Impact of nutritional supplementation on immune response, body mass index and bioimpedance in HIV-positive patients starting antiretroviral therapy (NuStART)

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CNHR Creative and Novel Ideas in HIV Research
CRNU Thembalethu
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Background

- Challenges to HIV care in resource limited settings (RLS) include amongst others, significant malnutrition.
- HIV-positive patients often present late for care and are already affected by malnutrition.
- Studies have shown a strong correlation between poor nutritional status and clinical progression of HIV.
- FutureLife-Porridge® has been used in decentralized HIV programmes in South Africa.
- Limited evidence supports the benefit of nutritional supplementation when starting antiretroviral therapy (ART) in RLS.

We investigate the effect of a nutritional supplement (NS), taken concurrently with ART for six months, on body mass index, bioelectrical impedance and laboratory and biochemical markers

Methods (1)

- **Study site and subjects**
  - Randomized controlled pilot study
  - Themba Lethu HIV Clinic at the Helen Joseph Hospital
  - Between May 2010 – November 2011

- **Inclusion criteria**
  - HIV-positive ART-naive adults
  - Self-reported **unintentional weight loss** in last 3 months – defined as a drop in dress size or loss of 5-10% of normal body weight
  - Initiating ART according to SA DoH ART treatment guidelines
- **Exclusion criteria**
  - Pregnant women
  - Allergy to soya or iodine
  - Participating in any other supplemental feeding program

Ethics approval from University of the Witwatersrand (HREC M090802)

Methods (2)

Screened (eligibility criteria)

Initiated on ART at TLC

Randomized (1:1)

ART + NS

Control (ART)

100g = 388 kCal/day of FutureLife-Porridge® for 6 months

HIV care and treatment according to the SA Department of Health (DoH) ART treatment guidelines

Monthly assessments[&]

Weight	Physical activity	Bioimpedance
Height	- pedometer	- FFM
Blood pressure	- PA score	- TBW
Temperature	Food Frequency	- ICW
	- FFQ	- ECW
	- 5 day recall diary	- % fat

Blood samples at 0 and 6 months

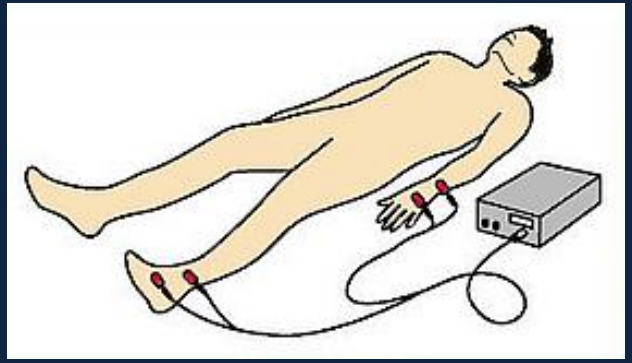
CD4 count*	ALT
Hemoglobin	albumin
MCV	iron
	ferritin
	magnesium
	selenium

*TherapyEdge-HIV™

[&]Questionnaire - adherence to ART, compliance to study protocol, tolerability

Methods (3)

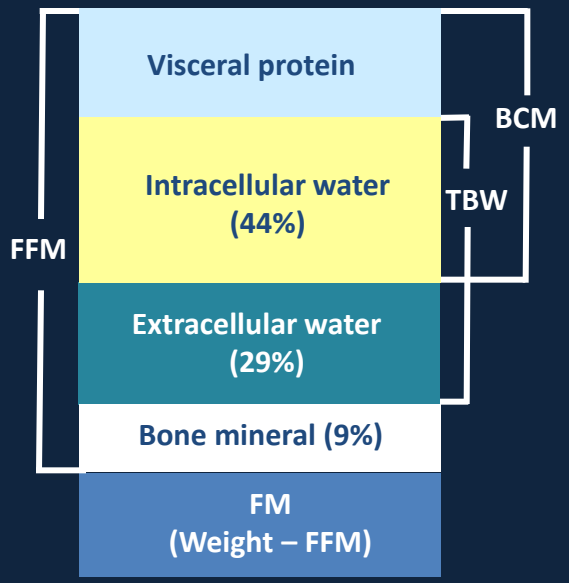
- **Bioelectrical impedance**
  - Performed using a RJL Quantum X analyzer
  - Commonly used method to estimate changes in body composition
  - Inexpensive, non-invasive, portable and can be performed on HIV-positive patients



Small current applied (50 kHz) to the body via surface electrodes – a drop in voltage occurs as the current encounters resistance in fluids and tissues

- **Resistance** – electrolyte containing total body water (ohms Ω)
- **Reactance** – condenser like properties of body cells

Fat Free Mass (FFM)	Everything that is not body fat
Lean dry mass (LDM)	Non-water portion of FFM (FFM – TBW)
Total body water (TBW)	ICW (within body cells) + ECW (outside body cells)
Body cell mass (BCM)	Protein rich compartment – loss of BCM is associated with poor clinical outcomes
Basal metabolic rate (BMR)	Number of calories a person will use per day
Phase angle	Membrane potential/cellular integrity (i.e. nourished "plump" cell = large phase angle)



Methods (4)

- **Outcomes**

Primary outcome: % increase in CD4 count, BMI, Hb, biochemistry and body composition at 6 and 12 months

Secondary outcomes:

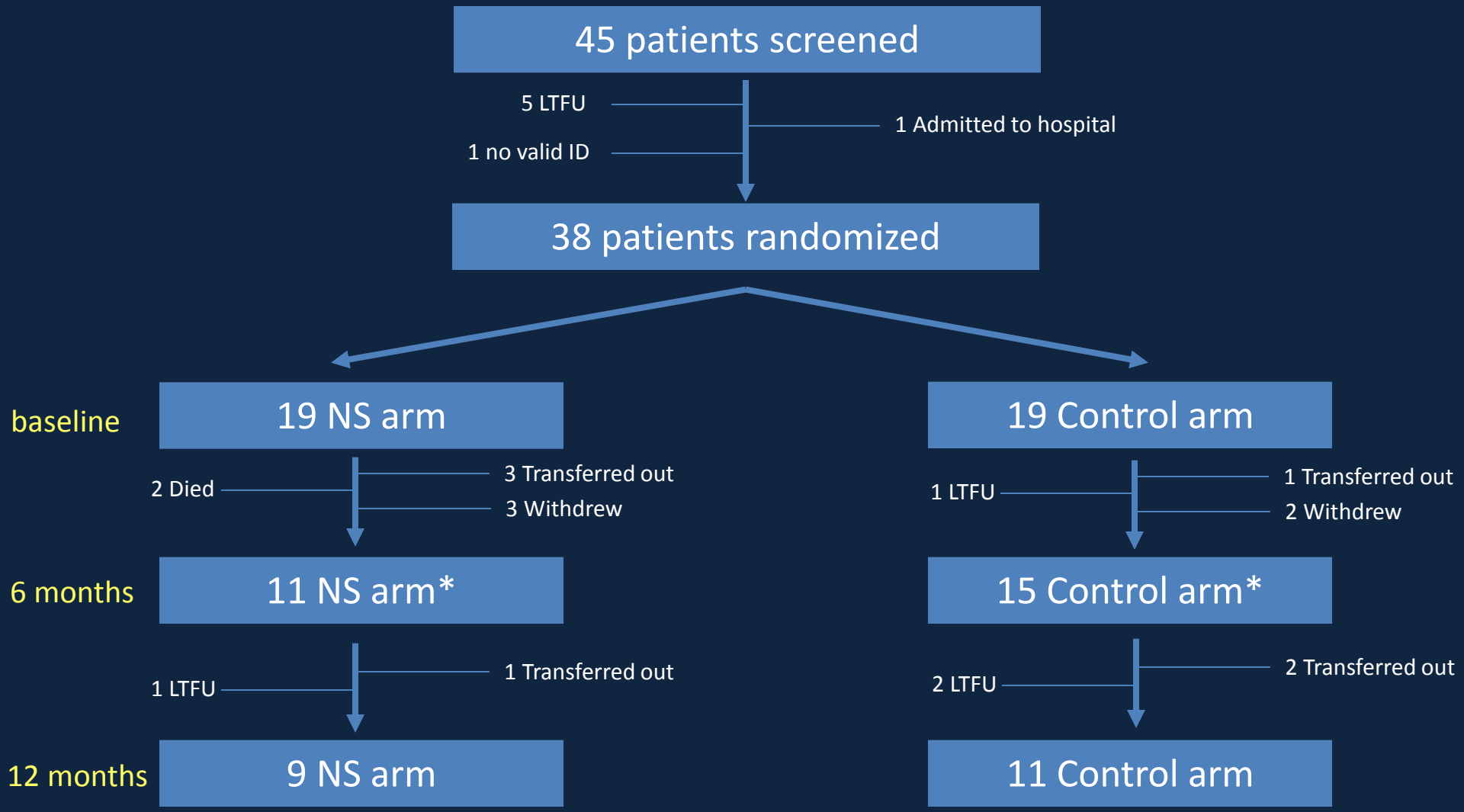
(i) any improvement in physical activity

(ii) any improvement in adherence to ART

(iii) % increase in CD4 count, BMI, hb, biochemistry and bioelectrical impedance, stratified by immune status at baseline (<100 vs. ≥100 cells/mm^3)

- **Statistical analysis**
  - Patient demographics and clinical characteristics at ART initiation (baseline) were summarized using proportions (n, %) or medians (IQR)
  - % change from ART initiation until 6 months follow-up were compared, by treatment arm, using paired T-test or Wilcoxon rank sum test for continuous data
  - Analysis were also adjusted for baseline CD4 cell count, hb, viral load, sex and age using repeated-measures analysis of variance (rANOVA)

Results (n=45)



*Time on ART (median days, IQR): died/LTFU 28 days (IQR 27 – 29); transferred out 63 days (IQR 23 – 119); withdrew of 135 days (IQR 84 – 140)

Results (n=38)

Characteristics		NS (n = 19)	Control (n = 19)	p value
Gender – Male	n,%	6 (31.6%)	7 (36.8%)	0.732
Age (years)	Median (IQR)	**37 (32 – 42)**	34 (30 – 43)	0.612
Employed	n,%	14 (73.7%)	11 (57.9%)	0.456
Education (≥ Grade 8)	n,%	17 (89.5%)	18 (94.7%)	0.222
Self-reported weight loss (kg)	Median (IQR)	5 (3 – 5)	5 (2 – 9)	0.094
Body mass index (BMI; kg/m^2) Fat (kg)	Median (IQR) Median (IQR)	20.4 (18.0 – 22.4) 10.6 (10.0 – 17.7)	19.3 (18.4 – 21.3) 11.1 (5.5 – 15.5)	0.197 0.560
Systolic blood pressure (mmHg) Diastolic blood pressure (mmHg)	Median (IQR) Median (IQR)	104 (90 – 125) 69 (46 – 76)	111 (107 – 127) 71 (66 – 84)	0.079 0.209
WHO stage III/IV	n,%	4/12 (33.3%)	7/16 (43.8%)	0.611
ART regimen (TDF/3TC/EFV)	n,%	14 (73.7%)	14 (73.7%)	1.000
CD4 cells/mm^3	Median (IQR)	**60 (12 – 105)**	107 (63 – 165)	0.149
Hemoglobin (g/dL) <10g/dL	Median (IQR) n,%	**10.3 (9.0 – 11.3)** **9 (47.4%)**	**13.1 (11.1 – 14.7)** **1 (5.3%)**	**0.001** **0.009**
Viral load (log10)	Median (IQR)	**5.4 (4.7 – 5.8)**	**5.6 (5.4 – 6.0)**	**0.042**
Mean cell volume (fL)	Median (IQR)	**85.0 (78.4 – 98.9)**	91.3 (84.0 – 94.8)	0.090

Results (n=38)

Characteristics		Completers (n=26)	Non-completers (n=12)	p value
Gender – Male	n,%	8 (30.8%)	5 (41.7%)	0.510
Age (years)	Median (IQR)	37 (32 – 42)	35 (32 – 43)	0.505
Employed	n,%	15 (57.7%)	10 (83.3%)	0.122
Education (≥ Grade 8)	n,%	24 (92.3%)	11 (91.7%)	0.114
Self-reported weight loss (kg)	Median (IQR)	5 (3 – 8)	5 (4 – 7)	0.356
Body mass index (BMI; kg/m^2) Fat (kg)	Median (IQR) Median (IQR)	20.2 (17.6 – 21.7) 11.1 (9.1 – 15.9)	19.7 (18.0 – 21.7) 10.5 (8.6 – 12.0)	0.842 0.791
Systolic blood pressure (mmHg) Diastolic blood pressure (mmHg)	Median (IQR) Median (IQR)	111 (102 – 127) 71 (66 – 87)	107 (95 – 120) 68 (56 – 75)	0.354 0.209
WHO stage III/IV	n,%	7/19 (36.8%)	4/9 (44.4%)	0.966
ART regimen (TDF/3TC/EFV)	**n,%**	**22 (84.6%)**	**6 (50.0%)**	**0.031**
CD4 cells/mm^3	Median (IQR)	86 (24 – 125)	99 (70 – 121)	0.405
Hemoglobin (g/dL) <10g/dL	Median (IQR) n,%	11.6 (10.3 – 13.6) 5 (19.2%)	11.0 (9.4 – 12.6) 5 (41.7%)	0.294 0.144
Viral load (log10)	Median (IQR)	5.5 (4.7 – 5.8)	5.2 (4.9 – 5.6)	0.851
Mean cell volume (fL)	Median (IQR)	90.1 (81.5 – 94.6)	83.2 (78.3 – 88.0)	0.096

Results - % change

From baseline to 6 months	NS	Control	P value
Body mass index	7.8	5.5	0.007
CD4 count	83.0	46.4	0.002
Hemoglobin	9.5	1.0	0.026
Fat Free Mass (FFM)	16.7	-3.5	0.036
Total Body Water (TBW)	13.0	-1.9	0.026
Intracellular Water (ICW)	16.1	-4.1	0.010
Phase angle	25.9	-1.5	0.063
Basal metabolic rate	5.3	-0.2	0.014
Ferritin	-90.3	-48.9	0.045

- NS patients increased CD4 count by 151cells/mm^3 vs. 77cells/mm^3 in the Controls (p=0.024)
- NS patients showed an improvement in physical activity compared to Controls (p=0.037)

From 6 to 12 months	NS	Control	P value
Body mass index	4.2	0.2	0.046
CD4 count	41.6	31.5	0.309

Conclusion

- We demonstrate that nutritional supplementation improves nutritional parameters (BMI, FFM, BMR) and immune function and promotes weight gain in HIV-positive patients that present at ART initiation with weight loss.
- Greatest gain in CD4 count and improvement in physical activity was observed in patients in the NS arm with a CD4 < 100cells/mm^3 at study entry.
- Additional benefits of nutritional supplementation include reversing malnutrition, reducing inflammation and improving physical activity, thereby improving quality of life and ultimately reducing HIV-associated complications.
- Larger studies with long-term follow-up are necessary to validate these data – protocol development

Acknowledgments

HE²RO/CHRU – WITS Health Consortium

Nicola Baines

Denise Evans

Mhairi Maskew

Lynne McNamara

Ian Sanne

Katerina Selibas

Desiree van Amsterdam

Tracey Webster

Right to Care

Patients and staff at CHRU and Themba Lethu Clinic – Helen Joseph Hospital

This presentation was made possible by the generous support of the American people through Cooperative Agreement AID 674-A-12-00029 from the United States Agency for International Development (USAID). The contents are the responsibility of the authors and do not necessarily reflect the views of USAID or the United States Government