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# The effect of nutritional supplementation on quality of life in people living with HIV: a randomised controlled trial

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**Abstract**

OBJECTIVE To determine the effects of lipid-based nutrient supplements (LNS) on the quality of life of people living with HIV (PLHIV) during the first 3 months of antiretroviral treatment (ART) and to investigate the effects of timing of supplementation by comparing with supplementation during the subsequent 3 months.

METHODS A randomised controlled trial was conducted in three ART clinics within public health facilities in Jimma, Ethiopia. Participants were PLHIV eligible to start ART with body mass index >17 kg/m$^2$ and given daily supplements of 200 g of LNS containing whey or soya either during the first 3 months or the subsequent months of ART. The outcome was measured in terms of total quality-of-life scores on the adapted version of the WHOQOL-HIV-BREF assessed at baseline, three and six months.

RESULTS Of the 282 participants, 186 (66.0%) were women. The mean age (SD) was 32.8 (±9.0) years, and the mean (SD) total quality-of-life score was 82.0 (±14.8) at baseline assessment. At 3 months, participants who received LNS showed better quality of life than those who only received ART without LNS ($\beta$ = 6.2, 95% CI: 2.9: 9.6). At 6 months, there was no difference in total quality-of-life score between the early and delayed supplementation groups ($\beta$ = 3.0, 95% CI: −0.4: 6.4). However, the early supplementation group showed higher scores on the social and spirituality domains than the delayed group.

CONCLUSIONS LNS given during the first three months of ART improves the quality of life of PLHIV.

**keywords** lipid-based nutrient supplement, HIV, quality of life, low-income setting, food insecurity, antiretroviral treatment

## Introduction

In sub-Saharan Africa, the availability of antiretroviral treatment (ART) over the past decade has greatly reduced the mortality rate among people living with HIV (PLHIV) [1]. As PLHIV now have near-normal life expectancies, their quality of life has become an important issue [2]. Although ART improves quality of life of PLHIV [3], other factors affecting quality of life remain to be addressed.

Interventions aimed at the alleviation of food insecurity and undernutrition, which were central to the management of PLHIV in the pre-ART era [4], could still play important roles in improvement of quality of life in the era of ART. Cross-sectional studies from low-income countries have found associations between lower quality of life of PLHIV, and food insecurity [5] and undernutrition [6]. Thus, the nutritional support services developed alongside HIV care programmes in sub-Saharan Africa may have positive effects on quality of life, despite being primarily aimed at treating undernutrition [7].

Studies from high-income settings indicate that nutritional support has little or no effect on the quality of life of PLHIV [8, 9]. There is some evidence for the effect of nutritional supplementation on weight gain and lean body mass of PLHIV in low-income countries [10–13]. However, the data regarding the effect of supplementation on quality of life are inconclusive [14]. The few studies from low-income settings suffered methodological limitations. They either compared two nutritional supplements with no control group [12, 15, 16] or were not

randomised [10, 11]. In a non-randomised study of a food support programme for PLHIV in Ethiopia, an improvement in functional status was observed among those who received food support compared to those who did not [17]. However, the programme had a high drop-out rate that could have biased the results towards those with better outcomes.

We conducted a nutritional supplementation trial and have previously reported the beneficial effects of lipid-based nutritional supplement (LNS) on lean body mass and grip strength of PLHIV as primary outcomes [13]. In this study, we report the effect of LNS on quality of life of PLHIV initiating ART as part of the randomised controlled trial. We also investigated the differential effects of timing of supplementation on quality of life.

## Methods

### Study design

This study reports the secondary outcome of quality of life for a randomised controlled trial of LNS given to PLHIV who initiated ART. The design of the study is described in detail elsewhere [13]. As part of the trial, PLHIV with a body mass index (BMI) >17 kg/m$^2$ were randomised to receive daily LNS with whey or soya, either for the first 3 months from the start of ART, that is early LNS, or for the subsequent 3 months, that is delayed LNS. For the purpose of this study, those receiving LNS with whey and soya were combined, as comparison between the two was not considered relevant for the outcome of quality of life. Thus, the design of the study allowed us to assess the effect of LNS supplementation *vs.* no supplementation on quality of life by comparing the two groups at 3 months (main comparison) and to assess the effect of timing, that is early *vs.* delayed supplementation, by comparing the two groups at 6 months.

### Participants

PLHIV eligible for ART were recruited from Jimma University Specialized Hospital, and two primary care facilities (Jimma and Agaro Health Centres). The inclusion criteria were as follows: age ≥18 years, BMI >17 kg/m$^2$ and living within 50 km of the respective healthcare facilities. Exclusion criteria were as follows: pregnancy, lactation, known diabetes mellitus or current use of nutritional supplements.

### Intervention

The participants received 200 g LNS (approximately 4600 KJ) daily for 3 months. Details of supplementation are described elsewhere [13]. The early groups received the LNS only in the first 3 months while the delayed group received LNS in the 4th–6th months after starting ART.

### Data collection

Research nurses collected data with supervision from the trial investigators. Data on quality of life and food security status were collected at baseline, 3 and 6-month follow-up. Adherence to the supplement was assessed monthly from participants' report of consumption of the supplement and by counting the empty sachets they returned. Data on baseline social, demographic and economic characteristics were collected using structured questionnaires in local languages (Amharic and Afaan Oromo). Data on food security were collected using the Household Food Insecurity Access Scale [18]. Quality of life was assessed using the WHOQOL-HIV-BREF, which had been adapted and validated previously for Ethiopian PLHIV to produce the WHOQOL-HIV-BREF-ETH. A rigorous process of cultural validation was undertaken to establish semantic and item equivalences, and known-groups and construct validity in this setting [19]. Height and weight were measured using calibrated scales and stadiometers, respectively. Data on the WHO clinical stage of HIV were extracted from the clinical charts. Viral load was measured using a PCR assay (RealTime HIV-1; Abbott Laboratories, IL, USA).

### Outcome

The total quality-of-life score on the 27-item WHOQOL-HIV-BREF-ETH was used as a measure of the outcome. The total quality-of-life score (minimum = 26 to maximum = 130, with higher scores indicating better quality of life) was calculated by summing the mean scores on all of the domains, namely physical (e.g. pain, sleep, energy), independence (e.g. mobility, work capacity), psychological (e.g. feelings, self-esteem), spirituality (e.g. fear of the future, blame about HIV status, worry about death), social (e.g. relationships, support) and environment (e.g. access to services, transport), as well as the scores on the two general items asking people to make a global rating on their general quality of life, and general health satisfaction. In addition, the mean scores on each of the domains were compared to see whether the LNS had different effects on the domains of quality of life of PLHIV.

### Randomisation and blinding

Participants were randomised to receive either early or delayed supplementation, and outcome assessors were blinded to group allocation. The pharmacist responsible

for supplement distribution was the only person with access to the random sequence list.

### Sample size

The sample size was determined by the requirements of the main trial outcome [13]. Thus, the aim was to recruit 100 participants with BMI >17 kg/m$^2$ in each of the early whey LNS, early soy LNS, and delayed LNS groups.

### Data analyses

All data were double-entered and cleaned with EpiData (EpiData Association, Odense, Denmark). Data were then analysed using STATA/IC version 12.0 (StataCorp LP, College Station, TX). Effect size estimates with *P*-values < 0.05 were considered significant. Mixed linear regression was used to examine the effect of supplementation on quality of life over the first 3 months. A comparison of quality of life between early and delayed LNS was made at 6 months. The regression models were adjusted for age, sex, educational level and baseline food security status. The analysis was repeated with additional adjustment for the viral load as a binary variable (detectable *vs.* undetectable) to explore whether the observed differences in the outcome measure were due to changes in the clinical parameters. All the analyses followed an intention to treat principle based on available data.

## Results

Of 453 PLHIV screened for eligibility, 282 with BMI ≥17 kg/m$^2$ were allocated 2:1 to receive early or delayed LNS. The remaining either declined participation ($n$ = 105) or were excluded because of a BMI ≤17 kg/m$^2$ ($n$ = 66). The most common reasons for declining to participate were not having time for assessment (31 patients), did not wish to give any reason (19 patients), did not like the taste of the LNS (18 patients), did not wish to give a blood sample (17 patients) or spouse did not give permission (6 patients).

Table 1 shows the baseline characteristics of participants who were allocated randomly to early and delayed intervention. The scores on the different domains of quality of life were roughly similar between the two groups at enrolment into the trial.

**Table 1** Baseline characteristics of PLHIV (BMI >17 kg/m$^2$) randomised to early or delayed supplementation with lipid-based nutrient supplement (LNS) ($n$ = 282)

| | Delayed LNS† ($n$ = 93) | Early LNS† ($n$ = 189) |
|---|---|---|
| Age (years)‡ | 31.7 (±8.5) | 33.3 (±9.3) |
| Sex | | |
| Female | 65 (69.9) | 121 (64.0) |
| Marital status | | |
| Married | 29 (31.5) | 79 (42.0) |
| Divorced or widowed | 54 (58.7) | 89 (47.3) |
| Never married | 9 (9.8) | 20 (10.6) |
| Education | | |
| No formal education | 32 (34.4) | 52 (27.5) |
| Primary | 43 (46.2) | 97 (51.3) |
| Secondary and above | 18 (19.4) | 40 (21.2) |
| Body mass index‡ (kg/m$^2$) | 19.8 (2.1) | 19.9 (2.3) |
| Food insecurity | | |
| None | 12 (13.2) | 27 (14.4) |
| Mild | 17 (18.7) | 39 (20.9) |
| Moderate | 30 (33.0) | 48 (25.7) |
| Severe | 32 (35.2) | 73 (39.0) |
| WHO HIV stage | | |
| Stage I | 25 (28.1) | 63 (33.7) |
| Stage II | 27 (30.3) | 59 (31.6) |
| Stage III | 29 (32.6) | 48 (25.7) |
| Stage IV | 8 (9.0) | 17 (9.1) |
| Quality of life‡ | | |
| General quality of life | 2.6 (1.2) | 2.6 (1.1) |
| General health satisfaction | 3.1 (1.1) | 2.9 (1.0) |
| Physical domain | 12.1 (3.1) | 12.3 (3.0) |
| Independence domain | 11.9 (3.1) | 12.4 (3.1) |
| Psychological domain | 11.9 (3.4) | 12.3 (3.1) |
| Spirituality domain | 13.5 (3.6) | 13.2 (4.2) |
| Social domain | 11.1 (3.0) | 11.4 (3.1) |
| Environment domain | 12.3 (2.7) | 12.1 (2.6) |
| Total quality of life scores | 81.7 (14.9) | 82.2 (14.9) |

†Data in brackets are percentages unless otherwise specified.
‡Data indicate mean ± SD.

### Total quality of life scores

At the 3-month assessment, the early intervention group had a total quality-of-life score of 92.1 (95% CI: 89.6: 94.6), which was higher than that of the control group ($\beta$ = 6.2, 95% CI: 2.9: 9.6, $P$ < 0.001) (Figure 1). At the 6-month assessment, when both groups had received LNS, the difference between the early and delayed intervention was not significant ($\beta$ = 3.0, 95% CI: −0.4: 6.4, $P$ = 0.1). As shown in Figure 1, the early intervention group had a sharp increase in the quality-of-life scores in the first 3 months that levelled off in the subsequent 3 months after supplementation had ended. The delayed intervention group had a steady increase in the quality-of-life scores throughout the 6-month follow-up period.

### Quality of life domains

As shown in Table 2, the supplementation had positive effects on general health satisfaction and on the physical,

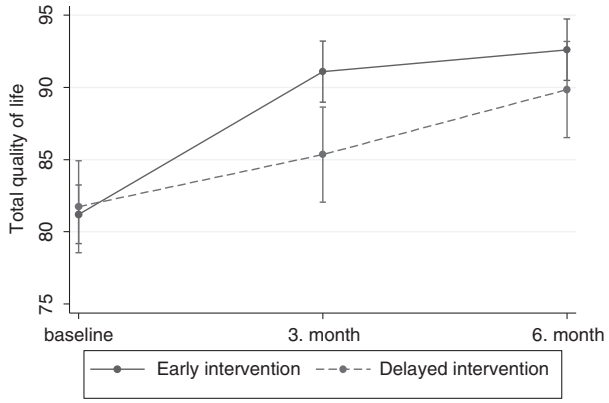


**Figure 1** Changes in the total quality-of-life scores with means and 95% confidence intervals by intervention group among PLHIV adjusted for age, sex, education and food security.

**Table 2** Quality-of-life scores at 3 months among 282 PLHIV starting ART (BMI >17 kg/m$^2$) randomised to delayed or early supplementation with lipid-based nutrient supplement (LNS)†

| Quality-of-life domains | Delayed LNS‡ ($n$ = 93) Adjusted mean (SE)§ | Early LNS‡ ($n$ = 189) Mean difference (95% CI)¶ | $P$-value |
|---|---|---|---|
| General quality of life | 2.86 (0.11) | 0.04 (−0.23: 0.30) | 0.777 |
| General health satisfaction | 3.20 (0.10) | 0.36 (0.12: 0.61) | 0.004 |
| Physical | 13.08 (0.32) | 1.06 (0.30: 1.82) | 0.006 |
| Independence | 13.51 (0.32) | 0.64 (−0.11: 1.39) | 0.097 |
| Psychological | 13.30 (0.33) | 0.54 (−0.21: 1.30) | 0.160 |
| Spirituality | 13.30 (0.37) | 1.20 (0.36: 2.05) | 0.005 |
| Social | 11.70 (0.31) | 0.97 (0.26: 1.69) | 0.008 |
| Environment | 11.84 (0.26) | 1.05 (0.44: 1.66) | 0.001 |

SE, standard error; CI, confidence interval.
†Effect estimates are adjusted for sex, age, education and baseline food security status.
‡Early LNS received LNS during the first 3 months (intervention group) and delayed LNS did not receive LNS (control group).
§The mean scores for the PLHIV in the delayed LNS group.
¶The difference between the mean of the early LNS group and the delayed LNS group.

spiritual, social and environment domains of quality of life over the first 3 months. The effect of supplementation on the independence domain was not significant ($\beta$ = 0.6, 95% CI: −0.1: 1.4; $P$ = 0.1). Neither there were differences in the general quality-of-life and psychological domain scores ($P$ > 0.05). The findings remained similar when the analysis was adjusted for viral load at the 3-month assessment (data not shown). At the 6-month assessment, the early supplementation led to higher scores only on the spirituality domain ($\beta$ = 0.9, 95% CI: 0.1: 1.8; $P$ = 0.04) and the social domain ($\beta$ = 0.8, 95% CI: 0.1: 1.5; $P$ = 0.03) (Table 3).

**Table 3** Quality-of-life scores 6 months among 282 PLHIV starting ART (BMI >17 kg/m$^2$) randomised to delayed or early supplementation with lipid-based nutrient supplement (LNS)†

| Quality-of-life domains | Delayed LNS‡ ($n$ = 93) Adjusted mean (SE)§ | Early LNS‡ ($n$ = 189) Mean difference (95% CI)¶ | $P$-value |
|---|---|---|---|
| General quality of life | 2.86 (0.11) | 0.21 (−0.06: 0.48) | 0.131 |
| General health satisfaction | 3.52 (0.11) | 0.05 (−0.20: 0.30) | 0.719 |
| Physical | 13.92 (0.33) | 0.40 (−0.37: 1.17) | 0.312 |
| Independence | 14.08 (0.32) | 0.29 (−0.47: 1.06) | 0.452 |
| Psychological | 13.96 (0.33) | 0.16 (−0.61: 0.93) | 0.677 |
| Spiritual | 13.76 (0. 38) | 0.92 (0.06: 1.77) | 0.036 |
| Social | 11.96 (0.31) | 0.80 (0.07: 1.52) | 0.032 |
| Environment | 12.86 (0.27) | 0.16 (−0.46: 0.78) | 0.616 |

SE, standard error; CI, confidence interval.
†Effect estimates are adjusted for sex, age, education and baseline food security status.
‡Early LNS received LNS during the first 3 months and delayed LNS received LNS during the subsequent 3 months.
§The mean scores for the PLHIV in the delayed LNS group.
¶The difference between the mean of the early LNS group and the delayed LNS group.

### Food insecurity

In the first 3 months, the early LNS group showed a decrease in the proportion of severe food insecurity by approximately 14.3% and an increase in the proportion of food secure group by a similar magnitude. The delayed LNS group showed a decrease in the proportion of severe food insecurity by approximately 9.5%, while the proportion of moderate food insecurity increased by 17.0% during the first 3 months (Figure 2).

## Discussion

LNS given in the first 3 months after initiation of ART resulted in significant improvement in health-related quality of life of PLHIV compared to people who did not receive supplementation. LNS given in the first 3 months of initiation of ART did not have superior effects on

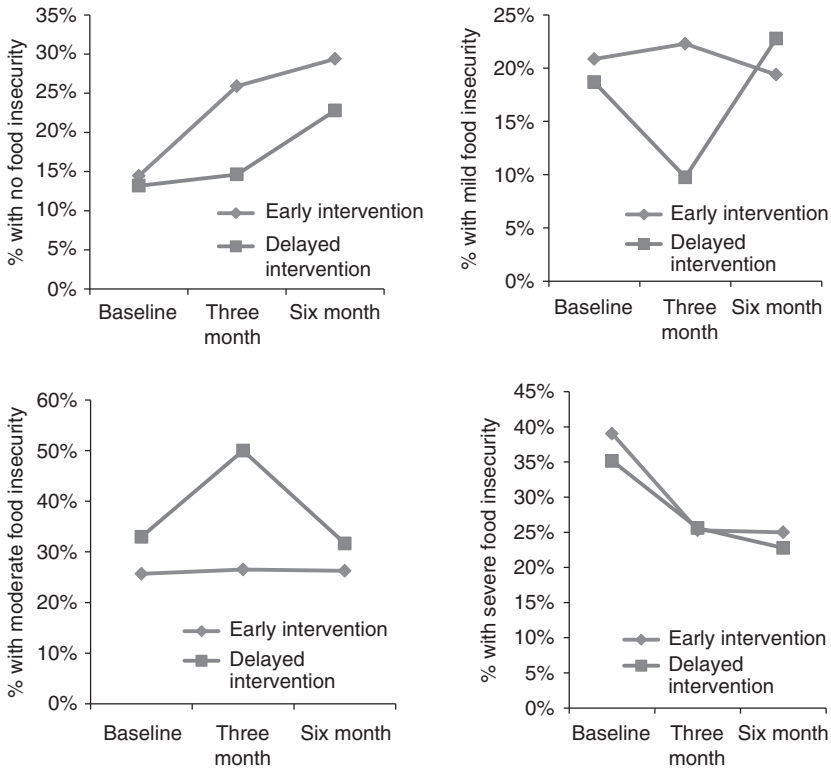


**Figure 2** Changes in the proportion of different food security groups of PLHIV receiving early supplements and delayed supplementation with BMI>17 kg/m$^2$ over the 6-month follow-up period.

quality of life after 6 months, compared to delayed LNS given between 4 and 6 months after initiation of ART. The total quality-of-life scores at the end point in both groups were lower than that for 100 HIV-negative adults recruited from JUSH, that is mean (SD) of 98.3 (16.2) (Table S1). Supplementation in the first 3 months was associated with significantly higher scores in the spirituality and social domains of quality of life of PLHIV at 6 months; however, this could have been a chance finding in the light of testing for multiple outcomes.

The observed effect of LNS at initiation of ART on the quality of life of PLHIV is consistent with the limited existing data from low-income country settings, indicating that nutritional supplementation improved quality of life or functional outcomes [10, 15–17]. However, it is not clear how nutritional supplementation resulted in improved quality of life. Food insecurity, a common issue among PLHIV in low-income settings [20–22], is known to be associated with poor quality of life [5]. The nutritional supplements may have improved the quality of life of PLHIV through reducing food insecurity, as we found that moderate and/or severe food insecurity decreased during the periods of supplementation. Also, food assistance for PLHIV in Ethiopia has been found to improve quality of life, especially mobility [17]. Nutritional assistance programmes in high-income settings, where food insecurity was not prevalent, had little or no effect on the quality of life of PLHIV [8, 9]. Somewhat unexpectedly, the prevalence of severe food insecurity decreased in both groups during the first 3 months of follow-up. However, in the delayed LNS group, there was a concomitant increase in the prevalence of moderate food insecurity while this was not observed in the early LNS group. Perhaps the health status of the delayed LNS group had improved as a result of ART, which might have improved the family's financial status.

As part of the primary analysis of this study, we found that supplementation had an effect on weight gain [13]. The association between low health-related quality of life and low BMI among PLHIV in low-income settings has been reported previously [23]. Thus, the observed improvement in quality of life may also be due to the improved nutritional status resulting from supplementation.

The observed positive effect of LNS on quality of life in those who had mild or no undernutrition indicates that PLHIV benefit from nutritional supplementation while initiating ART irrespective of their nutritional status. As food insecurity is a common issue in this population, concerns regarding an imminent need for more food at

initiation of ART could have lowered their quality of life even when they did not have undernutrition. Accordingly, our qualitative interviews have revealed that PLHIV perceived the LNS as 'beneficial in their recovery' and 'protective against the adverse effect of ART' [24]. The perceived beneficial effect of macronutrient supplements by PLHIV has also been reported in a Ugandan study [25]. Another study found that PLHIV perceived ART as harmful when taken without adequate food [26]. PLHIV who received the LNS at the initiation of ART might perceive themselves as particularly advantaged and protected from the harmful effects of ART. As quality of life is a patient-rated outcome, the results may have a lot to do with how the nutritional supplement was perceived by those who received it. This might explain the observed improvement in the general health satisfaction and spirituality domain of quality of life. The latter is comprised of items such 'fear of dying' and 'fear of the future', which are common existential issues during periods of acute illness or at the start of new treatments.

Our finding that nutritional supplementation improved quality of life even when people were adequately nourished is important, in the light of fact that current HIV care programmes only provide nutritional supplementation to PLHIV with moderately to severely low BMI [17, 27]. These programmes exclude those with BMI >17 kg/m$^2$ who, according to the findings from this study, could have attained better quality of life from nutritional support during the first 3 months of ART.

The observed positive effects of LNS on the physical domain of quality of life are consistent with the increased functional capacity, such as grip strength as reported in our previous study [13]. The positive effect of nutritional support programmes on functional capacity (e.g. ability to walk) has also been reported from Ethiopia [17]. The marginal effects on the independence domain might be due to the study being under powered to detect the differences, as evidenced by the wide confidence interval. The effects of LNS on the social and environment domains need further qualitative exploration to understand potential mechanisms. Surprisingly, the general quality-of-life item, which is supposed to indicate the 'overall' quality of life, did not differ between the two groups. This is likely due to difficulties with understanding the concept behind the item by respondents as reported in our validation study. It was difficult to find an equivalent term to 'quality of life' in the translation process, and PLHIV often misunderstood the question during the pilot test, as described elsewhere [19].

Our findings add to the limited scientific evidence on the effect of nutritional supplement on the quality of life of PLHIV in a low-income country. Our finding that LNS given only during the first 3 months had a sustained effect of improved quality of life at the 6-month assessment means that cost-effective nutrition supplementation programmes can be designed in low resource settings. Although the minimal clinically important difference has not been established for the short version of WHOQOL-HIV, a difference as big as 6.2 appears to be bigger than the 1.0 reported for a related tool, that is WHOQOL-100 for women with breast cancer [28].

The fact that study participants were not blinded to the status of receiving LNS, and that they were told LNS 'was good for them' and that it was expected to fill a nutritional need during ART could potentially introduce bias to the findings on patient-rated outcome. Nevertheless, the early intervention group maintained improved quality-of-life scores at 6 months despite not receiving the LNS between the 4th and 6th months. At the 3-month assessment, the supplemented group knew they were going to stop the supplement, and the non-supplemented group knew they were going to receive the supplement. Therefore, any anxiety or excitement that might arise in anticipation of the future would lead to underestimation of the effect of LNS on quality of life. Hence, the actual effect of LNS on quality of life could be greater than that observed in this study. The absence of a control group with no supplementation during the entire 6-month period precludes us from understanding whether delayed LNS has any additional benefits (compared to ART alone) on quality of life at the 6-month assessment point. Furthermore, the long-term benefits of LNS supplements on quality of life cannot be ascertained from this study. Although the proportion of PLHIV who declined to participate in the trial is significant, we do believe it is acceptable and lower than reported from other trials.

The findings call for improved nutritional supplementation of PLHIV irrespective of their nutritional status particularly in low-income countries where food insecurity is common. National guidelines, which are often based on clinical parameters, need to consider results from patient-rated outcome measures and address the nutritional needs of PLHIV who are otherwise excluded from nutrition support programmes. The fact that the level of quality of life of PLHIV at the end of nutritional supplementation was still below that of HIV-negative adults means that other factors need to be identified and addressed.

## Conclusion

LNS supplementation for PLHIV in the first 3 months of initiation of ART has beneficial effects on quality of life. Early supplementation may have more beneficial effects on certain domains of quality of life than delayed

supplementation. Guidelines need to address the benefits of nutritional supplements to PLHIV in settings when food insecurity is widespread even when there is no apparent undernutrition. Further studies are needed to explore the cost implications of providing nutritional supplements to PLHIV who are not malnourished.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Table S1.** Characteristics and quality of life of HIV negative adults who visited Jimma University Specialized Hospital for HIV testing ($n$ = 100).

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