (6.1)	354
	LMS-VM	20.0 (6.9)	884	23.7 (6.9)	408	24.9 (7.8)	145	3.0 (6.2)	395
Sex[2]	women	16.6 (5.1)	860	20.3 (5.5)	406	20.9 (5.2)	178	2.8 (5.3)	388
	men	22.8 (6.8)	882	26.5 (6.9)	372	32.6 (7.5)	95	2.9 (7.0)	361
Age (years) [3]	18-29	18.2 (6.5)	440	22.7 (7.4)	172	23.8 (7.4)	26	3.3 (6.6)	164
	30-39	20.7 (7.0)	760	24.2 (6.9)	327	26.2 (8.3)	96	3.3 (6.4)	316
	40-49	20.1 (6.4)	394	23.3 (6.6)	207	25.0 (8.6)	101	2.5 (5.7)	199
	≥ 50	18.7 (6.2)	148	20.4 (5.9)	72	23.1 (7.2)	50	1.0 (5.1)	70
Socioeconomic quintiles[4]	Lowest	19.1 (6.8)	351	23.1 (7.0)	126	24.6 (9.5)	58	3.7 (5.8)	122
	Low	20.1 (6.4)	359	23.1 (6.8)	162	24.7 (8.0)	64	2.1 (5.9)	155
	Middle	19.6 (6.5)	346	22.9 (6.9)	168	25.4 (8.7)	53	3.5 (6.7)	164
	High	19.6 (7.4)	343	23.6 (7.2)	154	25.5 (7.5)	48	3.2 (6.1)	148
	Highest	20.4 (6.8)	343	23.5 (6.9)	168	24.8 (7.2)	50	1.9 (6.1)	160

[1] ART=antiretroviral therapy, LNS=lipid-based nutritional supplement, LNS-VM=lipid-based nutritional supplement with added vitamins and minerals

[2] Men had greater grip strength than women at all time points (P<0.001) but there was no significant sex difference (P=0.85) in change from recruitment to 12 weeks; Tanzanian women measured at all three times (n=125) had mean 17.6 (SD 5.4) kg at recruitment, mean 20.1 (SD 5.0) kg at 12 weeks ART and mean 21.6 (SD 5.3) kg at 2-3 years ART; Tanzanian men measured at all three time points (n=60) had mean 25.2 (SD 5.9) kg at recruitment, mean 29.1 (SD 7.0) kg at 12 weeks ART and mean 32.6 (SD 7.5) kg at 2-3 years ART.

[3] Age was associated with grip strength p<0.001 at recruitment and 12 weeks, p=0.13 at 2-3 years, and change in grip strength p=0.02.

[4] Socio economic status at recruitment

Table 3. Factors affecting grip strength (kg) at referral for antiretroviral therapy, stratified by sex [1, 2]

Variable		Mean (SD) or N (%)	Adjusted for age and height		Model 1[3]		Model 2[4]	
			Coefficient (95% CI)	P	Coefficient (95% CI)	P	Coefficient (95% CI)	P
Women, (N=860)								
BMI (kg/m^2)		16.4 (1.4)	1.10 (0.87, 1.33)	<0.001	-		-0.08 (-0.64, 0.47)	0.77
MUAC (cm)		21.2 (2.1)	0.96 (0.81, 1.11)	<0.001	-		0.54 (0.28, 0.79)	<0.001
Waist circumference (cm)		65.0 (4.8)	0.16 (0.09, 0.23)	<0.001	-		0.02 (-0.07, 0.11)	0.59
Hip circumference (cm)		79.4 (4.4)	0.28 (0.19, 0.36)	<0.001	-		-0.04 (-0.16, 0.07)	0.47
Calf circumference (cm)		28.0 (2.1)	0.75 (0.58, 0.92)	<0.001	-		0.30 (0.06, 0.54)	0.01
FMI (kg/m^2)		3.0 (0.7)	1.45 (1.00, 1.90)	<0.001	-0.41 (-0.90, 0.09)	0.11	-	
FFMI (kg/m^2)		13.6 (0.7)	2.09 (1.65, 2.53)	<0.001	2.01 (1.52, 2.51)	<0.001	-	
Haemoglobin (g/L)		93 (22)	0.05 (0.03, 0.06)	<0.001	0.04 (0.02, 0.05)	<0.001	0.02 (0.005, 0.04)	0.01
CD4 count N (%)	>=200 cells/μl	242 (28%)	Reference	0.005	Reference	0.38	Reference	0.22
	100-199 cells/μl	251 (29%)	-0.86 (-1.76, 0.03)		-0.22 (-1.03, 0.58)		-0.22 (-1.02, 0.59)	
	50-99 cells/μl	162 (19%)	-0.89 (-1.89, 0.11)		-0.10 (-1.01, 0.58)		-0.16 (-1.08, 0.75)	
	<50 cells/μl	205 (24%)	-1.74 (-2.68, -0.80)		-0.73 (-1.61, 0.14)		-0.89 (-1.76, -0.008)	
CRP N (%)	<10 mg/L	162 (19%)	Reference	<0.001	Reference	0.004	Reference	0.01
	10-50 mg/L	220 (26%)	-0.96 (-1.88, -0.03)		-0.45 (-1.31, 0.42)		-0.23 (-1.08, 0.63)	
	50-160 mg/L	216 (26%)	-2.53 (-3.45, -1.60)		-1.14 (-2.02, -0.25)		-0.88 (-1.77, 0.01)	
	>160 mg/L	174 (21%)	-2.82 (-3.79, -1.84)		-1.65 (-2.61, -0.70)		-1.46 (-2.42, -0.49)	

SBP (mmHg)	96 (13)	0.10 (0.07, 0.13)	<0.001	0.06 (0.03, 0.09)	<0.001	0.06 (0.03, 0.08)	<0.001
On TB treatment, N (%)	119 (14%)	-2.23 (-3.21, -1.25)	<0.001	-2.04 (-2.95, -1.13)	<0.001	-1.39 (-2.31, -0.47)	0.003
With oedema, N (%)	29 (3%)	-4.98 (-6.83, -3.13)	<0.001	-4.90 (-6.65 (-3.15)	<0.001	-3.51 (-5.23, -1.79)	<0.001
Men (N=882)							
BMI (kg/m^2)	16.5 (1.3)	1.74 (1.42, 2.06)	<0.001	-		-0.58 (-1.21, 0.06)	0.08
MUAC (cm)	21.4 (2.1)	1.67 (1.48, 1.86)	<0.001	-		1.39 (1.08, 1.69)	<0.001
Waist circumference (cm)	67.7 (4.2)	0.29 (0.18, 0.40)	<0.001	-		0.03 (-0.09, 0.16)	0.61
Hip circumference (cm)	79.0 (4.0)	0.59 (0.46, 0.71)	<0.001	-		0.14 (-0.02, 0.30)	0.09
Calf circumference (cm)	28.9 (2.2)	0.93 (0.72, 1.15)	<0.001	-		0.29 (0.03, 0.54)	0.03
FMI (kg/m^2)	2.2 (0.6)	2.73 (2.01, 3.44)	<0.001	0.75 (-0.02, 1.51)	0.06	-	
FFMI (kg/m^2)	14.6 (0.7)	1.92 (1.33, 2.51)	<0.001	1.67 (1.05, 2.30)	<0.001	-	
Haemoglobin (g/L)	99 (24)	0.08 (0.06, 0.10)	<0.001	0.07 (0.05, 0.09)	<0.001	0.04 (0.02, 0.06)	<0.001
CD4 count N (%) >=200 cells/μl	231 (26%)	Reference	0.04	Reference	0.33	Reference	0.36
100-199 cells/μl	260 (29%)	-0.65 (-1.83, 0.54)		0.37 (-0.72, 1.45)		0.07 (-0.96, 1.11)	
50-99 cells/μl	170 (19%)	-1.77 (-3.10, -0.45)		-0.75 (-1.98, 0.48)		-0.83 (-2.00, 0.34)	
<50 cells/μl	221 (25%)	-1.36 (-2.60, -0.12)		-0.17 (-1.34, 0.99)		-0.52 (-1.63, 0.59)	
CRP N (%) <10 mg/L	122 (14%)	Reference	0.001	Reference	0.48	Reference	0.92
10-50 mg/L	213 (25%)	-0.93 (-2.40, 0.54)		-0.23 (-1.59, 1.12)		-0.11 (-1.38, 1.17)	
50-160 mg/L	254 (30%)	-2.38 (-3.82, -0.94)		-0.82 (-2.18, 0.54)		-0.35 (-1.65, 0.94)	
>160 mg/L	269 (31%)	-2.44 (-3.86, -1.01)		-0.85 (-2.23, 0.52)		-0.06 (-1.36, 1.25)	
SBP (mmHg)	98 (13)	0.13 (0.09, 0.16)	<0.001	0.06 (0.02, 0.09)	0.002	0.02 (-0.01, 0.06)	0.10

On TB treatment, N (%)	174 (20%)	-2.22 (-3.33, -1.12)	<0.001	-1.65 (-2.69, -0.62)	0.002	-0.44 (-1.44, 0.56)	0.39
With oedema, N (%)	35 (4%)	-5.11 (-7.36, -2.87)	<0.001	-4.22 (-6.33, -2.11)	<0.001	-1.84 (-3.85, 0.16)	0.07

[1] ART=antiretroviral therapy, BMI=body mass index, CI=confidence interval, CRP=C-reactive protein, FMI=fat mass index, FFMI=fat-free mass index, MUAC=mid-upper arm circumference, IQR=interquartile range, SBP=systolic blood pressure, SD=standard deviation, TB=tuberculosis.

[2] Missing data at referral for which values were imputed: 12 MUAC, 14 waist, hip and calf circumferences, 336 body composition, 139 haemoglobin, 7 SBP, 52 CRP

[3] Model 1 is adjusted for age, height, site, trial arm, SES, haemoglobin, CD4 count, CRP, tuberculosis treatment, SBP, oedema, and body composition variables FMI and FFMI

[4] Model 2 is adjusted for age, height, site, trial arm, SES, haemoglobin, CD4 count, CRP, tuberculosis treatment, SBP, oedema, and anthropometric variables, BMI, MUAC, waist, hip and calf circumferences

Table 4. Factors affecting grip strength (kg) 12 weeks after starting antiretroviral therapy, stratified by sex [1, 2]

Variable	Mean (SD) or N (%)	Adjusted for age and height		Model 1[3]		Model 2[4]	
		Coefficient (95% CI)	P	Coefficient (95% CI)	P	Coefficient (95% CI)	P
Women, (N=406)							
BMI (kg/m^2)	18.6 (1.9)	0.51 (0.23, 0.79)	<0.001	-		-0.57 (-1.33, 0.18)	0.14
MUAC (cm)	23.6 (2.2)	0.63(0.40, 0.87)	<0.001	-		0.61 (0.23, 0.99)	0.002
Waist circumference (cm)	70.7 (5.5)	0.06 (-0.04, 0.16)	0.25	-		-0.11 (-0.27, 0.06)	0.22
Hip circumference (cm)	84.5 (5.1)	0.25 (0.14, 0.35)	<0.001	-		0.16 (-0.03, 0.35)	0.09
Calf circumference (cm)	29.7 (2.2)	0.53 (0.29, 0.78)	<0.001	-		0.37 (-0.003, 0.75)	0.05
FMI (kg/m^2)	4.1 (1.0)	0.61 (0.11, 1.11)	0.02	-0.48 (-1.20, 0.24)	0.19	-	
FFMI (kg/m^2)	14.5 (0.9)	1.12 (0.56, 1.68)	<0.001	1.38 (0.56, 2.20)	0.001	-	
Haemoglobin (g/L)	111 (16)	0.04 (-0.01, 0.10)	0.12	0.06 (-0.002, 0.12)	0.06	0.05 (-0.005, 0.10)	0.08
CD4 count N (%) >=200 cells/μl	126 (31%)	Reference	0.60	Reference	0.52	Reference	0.79
100-199 cells/μl	123 (30%)	-0.79 (-2.10, 0.52)		-0.93 (-2.21, 0.35)		-0.62 (-1.89, 0.66)	
50-99 cells/μl	73 (18%)	-0.45 (-2.42, 1.52)		-0.70, (-2.65, 1.24)		-0.30 (-2.19, 1.58)	
<50 cells/μl	84 (21%)	-1.33 (-4.75, 2.10)		-0.99 (-4.39, 2.41)		-0.85 (-4.15, 2.46)	
CRP N (%)[6] <10 mg/L	88 (24%)	Reference	0.22	Reference	0.68	Reference	0.98

10-50 mg/L	151 (41%)	-1.11 (-2.51, 0.30)		-0.51 (-2.00, 0.98)		-0.29 (-1.78, 1.20)	
50-160 mg/L	79 (21%)	-1.21 (-2.80, 0.38)		-0.71 (-2.36, 0.94)		-0.12 (-1.78, 1.55)	
>160 mg/L	53 (14%)	-1.76 (-3.58, 0.06)		-1.22 (-3.28, 0.84)		-0.02 (-2.10, 2.06)	
SBP (mmHg)	99 (13)	0.08 (0.03, 0.13)	0.001	0.06 (0.01, 0.11)	0.02	0.06 (0.01, 0.11)	0.02
On TB treatment[7], N (%)	100 (25%)	-1.34 (-2.56, -0.12)	0.03	-1.36 (-2.57, -0.14)	0.03	-0.95 (-2.16, 0.26)	0.32
Men (N=372)							
BMI (kg/m^2)	18.3 (1.8)	1.22 (0.85, 1.59)	<0.001	-		0.32 (-0.61, 1.25)	0.50
MUAC (cm)	23.6 (2.2)	1.28 (0.98, 1.57)	<0.001	-		0.86 (0.33, 1.40)	0.002
Waist circumference (cm)	73.0 (4.9)	0.24 (0.10, 0.38)	0.001	-		-0.21 (-0.44, 0.02)	0.07
Hip circumference (cm)	83.6 (4.9)	0.46 (0.30, 0.61)	<0.001	-		-0.05 (-0.32, 0.22)	0.71
Calf circumference (cm)	30.6 (2.3)	0.76 (0.46, 1.07)	<0.001	-		0.11 (-0.32, 0.53)	0.62
FMI (kg/m^2)	3.2 (0.9)	1.56 (0.82, 2.30)	<0.001	-1.58 (-2.57, -0.41)	0.002	-	
FFMI (kg/m^2)	15.3 (1.0)	2.37 (1.72, 3.02)	<0.001	2.31 (1.45, 3.16)	<0.001	-	
Haemoglobin (g/L)	123 (21)	0.05 (0.005, 0.10)	0.03	0.11 (0.06, 0.16)	<0.001	0.07 (0.01, 0.12)	0.01
CD4 count N (%) >=200 cells/μl	114 (31%)	Reference	0.25	Reference	0.08	Reference	0.09
100-199 cells/μl	110 (30%)	-0.93 (-2.57, 0.72)		-0.55 (-2.05, 0.95)		-0.66 (-2.09, 0.78)	
50-99 cells/μl	75 (20%)	2.26 (-1.03, 5.56)		2.34 (-0.46, 5.14)		2.11 (-0.70, 4.92)	
<50 cells/μl	73 (20%)	1.49 (-3.08, 6.07)		4.10 (-0.69, 8.89)		3.76 (-0.60, 8.12)	
CRP N (%)[6] <10 mg/L	62 (20%)	Reference	0.004	Reference	0.31	Reference	0.28
10-50 mg/L	122 (38%)	2.87 (0.81, 4.93)		1.33 (-0.57, 3.24)		1.81 (-0.15, 3.76)	

50-160 mg/L	88 (28%)	0.44 (-1.75, 2.64)		-0.21 (-2.16, 1.75)		0.81 (-1.29, 2.91)	
>160 mg/L	46 (14%)	-0.38 (-2.89, 2.13)		-0.52 (-3.51, 2.47)		0.33 (-2.42, 3.08)	
SBP (mmHg)	102 (12)	0.10 (0.03, 0.17)	0.005	0.04 (-0.02, 0.11)	0.18	0.03 (-0.03, 0.10)	0.30
On TB treatment, [7] N (%)	123 (33%)	-2.09 (-3.55, -0.62)	0.005	-2.01 (-3.37, -0.65)	0.004	-1.32 (-2.70, 0.05)	0.06

[1] ART=antiretroviral therapy, BMI=body mass index, CI=confidence interval, CRP=C-reactive protein, FMI=fat mass index, FFMI=fat-free mass index, MUAC=mid-upper arm circumference, IQR=interquartile range, SBP=systolic blood pressure, SD=standard deviation, TB=tuberculosis.

[2] Missing data at 12 weeks after starting ART for which values were imputed: 8 MUAC, 7 hip, 6 waist, and calf circumferences, 33 body composition, 378 hemoglobin, 237 systolic blood pressure, 48 CD4 count, 89 CRP (measured at 6 weeks after starting ART)

[3] Model 1 is adjusted for age, height, site, trial arm, SES, haemoglobin, CD4 count, CRP, tuberculosis treatment, SBP, oedema, and body composition variables FMI, and FFMI

[4] Model 2 is adjusted for age, height, site, trial arm, SES, haemoglobin, CD4 count, CRP, tuberculosis treatment, SBP, oedema, and anthropometric variables BMI, MUAC, waist, hip and calf circumferences

[5] Median and interquartile range for CD4; regressions used square root transformed data

[6] CRP data is from week 6 after starting ART

[7] Patient on anti-tuberculosis treatment prior to starting ART

Table 5. Factors affecting grip strength (kg) 2-3 years after starting antiretroviral therapy, stratified by sex [1, 2]

Variable		Mean (SD) or N (%)	Adjusted for age and height		Model 1[3]		Model 2[4]	
			Coefficient (95% CI)	P	Coefficient (95% CI)	P	Coefficient (95% CI)	P
Women, N=178								
BMI (kg/m^2)		20.2 (3.1)	0.14 (-0.1, 0.4)	0.21			-0.26 (-1.1, 0.6)	0.56
MUAC (cm)		25.3 (2.9)	0.33 (0.1, 0.6)	0.007			0.83 (0.3, 1.3)	0.001
Waist circumference (cm)		76.3 (8.1)	0.01 (-0.1, 0.1)	0.83			-0.01(-0.19, 0.17)	0.91
Hip circumference (cm)		89.7 (7.5)	0.04 (-0.1, 0.1)	0.41			-0.15 (-0.4, 0.1)	0.19
Calf circumference (cm)		30.6 (3.8)	0.15(-0.04, 0.3)	0.12			-0.02 (-0.26, 0.23)	0.90
FMI (kg/m^2)		5.2 (1.9)	0.13 (-0.2, 0.5)	0.48	-0.71(-1.5, 0.05)	0.07		
FFMI (kg/m^2)		15.0 (1.3)	0.57 (1.1, 3.5)	0.04	1.39 (0.2, 2.6)	0.02		
CRP N (%)	<10 mg/L	119 (66.9)	Reference	0.01	Reference	0.06	Reference	0.02
	10-50 mg/L	52 (29.2)	-1.56 (-3.1, -0.04)		-1.25 (-2.8, 0.3)		-1.38 (-2.9, 0.1)	
	50-160 mg/L	6 (3.4)	2.17 (-1.6, 6.0)		2.1 (-1.7, 5.9)		1.56 (-2.2, 5.4)	
	>160 mg/L	1 (0.5)	-10.50 (-19.6, 1.4)		-8.8 (-18.0, 0.4)		-11.9 (-20.8, -2.9)	
SBP (mmHg)		109 (16.6)	0.05 (0.01, 0.09)	0.02	0.05 (0.01, 0.1)	0.02	0.05 (0.01, 0.09)	0.02
Any TB treatment since baseline, N (%)		48 (27.0)	-0.81 (-2.4, 0.8)	0.31	-0.51 (-2.0, 1.0)	0.51	-0.14 (-1.7, 1.4)	0.86
Pre-diabetes/diabetes, N (%)		37 (20.8)	0.39 (-1.4, 2.1)	0.66	0.56 (-1.2, 2.3)	0.53	0.6 (-1.2, 2.3)	0.52

Men (N=95)								
BMI (kg/m^2)		19.4 (1.9)	1.43 (0.8, 2.1)	<0.0001			1.24 (-0.8, 3.2)	0.22
MUAC (cm)		25.0 (2.2)	1.62 (1.1, 2.2)	<0.0001			1.53 (0.5, 2.6)	0.004
Waist circumference (cm)		75.5 (5.1)	0.29 (0.02, 0.6)	0.04			-0.35 (-0.8, 0.2)	0.17
Hip circumference (cm)		86.4 (5.1)	0.46 (0.2, 0.7)	0.001			0.18 (-0.2, 0.6)	0.37
Calf circumference (cm)		30.9 (2.6)	0.73 (0.2, 1.3)	0.009			0.67 (-1.5, 0.10	0.10
FMI (kg/m^2)[2]		4.2(1.1)	1.96 (0.8, 3.1)	0.001	1.28 (-0.1, 2.7)	0.07		
FFMI (kg/m^2)[2]		15.2 (1.0)	2.28 (1.1, 3.5)	<0.0001	1.10(-0.4, 2.6)	0.15		
CRP N (%)[3]	<10 mg/L	65 (69.1)	Reference	0.58	Reference	0.64	Reference	0.77
	10-50 mg/L	25 (26.6)	-0.01 (-3.1, 3.1)		0.61 (-2.3, 3.6)		0.37 (-2.4, 3.1)	
	50-160 mg/L	3 (3.2)	-1.39 (-9.4, 6.6)		-2.95 (-9.9, 3.9)		-1.78 (-8.7, 5.1)	
	>160 mg/L	1 (1.1)	-9.34 (-22.9, 4.3)		-5.82 (17.8, 6.2)		-5.10 (-17.3, 7.1)	
SBP (mmHg)		117 (34.5)	-0.03 (-0.07, 0.01)	0.13	0.14 (0.02, 0.2)	0.02	-0.003 (-0.04, 0.04)	0.88
Any TB treatment since baseline , N (%)		29 (30.5)	-2.28 (-5.2, 0.7)	0.13	-2.4 (-5.2, 0.3)	0.08	-2.2 (-4.9, 0.4)	0.10
Pre-diabetes/diabetes, N (%)		24 (25.3)	-0.39(-3.5, 2.8)	0.80	0.62 (-2.3, 3.6)	0.67	-0.20 (-3.1, 2.7)	0.89

[1] ART=antiretroviral therapy, BMI=body mass index, CI=confidence interval, CRP=C-reactive protein, FMI=fat mass index, FFMI=fat-free mass index, MUAC=mid-upper arm circumference, IQR=interquartile range, SBP=systolic blood pressure, SD=standard deviation, TB=tuberculosis.

[2] Missing 4 body composition, [3]1 CRP

[3] Model 1 is adjusted for age, height, haemoglobin, CRP, tuberculosis treatment, SBP, oedema, and body composition variables FMI, and FFMI

[4] Model 2 is adjusted for age, height, haemoglobin, CRP, tuberculosis treatment, SBP, oedema, and anthropometric variables BMI, MUAC, waist, hip and calf circumferences

Table 6. Factors measured at recruitment affecting change in grip strength (kg) from recruitment to 12 weeks after starting antiretroviral therapy, controlling for recruitment grip strength and stratified by sex [1, 2]

Variable	Adjusted for age, height and recruitment grip strength		Model 1[3]		Model 2[4]	
	Coefficient (95% CI)	P	Coefficient (95% CI)	P	Coefficient (95% CI)	P
Women, (N=388)						
BMI (kg/m^2)	0.29 (-0.10, 0.68)	0.14	-		0.24 (-0.62, 1.10)	0.58
MUAC (cm)	0.25 (-0.005, 0.50)	0.05	-		0.34 (-0.07, 0.75)	0.10
Waist circumference (cm)	-0.09 (-0.20, 0.01)	0.08	-		-0.23 (-0.36, -0.09)	0.001
Hip circumference (cm)	0.09 (-0.04, 0.21)	0.17	-		0.04 (-0.13, 0.21)	0.64
Calf circumference (cm)	0.19 (-0.07, 0.46)	0.14	-		0.05 (-0.34, 0.43)	0.81
FMI (kg/m^2)	0.10 (-0.58, 0.79)	0.77	-0.30 (-1.10, 0.50)	0.46	-	
FFMI (kg/m^2)	0.92 (0.19, 1.66)	0.01	1.02 (0.14, 1.90)	0.02	-	
Haemoglobin (g/L)	-0.002 (-0.02, 0.02)	0.88	-0.001 (-0.03, 0.02)	0.96	-0.02 (-0.04, 0.01)	0.23
CD4 count N (%) >=200 cells/μl	Reference	0.85	Reference	0.84	Reference	0.51
100-199 cells/μl	-0.31 (-1.51, 0.89)		-0.47 (-1.67, 0.73)		-0.69 (-1.88, 0.50)	
50-99 cells/μl	-0.11 (-1.53, 1.30)		-0.39 (-1.84, 1.05)		-1.12 (-2.50, 0.27)	
<50 cells/μl	-0.57 (-1.91, 0.77)		-0.56 (-1.95, 0.83)		-0.69 (-2.16, 0.79)	
CRP category <10 mg/L	Reference	0.10	Reference	0.12	Reference	0.09
10-50 mg/L	0.57 (-0.65, 1.79)		0.41 (-0.85, 1.66)		0.61 (-0.63, 1.85)	

50-160 mg/L	-1.12 (-2,45, 0.22)		-1.22 (-2.62, 0.17)		-1.12 (-2.50, 0.27)	
>160 mg/L	-0.57 (-2.02, 0.87)		-0.68 (-2.18, 0.81)		-0.97 (-2.17, 0.79)	
SBP (mmHg)	0.01 (-0.03, 0.05)	0.53	0.001 (-0.04, 0.04)	0.98	-0.001 (-0.04, 0.04)	0.97
On TB treatment, N (%)	1.43 (0.14, 2.73)	0.03	1.54 (0.18, 2.89)	0.03	1.98 (0.61, 3.35)	0.005
Oedema at recruitment	-0.18 (-3.08, 2.72)	0.90	-1.53 (-4.54, 1.48)	0.32	-0.64 (-3.59, 2.32)	0.67
<u>Men (N=361)</u>						
BMI (kg/m^2)	0.60 (0.06, 1.13)	0.03	-		0.97 (-0.10, 2.03)	0.08
MUAC (cm)	0.36 (-0.02, 0.74)	0.06	-		-0.19 (-0.73, 0.36)	0.50
Waist circumference (cm)	0.05 (-0.11, 0.21)	0.51	-		-0.12 (-0.33, 0.09)	0.27
Hip circumference (cm)	0.15 (-0.05, 0.34)	0.15	-		-0.10 (-0.36, 0.16)	0.44
Calf circumference (cm)	0.25 (-0.08, 0.58)	0.13	-		0.12 (-0.29, 0.53)	0.57
FMI (kg/m^2)	-0.17 (-1.19, 0.86)	0.75	-1.26 (-2.36, -0.15)	0.03	-	
FFMI (kg/m^2)	1.20 (0.27, 2.14)	0.01	1.69 (0.71, 2.68)	0.001	-	
Haemoglobin (g/L)	0.02 (-0.01, 0.05)	0.26	0.04 (0.003, 0.07)	0.03	0.02 (-0.01, 0.05)	0.23
CD4 count N (%) >=200 cells/μl	Reference	0.15	Reference	0.28	Reference	0.28
100-199 cells/μl	-0.40 (-2.03, 1.23)		-0.37 (-1.97, 1.22)		-0.30 (-1.94, 1.34)	
50-99 cells/μl	1.00 (-0.80, 2.80)		1.02 (-0.77, 2.81)		1.10 (-0.74, 2.94)	
<50 cells/μl	1.48 (-0.34, 3.31)		1.11 (-0.73, 2.94)		1.16 (-0.72, 3.03)	
CRP category <10 mg/L	Reference	0.07	Reference	0.14	Reference	0.12
10-50 mg/L	0.70 (-1.19, 2.58)		0.75 (-1.13, 2.63)		0.41 (-1.49, 2.30)	
50-160 mg/L	-1.33 (-3.21, 0.54)		-0.65 (-2.55, 1.24)		-0.79 (-2.72, 1.15)	

>160 mg/L	-1.17 (-3.06, 0.73)		-1.24 (-3.18, 0.70)		-1.66 (-3.66, 0.33)	
SBP (mmHg)	0.05 (-0.002, 0.10)	0.06	0.02 (-0.04, 0.07)	0.58	0.02 (-0.04, 0.07)	0.50
On TB treatment, N (%)	-0.65 (-2.14, 0.84)	0.39	-0.19 (-1.65, 1.28)	0.80	-0.18 (-1.71, 1.35)	0.82
Oedema at recruitment	-5.81 (-10.06, -1.56)	0.008	-5.95 (-10.24, -1.67)	0.007	-5.13 (-9.39, -0.87)	0.02

[1] ART=antiretroviral therapy, BMI=body mass index, CI=confidence interval, CRP=C-reactive protein, FMI=fat mass index, FFMI=fat-free mass index, MUAC=mid-upper arm circumference, IQR=interquartile range, SBP=systolic blood pressure, SD=standard deviation, TB=tuberculosis.

[2] Missing data at referral for which values were imputed: 6 MUAC, 6 waist, hip and calf circumferences, 101 body composition, 72 hemoglobin, 2 systolic blood pressure, 20 CRP

[3] Model 1 is adjusted for age, height, site, trial arm, SES, recruitment grip strength, haemoglobin, CD4 count, CRP, tuberculosis treatment, SBP, oedema, and body composition variables FMI, and FFMI

[4] Model 2 is adjusted for age, height, site, trial arm, SES, recruitment grip strength, haemoglobin, CD4 count, CRP, tuberculosis treatment, SBP, oedema, and anthropometric variables BMI, MUAC, waist, hip and calf circumferences