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Effectiveness of Macronutrient Supplementation on Nutritional Status and HIV/AIDS Progression: A Systematic Review and Meta-Analysis

Hyejeong Hong, PhD(c), MSN, FNP,

Johns Hopkins University School of Nursing, Department of Community-Public Health, 525 North Wolfe Street, Baltimore, MD, 21205, USA, hhong13@jhu.edu

Chakra Budhathoki, PhD, and

Johns Hopkins University School of Nursing, Department of Acute and Chronic Care, 525 North Wolfe Street, Baltimore, MD, 21205, USA, cbudhat1@jhu.edu

Jason E. Farley, PhD, MPH, ANP-BC, FAAN, AACRN

Johns Hopkins University School of Nursing, Department of Community-Public Health, REACH Initiative, 1909 McElderry Street, SON House, Baltimore, MD, 21205, USA, jfarley1@jhu.edu

Abstract

Background & Aims: Malnutrition is common in Sub-Saharan Africa, weakening the immune function of persons living with HIV infection (PLWH). Being malnourished at the initiation of antiretroviral therapy (ART) leads to higher risk of early mortality and reduced quality of life. Thus, introduction of protein-energy-fortified macronutrient supplements at ART initiation may improve HIV treatment outcomes. This review aimed to evaluate the effectiveness of macronutrient interventions.

Methods: This systematic review and meta-analysis included 15 studies conducted from 2000 to 2015 among Sub-Saharan African adults.

Results: Six randomized controlled trials and 4 retrospective cohort studies provided data eligible for a meta-analysis. Supplementation significantly increased the overall standardized mean difference (SMD) between baseline and follow-up data in weight (SMD=0.382, $p<.001$), BMI (SMD=0.799, $p<.001$); fat-free mass (SMD=0.154, $p=.009$); and CD4 count (SMD=0.428, $p<.001$).

Conclusion: Protein-energy-fortified macronutrient supplementation at ART initiation may positively influence nutritional status and immunologic response in PLWH in Sub-Saharan Africa.

Correspondence to: Hyejeong Hong.

CONFLICT OF INTEREST The authors declare that they have no conflict of interest.

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Keywords

malnutrition; macronutrient; nutritional supplement; HIV; Sub-Saharan Africa

INTRODUCTION

Malnutrition—an insufficiency or unbalance of nutrition [1]—is a significant health issue in persons living with HIV (PLWH) [2, 3]. In resource-limited countries, the availability of food resources to meet daily needs may not be sufficient for PLWH [4]. Since imbalanced distribution of social determinants such as socioeconomic status, local food markets, and transportation options impacts food availability [5–7], this is particularly salient in Sub-Saharan Africa where food insecurity along with many other social determinants of health [4, 8, 9] and co-infections such as *Mycobacterium tuberculosis* complicate the picture [10]. Malnutrition is a result of a deficiency of both macronutrients (nutrients that provide calories or energy, including carbohydrates, proteins, and fat) and micronutrients (vitamins and minerals), vital dietary components necessary for physical and mental development, disease prevention, and well-being [11, 12]. Malnutrition contributes to physiological, psychological, compositional, or functional alterations [13, 14].

HIV-associated wasting—involuntary weight loss greater than 10% of baseline—plus chronic diarrhea or chronic weakness are identified as acquired immunodeficiency syndrome (AIDS)-defining conditions [15]. HIV-associated wasting is specifically characterized as protein-energy malnutrition—the insufficient intake of both protein and energy—and is one of the most common conditions associated with AIDS in resource-limited settings such as Sub-Saharan Africa [16]. Protein-energy malnutrition as a cause of secondary immune deficiency accelerates susceptibility to opportunistic infections in PLWH [17, 18]. Consequently, the nutritional status of the host regulates the outcome of infection, and the co-existence of HIV infection and malnutrition may lead to increased mortality [2, 19–22] as well as lower quality of life (QOL) [23–25]. Therefore, correction of nutritional status for PLWH with protein-energy fortified interventions in Sub-Saharan Africa is necessary not only to reduce mortality but also to improve QOL. Nevertheless, few recommendations exist for healthcare providers to manage nutritional status for PLWH in Sub-Saharan Africa. Recognition of malnutrition in adults and its relation to HIV and AIDS progression as well as clinical implementation of appropriate supplementation are understudied. There is a strong need to improve nutritional status prior to initiation of antiretroviral therapy (ART); however, no clear consensus exists as to whether the introduction of protein-energy fortified macronutrient supplements with ART initiation is more effective for improving both nutritional status and immunologic response compared to ART alone. Thus, the purpose of this meta-analysis was to evaluate the effects of oral macronutrient energy-fortified nutritional interventions on nutritional and immunologic outcomes in adults living with HIV infection in Sub-Saharan Africa.

MATERIALS AND METHODS

The overall process of our systematic review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations [26]. Institutional Review Board approval was not required for this review.

Data Search and Inclusion/Exclusion Criteria

PubMed, Embase, CINAHL, and Cochrane Review were searched using the terms nutritional supplements, nutrition, supplementation, nutritional support, HIV, AIDS, and Sub-Saharan Africa. Reference lists of identified articles and bibliographies of books were also reviewed. Nutritional studies involving adults with HIV/AIDS were included, while those involving pregnant women, children, and non-energy-fortified nutritional interventions (calories less than 100 kcal/day or micronutrient supplementation only) in PLWH were excluded. During the initial search, the search was not limited by year to aid in identification of classic works and was later restricted to the years from 2000 to July 2017 to provide the most current literature. Study inclusion criteria were as follows: (1) participants are HIV-infected adults age 15 years and older based on WHO classification of adults (ages 15–64 years) for an HIV epidemic and also due to higher prevalence of HIV infection among young adults (ages 15–49 years) in Sub-Saharan Africa [3], (2) our study used macronutrient supplements, (3) all study participants had the same chance to receive ART regardless of randomization, and (4) absence of comorbidities except for pulmonary mycobacterium tuberculosis (PTB). Among comorbidities, only PTB patients were accepted for review, while other comorbidities were excluded because comorbidity of PTB is the most common cause of HIV-associated death [7] as an end-stage of AIDS [15]. Even though PTB co-infection may require higher nutritional demand, modifying the effects of oral nutritional supplements on physiological outcomes, it might be impractical to exclude PTB-infected individuals from study samples of primary studies because most countries in Sub-Saharan Africa are PTB-endemic areas [7].

When duplicate reports or studies were removed, the electronic and hand search yielded 281 studies, of which 89 studies were initially screened; 41 studies then met our inclusion criteria. Through a full text review and quality assessment process for the original studies, 26 studies were dropped because of the following: (a) inadequate intervention use such as micronutrient supplementation, total parenteral nutrition, or nutritional education only; (b) non-target populations such as ART-naïve patients only, pregnant women, children, adults with other comorbidities (except for PTB or countries outside Sub-Saharan Africa); and (c) ineligible reported data for a meta-analysis such as small sample size less than 25, and studies published before 2000 (Figure 1).

To increase confidence in the results related to the association between macronutrient intervention and outcomes and also to provide information on whether the intervention was effective [27], a meta-analysis was used where the following eligible data were utilized from randomized controlled trials (RCTs) and cohort studies: (1) baseline and follow-up mean with standard deviation (SD) or confidence intervals (CI)—6 RCTs and 4 retrospective cohort studies met this criteria; or (2) mean differences between baseline and follow-up with a type of significance values such as *p*-values or CI—2 RCTs met this criteria. Although

primary studies collected data and were reported slightly differently in the published works, we utilized their summary data as mean difference, 95% confidence interval, and sample size. Thus, 12 studies were included in the meta-analysis (Table 1). We contacted 13 corresponding authors of the eligible studies with a request to provide summary data; only 1 corresponding author provided requested data, which were included in the meta-analysis. Summary statistics from eligible primary studies were abstracted by the first author and verified by the last author.

Data Quality Assessment

To identify the potential risk of bias of each study, the quality and rigor of the original studies were evaluated using two published quality-rating scales: the Jadad Scale [28] for RCTs and the Newcastle-Ottawa Quality Assessment Scale (NOS) [29] for cohort studies. When published literature was unrepresentative of the population of the conducted studies, a publication bias was assumed to exist [30], possibly distorting the results of data synthesis [31]. Thus, the presence of publication bias in the extracted outcomes was evaluated by Begg's test with funnel plots [32], which are a graphical plot of effect size against sample size or other indicators of the precision of the estimate such as standard error of the treatment effect or inverse variance of the treatment effect (weight) [32]. Asymmetry of the funnel plot indicates possible publication bias [32].

Data Synthesis and Meta-analysis

The studies included in this review were deemed comparable in relevance (research question and closeness in design) as well as for measurement of the same outcome, and were therefore pooled for a summary effect. Due to high risk of bias, studies with quality assessment scores lower than 2 out of 5 from Jadad and 4 out of 9 from NOS were not included in the metaanalysis. For these studies, only a narrative synthesis was included.

The effectiveness of intervention from 6 RCTs out of 8 were statistically measured by overall standardized mean difference (SMD or Cohen's *d*) [33]. The SMD was computed with the following formula: *SMD* = {*new treatment improvement* – *comparator (placebo) improvement*} / *pooled standard deviation*.

We also used 95% confidence interval for the mean difference and sample size with the *metan* command in meta-analysis by STATA 14 software [34]. The presence of heterogeneity of each trial was tested by Q statistics to choose between the fixed effect model and the random effect model and presented by I^2 index.

Descriptive Analysis

Randomized controlled trials—Table 1 shows the study locations, type of interventions, length of interventions, and primary outcomes of the included eight RCTs. Five out of eight studies examined the effects of two different interventions by using a different type of nutritional supplements; four of the studies reported the mean differences between pre- and post-intervention in each intervention group [35–38], and one study reported the mean differences between two different intervention groups [39]. For meta-analysis, unpublished raw data of mean and SD for weight, BMI, FFM, and CD4 count before and after

intervention for both groups were received from the corresponding author [39]. The remaining three RCTs examined the effect of one nutritional intervention and compared outcomes with a control group not introduced to any nutritional supports (referred to as the supplement-free control) among them; two studies reported mean differences between before and after the interventions [40, 41]; one study reported median and interquartile range [42]. Five among eight RCTs used purposive sampling methods recruiting underweight subjects ($\text{BMI} < 18.5\text{kg/m}^2$) [35, 36, 38, 39, 41], and two studies recruited subjects with self-reported, unintended weight loss and underweight who had been referred by healthcare providers or community leaders [37, 42]. No studies provided the theoretical or scientific rationale for determination of the length of intervention as well as for smell, texture, taste, or volumes of supplements.

In terms of methodological quality of the RCTs, Jadad scores ranged from 2 to 5 out of 5. One study did not specify the method of randomization [41], and five did not specify an appropriate method of blinding [35, 36, 40–42]. Attrition rates varied between 3.4% and 19.5% for the majority of studies; however, two studies had substantially higher attrition rates of 34% [39] and 30% [42], indicating the possibility of selection bias; major causes of attrition were death and transfer-out, respectively. Only two trials showed evidence of power of 80% [37] and 90% [42] to determine significance at $\alpha < .05$; six did not have adequate power at the targeted level of 80%, which would suffer from the risk of committing a type II error as a threat to statistically valid conclusions [43].

Retrospective cohort studies—The characteristics of the included seven retrospective cohort studies are summarized in Table 1. Among seven studies, one study had three cohorts, two cohorts with two different interventions, and one of historical supplement-free control cohort [44]; two studies had two cohorts with two different nutritional supplements without supplement-free controls [45, 46]. The remaining four studies had only a single intervention cohort without a supplement-free control cohort [47–50]. One of the single-intervention cohort studies used a mixed methods design to assess the impact of food supplementation services on weight gain and associated factors [50], but only quantitative data were extracted for this review. In addition, one study selected a group of people receiving different nutritional interventions and participants from another nutrition program as a control group [45], but this selection of control group would also threaten the internal validity because of the possible variations in maturation or history [43]. The length of supplementation ranged from at least one month to more than 12 months, while two studies did not specify it [45, 50]. Cohort study methodological qualities quantified by NOS scale ranged from two to six out of nine.

RESULTS

Effects on Nutritional Status and Immunologic Response

We integrated four categories of physiological parameters based on the commonalities from eight RCTs and seven cohort studies as follows: (1) *body size* measured by anthropometric parameters such as body weight, BMI, arm/waist/hip/calf circumferences, triceps/subscapular skinfold; (2) *body composition* measured by bioelectrical impedance such as fat

mass, fat-free mass (FFM), muscle mass, fat area, muscle area, total body water, intracellular water, and extracellular water; (3) *serologic nutritional status* measured by laboratory blood tests such as hemoglobin and serum albumin levels; and (4) *HIV-specific immunologic recovery* measured by CD3, CD4, CD8 cell counts, and HIV viral load.

Common Effects on Underweight Participants

Among RCTs, six studies in which underweighted participants were targeted exclusively (BMI < 18.5kg/m²) had more significant improvement particularly on weight, BMI, FFM, and CD4 measures [35, 36, 38, 39, 41, 42]. Studies that recruited participants regardless of their baseline nutritional status showed no significant differences before and after intervention on weight (5.4kg vs. 5.1kg, $p = .68$), muscle area (−0.4 cm², 95% CI −1.9, 1.2), and CD4 count (154 cells/mm³ vs. 171 cells/mm³, $p = .50$) (Table 1) [37, 40, 45].

Types of Macronutrient-Energy Fortified Supplements

Comparably older studies conducted before 2011 (regardless of year of publication) used micronutrient-dense food rations such as Ready-to-Use Therapeutic Foods (RUTF) and Corn-Soya Blends (CSB) flour that were mainly designed for severe malnutrition, starvation, or nutritional rehabilitation [39, 40, 44, 46, 47]. Several studies designed their own food packages composed of multiple ingredients. Serrano et al. introduced a Family Nutritional Support, which included cereal, legume (dry peas and not containing vegetables) and vegetable oil strengthened with vitamin A [41]. Nagata et al. used a food package consisting of a ration of cereals (rice or corn), pulses, peanuts, sugar, sunflower seed oil, and fortified corn soy blend [48]. Mensah et al. used dry micronutrient dense food rations composed of soy-fortified wheat and vegetable oil [50]. More recent studies published after 2012 used pharmaceutical company-developed high-protein and high-energy supplements including various micronutrients targeting calories ranging from 150 kcal/day to 4600 kJ/day (about 1,104 kcal/day) [36, 38, 42, 49]. Instead of using macro- and micronutrient compounds, use of single food interventions was also attempted by two studies: (1) The effect of *Spirulina Plantensis*, a blue-green algae with a very high-protein content as food supplementation, was examined by comparing it to that of soya bean powder [35]. (2) The effect of (2) probiotic yogurt was examined by comparing it to that of maize flour and beans [45]. There was a significant increase of body weight, hemoglobin level, and viral load after 3-months use of *Spirulina* powder. The change of physiological measures before and after use of probiotic yogurt was not examined because the outcomes were compared with the other intervention cohorts, not with supplement-free control cohorts [45]. However, there was significantly greater mitigation of stomach pain (29%) in the probiotic yogurt consumption cohort than in the counterpart cohort (50%).

Effects on body weight, BMI, FFM, and CD4 count from a meta-analysis

The effectiveness of nutritional supplements on body weight, BMI, FFM, and CD4 were strengthened by a meta-analysis outcome nested within the systematic review that produced pooled supplementation effect estimates. Since the results of weight gain (N = 9: five RCTs and four cohorts), BMI (N = 11: seven RCTs and four cohorts), and CD4 count (N = 9: seven RCTs and two cohorts) appeared statistically heterogeneous ($I^2 = 37.17$, $I^2 = 368.72$, $I^2 = 103.44$, respectively), a random effects model was applied to combine the results in a

more conservative way. Conversely, the fixed effects model was applied to FFM (N = 6: four RCTs and two cohorts) due to homogeneity ($I^2 = 2.11$). Supplementations with protein-energy-based macronutrients significantly increased overall SMD between baseline and follow-up data in all four parameters: (1) body weight: SMD = 0.382; 95% CI = 0.318, 0.445; $p < .001$ (Table 2); (2) BMI: SMD = 0.799; 95% CI = 0.742, 0.855; $p < .001$ (Table 3); (3) FFM: SMD = 0.154; 95% CI = 0.039, 0.270; $p = 0.009$ (Table 4); and (4) CD4 count: SMD = 0.428; 95% CI = 0.353, 0.502; $p < .001$ (Table 5).

Publication bias

Although some visual evidence of publication bias was detected from asymmetric Begg's funnel plot of body weight, BMI, and CD4 count, due to small sample size less than the minimum requirement of 10 literature articles, it was difficult to determine whether publication bias was present [32]. Interestingly, the effect size on the homogeneous variable of FFM was very small while that of heterogeneous variables—weight, BMI, and CD4 count—were comparatively larger. But because weight, BMI, and CD4 count showed possible evidence of publication bias, supporting high heterogeneity, we can assume that the true effect size of weight, BMI, and CD4 count may have varied depending on study settings. For this reason, although the effect size of FFM was considered small, the homogeneity from Q statistics and significant p -values for effect size supported characteristics of its stability, suggesting less publication bias.

DISCUSSION

This study was limited to small trials, each evaluating different macronutrient supplements and the heterogeneity of the patient populations regarding immunologic parameters and stage of disease. Nevertheless, it can be concluded that protein-energy fortified macronutrient supplementation along with ART initiation are effective in improving physiological nutritional status and immune responses in PLWH. Moreover, this study provides statistical evidence of the effectiveness of various types of macronutrient interventions through quantitative data synthesis. According to the results of hypercaloric feeding studies, including the use of appetite stimulants, weight gain was predominantly fat, while anabolic agents such as steroids and resistance training exercise presented increased body cell mass and skeletal muscle mass (term used interchangeably with fat-free mass or lean body mass) [51]. Although only one included study reported increased fat mass [35], it can be hypothesized that improved nutritional status from the use of macronutrient supplements might enhance the level of energy expenditure, allowing individuals to be more physically active. This improvement in physical activity levels would facilitate daily resistance exercise, which would stimulate skeletal muscle mass development, which was confirmed by increased hand-grip strength [36, 37]. Moreover, the improved physical activities derived from nutritional support may also assist not only employment stability and local economies but also participants' quality of life [4, 52].

This study has several strengths. First, in order to avoid selection bias, study selection was based on strict criteria of PRISMA. Second, we conducted an extensive search of the literature with the help of an academic librarian to ensure sensitivity and specificity. Third,

we followed the quality assessment tool (Jadad for RCTs and NOS for retrospective cohort studies) to appraise the included studies so that results could be interpreted in the context of their quality. Finally, we took a conservative approach and conducted a meta-analysis of studies with the least risk of bias.

This review also has several limitations. First, a small number of studies met the inclusion criteria. We attempted to offer a more comprehensive review by expanding our search to also include retrospective cohort studies. Second, inclusion of comorbidity of PTB from six RCTs [35–40] and one cohort study [48] may alter the review findings because HIV/TB co-infection may modify the impact of nutritional interventions [53]. Third, two RCTs did not meet the basic requirements for quality of clinical trials, particularly blinding, but blinding may be difficult to achieve in nutritional intervention studies with counseling or clinical referrals [40, 41]. Finally, because most of studies included in this meta-analysis had no supplement-free control group, it was difficult from this review to distinguish the origin of nutritional and immunologic improvement and impossible to determine whether it was a result of the initiation of nutritional supplements versus ART only. Seven studies without supplement-free controls may have been influenced by a history effect (when treatment effect is not related to nutritional supplement intervention but occurs during the time of the study), affecting the internal validity of the study due to lack of environmental control [43]. However, if the nutritional supplements were utilizable in the study settings, withholding the supplements from patients would be unethical.

As mentioned, only three RCTs had control groups receiving ART only without nutritional support, but the conclusions diverged. Among them, two RCTs showed that there were no significant mean differences in body weight, BMI, or CD4 count [40, 41]. On the other hand, one pilot RCT reported that the intervention group that received porridge-type macronutrient supplements for six months showed a significantly higher mean percentage change in weight, BMI, and FFM than control groups that received ART only [42]. This pilot trial, however, had a very small sample size (11 subjects from the intervention group vs. 15 subjects from the control group), which limited the ability to determine the unilateral effectiveness of macronutrient supplementation because previous studies supported that highly active antiretroviral therapy (aka HAART: The standard treatment consists of a combination of at least three antiretroviral drugs) decreased the incidence and prevalence of malnutrition in HIV-infected adults, although body fat distribution and metabolism could be altered [54]. To evaluate what type of supplements were more effective on nutritional status and immunologic response, meta-regression should be applied; however, it was impossible to use meta-regression to provide the definitive effectiveness per type of supplement due to the small sample size and fewer than the required 10 studies [32].

For future research, if nutritional supports are not the usual care in the study settings, clinical trials utilizing innovative study designs such as stepped-wedge cluster randomized trials or randomized controlled crossover trials, including ethically acceptable control arms unexposed to nutritional supplements, should be considered to differentiate the effectiveness on nutritional status and immunologic response. In addition, because the development of malnutrition is multifactorial and results from changes not only in nutrient intake but also absorption and energy expenditure [51], investigators must reconsider the choice of

supplements, the length of supplements use, and the range of variables for health outcomes that can reflect the aspects of complexities. Our review indicates that tailored protein-energy fortified macronutrient supplements with essential micronutrients would result in the largest change in nutritional status and immunological response. To achieve the most effective nutritional and immunological outcomes and to decrease possible harm, the application of a meta-regression model or survival analysis is needed to examine the proper duration of macronutrient interventions and the timing of supplementation initiation. Finally, because qualitative studies or mixed methods studies provide different pictures and perspectives in greater depth, they are required to explore the psychophysiological changes in individual and social levels after introducing nutritional supplements and/or nutritional support programs. Therefore, the combination of quantitative and qualitative data would contribute to the development of a more complete understanding of the effectiveness of nutritional support.

There is increasing demand for the use of macronutrients, food supplements, and nutritional education in HIV/AIDS-endemic areas and an emerging need to expand the existing projects to other countries. Consequently, while the information gathered here will be useful in Sub-Saharan Africa and other HIV-affected regions, the pronounced contextual differences in various regions have to be considered when these findings are being generalized broadly. Evidence-based guidelines should also be developed for healthcare providers to assist their clinical decisions in terms of improving individuals' nutritional status and immunologic responses in resource-limited settings.

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STATEMENT AUTHORSHIP

Ms. Hong conducted the study and led the study design, data collection, data interpretation, article preparation, article review and correspondence as well as contributed to statistical analysis. Dr. Budhathoki led the statistical analysis and contributed to data collection, data interpretation, article preparation, and article review. Dr. Farley contributed to article preparation and review. All authors read and approved the final manuscript.

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Figure 1.
PRISMA Flow Diagram for Data Selection

Table 1.

Overview of the Studies and Primary Outcomes

Author <i>RCTs</i>	Year	N	Country	Source of Macronutrients	Control	F/U	BW	BMI	MU					Tri.		F/M		VL	Hb	Alb	BMR	BC	HGS	PA	Adh	QOL	Mort	QA
									AC	fold	FEM	area	CD4	F/M														
Cantrell et al.[40]	2008	636	Zambia	CSB + veg. oil	-	6m	↔					↔	↔										↑	↔	↔	↔	2	
Ndekha et al.[39]	2009	491	Malawi	RUTF	CSB	14w		↑				↔	↔	↔									↔	↔	↔	↔	5	
Serrano et al.[41]	2010	180	Niger	cereal + legume + veg oil	-	6m		↔				↑	↔	↔				↔					↑		↑		2	
Azabji-Kenfack et al.[35]	2011	52	Cameroon	<i>Spirulina platensis</i>	-	3m		↑				↑	↑	↓	↑	↔	↔										3	
				Soya bean	-	3m		↑				↑	↑	↓	↑	↔	↔											
PrayGod et al.[37]	2012	377	Tanzania	EPB (3690KJ/d)	EPB (615KJ/d)	2m				↔												↑					3	
Evans et al.[42]	2013	26	S. Africa	<i>FutureLife@ porridge</i>	-	6m		↑				↑	↑	↑	↑	↑	↑				↑		↑		↔	↔	3	
Olsen et al.[36]	2014	318	Ethiopia	early LNS + whey	delayed LNS	3m		↑						↔	↔	↔	↔					↑		↔			5	
				early LNS + soy	delayed LNS	3m		↑						↔	↔	↔	↔					↑		↔				
Rehman et al.[38]	2015	1876	Tanzania	LNS + VM	LNS only	12w		↔		↑	↔	↔	↔	↔	↔	↑											5	
<i>Retrospective Cohort Studies</i>																												
Ndekha et al.[46]	2009	336	Malawi	RUTF	CSB	3m		↔				↔											↔	↔	↔	↔	5	
van Oosterhout et al.[44]	2010	593	Malawi	RUTF	-	26w		↑																			6	
				CSB	-			↑																			6	
Scarcella et al.[48]	2011	106	Mozambique	Cereal-based food package	-	>3m		↑						↑													4	
Ahoua et al.[47]	2011	1106	Kenya, Uganda	RUTF		>1m		↑						↑			↑	↑									6	
Irvine et al.[45]	2011	171	Tanzania	Probiotic yogurt	Maize + beans	N/S		↔				↔	↔	↔	↔	↔	↔									2		
Nagata et al.[49]	2014	1017	Kenya	<i>Foundation Plus</i>	-	100d		↑						↔	↔	↔	↔										6	
Mensah et al.[50]	2015	200	Ghana	Soy + wheat + veg. oil		100d		↑																			4	

Note. Adh = adherence to ART; Alb = Serum albumin (g/L); BC = body composition; BMI = body mass index (kg/m²); BMR = basal metabolic rate; BW = body weight; CD4 = cluster of differentiation 4 (cells/mm³); CSB = corn-soya blends; d = day(s); EPB: Energy-protein biscuit; FFM = fat free mass (kg); F/M area = fat/muscle area; f/u = follow-up; Hb = hemoglobin (g/dL); HGS = hand grip strength (kg); m = month(s); MUAC = mid-upper arm circumference; Mort = mortality; LNS = Lipid Nutritional Supplement; LNS- VM = Lipid Nutritional Supplements-vitamins and minerals; NOS = Newcastle-Ottawa Quality Assessment Scale; N/S: not specified; PA = physical activity; QA = quality assessment; QOL = quality of life; RCT = randomized controlled trial; RUTF = high-energy Ready-to-Use Therapeutic Foods; S = South; Tri. Fold = triceps skinfold; Veg. = vegetable; VL = HIV 1+ viral load (copies/mL); wk = week(s)

Table 2.

Forest Plot of Body Weight

Note: CI = confidence interval; CSB = corn-soya blends; EPB = Energy-protein biscuit; LNS = Lipid Nutritional Supplement; RCT = randomized controlled trial; RUTF = highenergy Ready-to-Use Therapeutic Foods; SMD = standardized mean difference

Table 3.

Forest Plot of BMI

Note: BMI = body mass index; CI = confidence interval; CSB = corn-soya blends; LNS = Lipid Nutritional Supplement; RCT = randomized controlled trial; RUTF = high-energy Ready-to-Use Therapeutic Foods; SMD = standardized mean difference

Table 4.

Forest Plot of FFM

Note: CI= confidence interval; CSB = com-soya blends; FFM = fat-free mass; LNS = Lipid Nutritional Supplement; RCT = randomized controlled trial; RUTF = high-energy Ready-to-Use Therapeutic Foods; SMD = standardized mean difference

Table 5.

Forest Plot of CD4 Count

Note: CD4 = cluster of differentiation 4 (cells/mm³); CI = confidence interval; CSB = corn-soya blends; RCT = randomized controlled trial; RUTF = high-energy Ready-to-Use Therapeutic Foods; SMD = standardized mean difference