

The Enabling Effect of Food Assistance in Improving Adherence and/or Treatment Completion for Antiretroviral Therapy and Tuberculosis Treatment: A Literature Review

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Abstract Socioeconomic costs of HIV and TB and the difficulty of maintaining optimal treatment are well documented. Social protection measures such as food assistance may be required to offset some of the treatment related costs as well as to ensure food security and maintain good health of the affected individual and household. Programmes have started placing greater emphasis on treatment adherence and are looking for proven interventions that can optimize it. This paper looks at the effect of food assistance for enabling treatment adherence and reviews studies that used food assistance to promote adherence. Eight of ten studies found that provision of food can improve adherence and/or treatment completion for HIV care and treatment, ART and TB-DOTS. This indicates that food provision is not only a biological, but also a behavioural intervention, and underscores that unresolved food insecurity can be an impediment to treatment adherence and consequently to good treatment outcomes.

Keywords TB · DOTS · ART · Food assistance · Enabler · Adherence to treatment

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Introduction

Food insecurity is one of the multiple barriers that individuals face in initiating and adhering to long-term medical therapies such as ART and DOTS, especially in resource-limited settings [1–17]. Other patient-related barriers include the complexity of the medication regimen [18], emotional distress [7], illness costs to households [19], stigma [20], health beliefs and poverty [4], limited knowledge of the disease [21], difficulty remembering [22], intentional non-adherence due to adverse drug reactions [23] and harmful use of alcohol [24].

In the context of the rapid scale up of both HIV care and treatment and TB treatment services, especially in sub-Saharan Africa, there is an urgent need to understand the complex interplay of risk factors for non-adherence, including food insecurity, so that effective adherence support interventions can be designed, piloted, evaluated, adjusted and then implemented at scale. This is particularly important given the fact that the percentage of people in Sub Saharan Africa who are still on treatment 3 years after starting ART is only approximately 65 % [25], and incomplete adherence increases the risk of developing drug resistance.

Adherence support strategies may include directly observed treatment, education and counseling, patient reminder and late patient tracer systems, and incentive or enabler¹ systems, including food assistance. It is important to note that food assistance often has a dual role. In addition to being an enabler to start and continue treatment, it can together with the pharmacological treatment contribute

¹ The term incentive is widely used in much of the literature but for the purposes of this paper the term “enabler” is adopted except when necessary to preserve the language used in referenced publications.

Table 1 Overview of studies among PLHIV or TB patients that assessed impact of food or vouchers for food on adherence and/or completion of treatment ($n = 10$)

Reference	Country	TB patients or PLHIV	Design of study	Outcome indicators	Findings
28	US	TB patients	Intervention compared to historical controls: Non complying patients eligible to receive a grocery coupon (USD 5) for each DOTS appointment that was kept ($n = 55$) Historical controls who would have been eligible for incentive scheme ($n = 52$)	Completion of therapy	Patients of the incentive program more likely than controls to have completed therapy within 32 weeks (OR 5.73, 95 % CI [2.25–14.84]) and 52 weeks (OR 7.29 95 % CI [2.45–22.73])
29	Brazil	TB patients	Retrospective comparison of two groups of patients: TB treatment only ($n = 74$) (2001–2003) TB treatment + food basket at a value of approx. 72 USD/month ($n = 68$) (2004–2006)	Cured or abandoned treatment	In the group that also received food, 61 patients (87.1 %) were cured and 9 patients (12.9 %) abandoned treatment. In the treatment-only group, 46 patients (69.7 %) were cured and 20 patients (30.3 %) abandoned treatment ($p = 0.013$)
35	Niger	PLHIV	Intervention compared to historical control: PLHIV receiving ART, CD4 <200/mm ³ , WHO stage III or IV and/or BMI <18.5 kg/m ² —received food basket of 2,250 kcal/person/day per family member ($n = 62$) Historic control meeting same criteria, but not receiving a food basket ($n = 118$)	ART adherence, survival, CD4 count, nutritional status	98 % of food assisted and 77.4 % of non food assisted remained adherent to ART over 6 mo period ($p < 0.05$) (all PLHIV had been on ART for <12 months). Greater increase in CD4 in food assisted group (+114 vs +68 CD4 cells/mm ³ , $p < 0.05$). One death in food assisted group and 12 in non food assisted group ($p < 0.05$). No difference of changes of WHO stage or BMI
36	Zambia	PLHIV	Partly retrospective study, comparing data from PLHIV on ART at food assisted to non food assisted clinics. Food clinics provided food based on food insecurity status, consisting of 25 kg maize, 6 kg CSB, 4.5 kg peas, 1.8 L vegetable oil per month. Retrospective selection of PLHIV, interviews administered, selection of clinic and pharmacy records. In total 145 food assisted and 147 non food assisted PLHIV. Analysis used PSM of food assisted and non food assisted PLHIV	Adherence to ART, using pharmacy refill records	Food assistance recipients had higher ART adherence compared to non-recipients (98.3 vs 88.8 %, respectively; $p < 0.01$). No significant effects observed for weight or CD4 count change. Improvement in adherence rates was greater for participants on ART for less than 230 days and for those with BMI <18.5 kg/m ² , a higher HIV disease stage or a CD4 count ≤ 350 cells/ μ L
37	Mozambique	PLHIV	Retrospective study, comparing records from PLHIV on ART in two provinces, one with and one without food assistance. Food assistance provided monthly to PLHIV with low BMI (<18.5 kg/m ²) and no or low income, consisting of 25 kg maize, 10 kg soya, 5 kg cowpeas. Eligibility reviewed every 3 months. Analysis used PSM of food assisted and non food assisted PLHIV	Adherence to ART, using pharmacy refill records	Adherence was higher among non food recipients, both during food assistance and post food assistance periods. Expressed as periods of time during which patient's supply of medication was assumed to have been exhausted: during food assistance: 0.182 versus 0.137 in food and non-food groups, respectively ($p = 0.029$), and post food assistance, 0.199 versus 0.129, respectively ($p = 0.001$)

Table 1 continued

Reference	Country	TB patients or PLHIV	Design of study	Outcome indicators	Findings
32	Haiti	PLHIV	Prospective observational cohort study, comparing PLHIV (most but not all on ART) eligible for food assistance ($n = 300$) to those not eligible ($n = 300$). Eligibility based on also having TB, low BMI, low CD4 count ($<350/\text{mm}^3$) and/or severe socio-economic conditions. Food ration: 100 g CSB, 50 g cereal, 50 g dried legumes, 25 g vegetable oil, 5 g iodized salt per day per family member, for maximum of three members	Number of monthly visits attended, food security score, BMI at 6 and 12 months	At 6- and 12-months, 488 and 340 subjects were eligible for analysis. At 6 months, mean number of scheduled monthly visits attended was 5.49 versus 2.82 ($p < 0.0001$) for the food assisted versus the non-food group, and at 12 months 9.73 versus 8.34 ($p = 0.007$). At 6 months, food security had significantly improved in those who received food assistance versus who did not (-3.55 vs -0.16 ; $p < 0.0001$); and BMI had decreased significantly less (-0.20 vs -0.66 ; $p = 0.020$). At 12 months, food assistance was associated with improved food security (-3.49 vs -1.89 , $p = 0.011$) and BMI (0.22 vs -0.67 , $p = 0.036$)
33	India	PLHIV	Prospective longitudinal clinic-based observational study. HIV-positive, initially ART naive, children ($n = 100$) followed for 2 years. In year two ($n = 80$) children received food assistance as take-home ration providing 1/3 of child's caloric needs	Clinic attendance (at least once every 2 months), follow-up attrition, death, episodes of AIDS defining opportunistic infections, need for ART	In the first year, three children died and six were lost to follow-up, and ART was initiated in 14 children of whom two died and one was lost to follow-up. The odds for regular clinic attendance was 3.00 (95 % 1.27–7.08) during the second year compared to the first. The authors also report a decline of follow-up attrition (58.3 %), death rate (56.7 %), episodes of AIDS defining OIs (OR 1.87), progression of the disease to higher stages (OR 1.65), severe malnutrition (OR 1.97) and need for ART (14 vs 11.2 %) during the second year
34	Zambia	PLHIV	Prospective controlled design among food insecure PLHIV on ART Four clinics assigned to food assistance ($n = 442$). Amount and type of food varied by family size and income owner status of PLHIV—all received CSB + oil, some also maize meal and beans Four clinics no food assistance ($n = 194$)	MPR from pharmacy refill records	258 of 366 (70 %) of patients in the food group achieved an MPR of 95 % or greater versus 79 of 166 (48 %) among controls (RR 1.5; 95 %CI 1.2–1.8). No significant effect of food supplementation on weight gain or CD4 cell response was observed
30	Timor-Leste	TB patients	Prospective, individually-randomized, controlled design among TB patients at three clinics Food assistance ($n = 137$) consisting of a midday meal at clinic for first 2 months, and take home ration of red kidney beans, rice and oil for one meal/d for one person for rest of treatment Nutrition education only ($n = 133$)	Treatment success, compliance (not defined), weight gain	Treatment success before the violent conflict in Timor-Leste, was 84 % in the intervention and 85 % in the control group and after that 50 % and 56 % respectively. During the intensive phase, compliance was 86.7 % in the intervention and 91.4 % in the control group ($p = 0.02$). Weight gain was higher in the intervention than in the control group at both 8 weeks (5.2 vs 3.6 kg, $p = 0.04$) and 32 weeks (10.1 vs 7.5 kg, $p = 0.04$)

Table 1 continued

Reference	Country	TB patients or PLHIV	Design of study	Outcome indicators	Findings
31	India	TB patients	Prospective, individually-randomized, controlled design among wasted TB patients Food assisted group received dietary advice, sweet balls (600 kcal/day) of which consumption was observed daily and a take home ration of sprouted grams and nuts (100 g/day) No food assistance	Sputum conversion, treatment completion	Among smear positive patients (36 per group), the sputum conversion rate was 97.2 and 80.6 % in the food assisted and control groups, respectively. Treatment completion rate was 98 and 82 %, respectively

to the treatment of malnutrition, provided that the foods provided are of appropriate nutritional quality [26].

In the context of limited health care and programme resources, and especially in areas of widespread food insecurity, there is considerable interest in knowing the effectiveness of food interventions in improving adherence to ART and DOTS. However, as noted by Gross and Blumel, there is very little evidence on the impact of incentive programs (of any kind) because few have been evaluated and when an evaluation is done, it is often difficult to isolate the impact of the incentive from other aspects of the DOTS program [27].

The purpose of this paper was to assess the evidence that is available from published studies about the role and effectiveness of food interventions as enablers in improving adherence to long-term therapies for HIV and tuberculosis among poor and disadvantaged patients, and consider program implications and priorities for future research.

Methods

A literature search was conducted to identify studies that had reported adherence to treatment for either HIV/AIDS or tuberculosis and/or treatment completion for tuberculosis as a primary or secondary outcome, and that were based on randomized or non-randomized controlled trials, historical cohort studies or published program evaluations, and which provided food assistance as an enabler. Food assistance could be provided in the form of vouchers or food, with or without the additional aim to contribute to treating malnutrition. The studies were identified through an extensive search of the PubMed database using various combinations of key search terms, including (food, cash, intervention, transfer, incentive or enabler) and (adherence or compliance) and (ARV, ART, HAART, DOT, DOTS or TB treatment), assessing references from identified publications and through contacting colleagues in this area of research.

Findings

Four studies were identified that assessed impact of food assistance on completion and/or adherence to TB treatment [28–31], and six studies that assessed impact of food assistance on adherence to clinic appointments among PLHIV [32, 33] or adherence to ART [34–37]. Information about the studies has been summarized in Table 1.

A study among TB patients in the US compared treatment completion before and after a change of the incentive scheme [28]. A total of 55 patients who had demonstrated

non-adherence by missing at least 25 % of DOTS doses over a 4-week period, were provided a US\$5 grocery coupon for each DOTS appointment (approximately one per week) that was kept [29]. Completion of therapy amongst this group was compared to historic cases who would have been eligible for this incentives program based on their non-adherence record ($n = 52$). Patients of the incentive program were more likely than control patients to have completed therapy within 32 weeks (OR 5.73, 95 % CI [2.25–14.84]) and 52 weeks (OR 7.29 95 % CI [2.45–22.73]).

Two studies with a similar design were conducted among TB patients in Brazil [29] and PLHIV on ART in Niger [35]. Filho et al. [30] compared, retrospectively, TB patients who had received TB treatment only between 2001 and 2003 ($n = 68$) to TB patients who had received both TB treatment and a food basket between 2004 and 2006 ($n = 74$). The value of the food basket was 30 Brazilian Real per month (in 2005, equivalent to approximately 72 USD/month). In the treatment-only group, 46 patients (69.7 %) were cured and 20 patients (30.3 %) abandoned the treatment, whereas in the group that also received food, 61 patients (87.1 %) were cured and only 9 patients (12.9 %) abandoned treatment ($p = 0.013$).

The retrospective study by Serrano et al. conducted among PLHIV on ART at a clinic in Niamey, Niger compared survival, CD4 count, nutrition status and ART adherence among PLHIV who received food assistance to a historic control group that would have been eligible for food assistance if it had been offered when they started treatment [35]. The food basket provided 2,250 kcal/person/day per family member and consisted of 500, 100 and 30 g/person/day respectively of cereal, legume and vegetable oil fortified with vitamin A. PLHIV were eligible for food assistance when they received ART, had a CD-4 cell count under $200/\text{mm}^3$ at one of the two last blood samplings, developed a clinical advanced stage of AIDS (WHO stage III or IV) and/or had a body mass index (BMI) $<18.5 \text{ kg/m}^2$. Monthly collected clinic data of PLHIV who had been on ART for less than 1 year were used, and data from the first 6 months of receiving food assistance, and equivalent for the comparison group, were analysed. Sixty-two PLHIV were included in the food assisted group and 118 in the comparison group. Adherence was assessed on follow up consultation with help of patient interviews, checking remaining tablets in ART boxes and possible oversights of adherence. The authors report that 98 % of food assisted and 77.4 % of comparison PLHIV remained adherent to ART ($p < 0.05$), without specifying how they classified adherent and non-adherent. Furthermore, one patient who received food support and twelve controls died ($p < 0.05$). Increase in CD-4 cell count was around 1.7 times higher ($+114$ vs $+68 \text{ CD-4 cells/mm}^3$, $p < 0.05$) in

food supported groups. The changes of WHO stage and BMI did not differ between groups.

Posse et al. [37] and Tirivayi et al. [36] also conducted retrospective, or partly retrospective, studies, using clinic and pharmacy records, but they employed a quasi-experimental design in which propensity score matching (PSM) with difference in differences estimates was used to match, for the analysis, each randomly selected food assistance recipient to a sample of similar non-food assistance recipients based on key indicators (e.g. age, CD4 count, duration on ART, family size, asset ownership etc.).

The study by Posse et al. [37] used data from two provinces in Mozambique. In Sofala province, clinics provided food assistance to PLHIV on ART with a BMI below 18.5 kg/m^2 who were either earning no income or whose income was below the monthly national minimum income and many dependents. No food was provided in Zambezia province. Food assistance was provided once per month for a period of 3 months, after which it could be extended for another 3 or 6 months, if BMI was still below 18.5 kg/m^2 . Food assistance consisted of 10 kg of soya, 5 kg of cowpeas and 25 kg of maize. Adherence, which was the primary outcome variable, was determined from pharmacy refill records and expressed as periods of time during which the patient's supply of medication was assumed to have been exhausted. Only data from adults, non pregnant or lactating, were used. Mean adherence score, i.e. indicating the extent to which supplies were exhausted, of the food assistance recipients ($n = 171$) was significantly higher than of the control group ($n = 185$) during and post food assistance ($p = 0.029$ and $p < 0.001$ respectively), showing that food assistance recipients were less adherent to ART than the control group. Due to limitations in the completeness of data the authors were unable to correlate adherence to ART with other clinical outcomes such as BMI, CD4 count and opportunistic infections.

Tirivayi et al. [36] conducted a cohort study in Zambia incorporating interviewer-administered surveys and retrospective clinical data to compare ART patients receiving food assistance with a control group of non-recipients. Medication adherence was assessed using pharmacy dispensation records and expressed as medication possession ratio (MPR), which is calculated by dividing the total number of days the patient was late for pharmacy refills by the total days on ART during the study period, subtracting this ratio from 1 and converting it into percentages. At 'food clinics', eligibility for food assistance was strictly based on food security status and the monthly ration consisted of maize (25 kg), vegetable oil (1.8 L), peas (4.5 kg) and a corn and soy blend flour (6.0 kg). After food assistance had been provided for 6 months, to PLHIV who had been on ART for any length of time, intervention and control clinics were selected, matching control clinics to

intervention clinics according to active patient population, duration of operation and historical patient survival at 12 and 18 months post-ART initiation. Random sampling was used to select approximately 50 non-pregnant adult ART patients from each of the four intervention and control clinics, all with a food security status that had, or would have, made them eligible for food assistance. All 400 patients were interviewed and subsequently their clinic and pharmacy data were retrieved. Patients for whom required data were not available, were excluded from the analysis. Food assistance recipients ($n = 145$) had higher ART adherence compared to non-recipients ($n = 147$) (98.3 vs 88.8 %, respectively; $p < 0.01$). No significant effects were observed for weight or CD4+ lymphocyte count change. The improvement in adherence rates was greater for participants on ART for less than 230 days and for those with BMI $< 18.5 \text{ kg/m}^2$, a higher HIV disease stage or a CD4+ lymphocyte count $\leq 350 \text{ cells}/\mu\text{l}$.

Ivers et al. [32] conducted a prospective observational cohort study among adults living with HIV in Haiti, most of whom were on ART (eligibility based on CD4 count < 350 or meeting WHO clinical criteria). People were eligible for monthly food rations if they had TB, BMI $< 18.5 \text{ kg/m}^2$, CD4 cell count $< 350/\text{mm}^3$ (in the prior 3 months) and/or severe socio-economic conditions. The ration contained 50 g of cereal, 50 g of dried legumes, 25 g of vegetable oil, 100 g of corn-soya blend and 5 g of iodized salt for each of three family members (approximately 949 kcal) per person per day. A total of 600 individuals (300 eligible and 300 ineligible for food assistance) were interviewed before rations were distributed, at 6 months and at 12 months. At 6- and 12-month time-points, 488 and 340 subjects were eligible for analysis. The mean number of scheduled monthly visits attended by 6 months was 5.49 versus 2.82 ($p < 0.0001$) for the food assisted versus the non-food group, and at 12 months it was 9.73 versus 8.34, respectively ($p = 0.007$). At 6 months, food security had significantly improved in those who received food assistance versus who did not (-3.55 vs -0.16 ; $p < 0.0001$); and BMI had decreased significantly less (-0.20 vs -0.66 ; $p = 0.020$). At 12 months, food assistance was associated with improved food security (-3.49 vs -1.89 , $p = 0.011$) and BMI change (0.22 vs -0.67 , $p = 0.036$).

Kundu et al. [33] conducted a prospective longitudinal clinic-based observational study in the pediatric HIV/AIDS clinic, Medical College, Kolkata, India in which they followed a group of initially 100 HIV-positive ART naïve children for a period of 2 years. After the first year, food assistance was provided, outside the hospital, to all remaining and still eligible children ($n = 80$) in the form of a take-home ration providing 1/3 of the caloric needs of the child. The children were advised to come to the

clinic monthly or at least once in two months. Attending more than 90 % of the 2 monthly visits was considered regular. In the first year, three children died and six were lost to follow-up, and ART was initiated in 14 children of whom 2 died and 1 was lost to follow-up. It is not clear from the paper why some of the other 20 children who were not included during the second year were lost or excluded. The odds for regular clinic attendance was 3.00 (95 % 1.27–7.08) during the second year compared to the first. The authors also report a decline of follow-up attrition (58.3 %), death rate (56.7 %), episodes of AIDS defining OIs (OR 1.87), progression of the disease to higher stages (OR 1.65), severe malnutrition (OR 1.97) and need for ART (14 vs 11.2 %) during the second year.

Three trials with a prospective controlled design assigned half of the clinics or subjects to food assistance and the other half to the control group. In Zambia, a home-based adherence support program provided food supplements to PLHIV on ART with food insecurity attending four of a total of eight clinics [34]. The amount of food received depended on whether the infected adult was the family's primary income earner and on family size, and rations were modified during the course of program implementation. Corn soya blend and vegetable oil were received by all PLHIV, but some received more and also received maize meal and beans. A total of 636 food insecure adults were enrolled (442 receiving food assistance and 194 not receiving assistance). Food supplementation was associated with better adherence to therapy: 258 of 366 (70 %) of patients in the food group achieved an MPR of 95 % or greater versus 79 of 166 (48 %) among controls (relative risk, RR 1.5; 95 % CI [1.2–1.8]). No significant effect of food supplementation on weight gain or CD4 cell response was observed.

The trial by Martins et al. [30] was conducted among treatment naïve pulmonary TB patients in Dili, Timor-Leste who started TB treatment. Patients at three clinics were randomly allocated to receive food assistance ($n = 137$) or just nutrition advice ($n = 133$). Patients receiving food assistance received a warm meal at the clinic at mid day every day during the first 2 months of treatment and after that received a take home ration of red kidney beans, rice and oil, sufficient to prepare one meal for one adult per day. Treatment success before the violent conflict in Timor-Leste, which started on 28 April 2006, was 84 % in the intervention and 85 % in the control group and after the conflict it was 50 % in the intervention and 56 % in the control group. During the intensive phase, compliance was 86.7 % in the intervention and 91.4 % in the control group ($n = 0.02$), but it is not clear from the paper how 'compliance' was defined. Weight gain was higher in the intervention than in the control group at both

8 weeks (5.2 vs 3.6 kg, $p = 0.04$) and 32 weeks (10.1 vs 7.5 kg, $p = 0.04$).

The study by Jahvani and Sudha [31], which was conducted among wasted TB patients in India who started TB treatment, randomly allocated 50 of 100 patients to food assistance in the form of personalized dietary advice, sweet balls made from wheat flour, caramel, groundnuts and vegetable ghee (600 kcal/day) that had to be consumed in front of the Anganwadi worker daily as well as a take home ration of sprouted grams and nuts (100 g/day). Among smear positive patients (36 per group), the sputum conversion rate was 97.2 % in the food supplemented and 80.6 % in the control group. Treatment completion rate was 98 % in the food supplemented and 82 % in the control group.

Discussion

Each of the ten studies that were identified provided some form of food assistance to vulnerable people with either TB disease or HIV infection, and assessed adherence to clinic appointments, medication possession, compliance to treatment and/or treatment completion. Eight of the ten studies reported improved adherence or treatment completion among people that received food assistance. Below we compare different characteristics as well as the design of the ten studies.

The studies were conducted in very different settings, including the US (TB, [28]), Haiti (PLHIV, [32]), Brazil (TB, [29]), Zambia (PLHIV on ART, [34], [36]), Mozambique (PLHIV on ART, [37]), Niger (PLHIV on ART, [35]), India (TB, [31] and PLHIV, [33]) and Timor-Leste (TB, [30]). Some studies were conducted among a subgroup of most vulnerable patients, i.e. patients defaulting on TB treatment [28], wasted TB patients [31], food insecure PLHIV on ART [34–36], food insecure PLHIV with low BMI and/or other aggravating factors [37] or assigned treatment by vulnerability status ([32]—only PLHIV with food insecurity were eligible for food assistance, the non food insecure formed the control group). The more vulnerable the participants, the more likely it is that providing food assistance will have an impact on adherence and/or treatment completion.

The number of subjects involved in the studies was relatively small, ranging from a total across intervention and control groups of 100–107 [28, 31] to 600–636 [32, 34].

Outcomes differed, particularly among the TB compared to the HIV studies. In the TB studies [28–31] completion of TB treatment was the primary outcome. In the Martins study among TB patients [30], the secondary outcome, adherence, was measured by recording clinic attendance and directly observed treatment (daily in the intensive phase and fortnightly in the continuation phase)

and through interview and pill counts (in the continuation phase), but the authors did not state how they used this information to classify subjects into adherent and non-adherent. For the studies among PLHIV; three studies used pharmacy refill data to determine the MPR [34, 36] or the opposite, i.e. the days without treatment [37]; one study checked pill counts and discussed adherence with patients [35], but like in the Martins et al. [30] study did not state how adherence was classified; and two studies that also included PLHIV not on ART reported or classified by proportion of clinic appointments that were kept [32, 33]. The fact that ART is for life makes studies to assess the impact of different interventions on adherence to treatment and retention in care for PLHIV complicated and often limited to the initial phase of treatment and to medication possession, while long-term retention in care is the ultimate goal [38]. Also, assessing actual compliance with the treatment regimen is very difficult. When adherence expressed as MPR is related to clinical outcomes, this is interpreted as an indication that MPR represents compliance in terms of actually taking the medication [36, 37].

The form, amount and way in which food assistance was provided also varied widely. One study, in the US, provided grocery coupons [28]; the studies in Brazil [29], Haiti [32] and Africa [34–37] gave food that provided for needs of the infected family member as well as for other family members, whereas the studies in Timor-Leste [30] and India [31, 33] provided just a proportion of the needs of the infected individual, including a ready-made food that had to be consumed at the clinic in two of the studies [30, 31]. The study by Martins provided the smallest transfer value and consuming the meal that was provided during the 2 months-long intensive treatment phase at the clinic, daily, at mid-day was not convenient for several of the participants [30].

Also the reasons to provide the treatment and the way in which it was done differed. Some programs based eligibility on food insecurity, others also on clinical conditions (low BMI, low CD4 count, advanced stage of disease), others on demonstrated non-adherence, while others provided it to all participants in the program. Another important difference was that some programs made receiving the food conditional upon presenting for clinic appointments and/or medication refills, which makes it more likely that participants adhere. This could have been one of the reasons that Posse et al. [37] in their study in Mozambique did not find improved adherence among PLHIV that received food assistance. Food recipients were targeted based on low BMI and poor or low income and receipt of food was unconditional, i.e. it was given regardless of whether patients attended clinic appointments, and it was provided at a different place than the medication. It could be that patients prioritized obtaining food over medication, which would also indicate that they

Food and Nutrition Assistance as Enablers for Adherence to Treatment		
Levels of engagement	Behavioural	Biological
Community level	<ul style="list-style-type: none"> • Establish social safety nets serving PLHIV (HIV sensitive / HIV specific) <ul style="list-style-type: none"> ◦ Food as an enabler to remain in care/ food centers – short/medium term ◦ Economic strengthening activities linked with food and nutrition support – longer term ◦ School feeding • Nutrition knowledge among community health workers • Resilience building, e.g. food for assets • Education, including nutrition • Nutrition messaging, BCC¹ 	<ul style="list-style-type: none"> • Linkages of the communities with the health system for longer term solutions <ul style="list-style-type: none"> ◦ Task shifting – Delegation of tasks to staff with lower qualifications to alleviate burden on health systems in resource limited settings (e.g. Nutrition Assessment and Counseling, NAC) ◦ Referral through community workers ◦ Nutrition support centers - community role in food distribution for beneficiaries based on clear entry and exit criteria
Health systems level	<ul style="list-style-type: none"> • Linkages with sexual and reproductive health community programs • Nutrition messaging, BCC¹ • Linkages with government social safety nets with a food assistance component for PLHIV <ul style="list-style-type: none"> ◦ Example: Referral to resilience building activities • Support to pregnant women for the prevention of mother to child transmission 	<ul style="list-style-type: none"> • Regular nutrition assessment • Referral to food and nutrition assistance <ul style="list-style-type: none"> ◦ Therapeutic and supplementary foods ◦ Tracking malnourished individuals • Nutrition counselling • Referral to community health workers for follow up

(1) Behaviour change communication

Fig. 1 Role of food and nutrition support as enablers of adherence to treatment and retention in care, distinguishing behavioural and biological components and engagement at community and at health systems level

may have had a poor understanding of their need for ART. However, it could also be that they obtained their medication elsewhere or that the pharmacy records used for the study were of poor quality (note that intervention and control clinics were from different provinces).

This brings us to the variation of the strength of study designs. Only two studies were individually randomized controlled trials [30, 31], with Martins et al. [30] also reporting concealed treatment allocation. All the other studies were prospectively embedded in, or evaluated retrospectively, an actual program that aimed to improve clinic attendance or treatment adherence or completion by providing enablers in the form of food assistance. While non-randomized controlled trials have a weaker study design, research designs were strengthened by comparing baseline characteristics among intervention and control groups and/or by using PSM to maximize comparability among intervention and control groups. One important weakness of retrospective studies though is that they rely on routine data that are available at clinics and pharmacies, the quality of which may be lower than of data that are collected for research purposes. However, despite these limitations, the reported findings of better TB treatment outcomes and better adherence to clinic visits or medication possession among PLHIV who received food assistance in all but one of the eight non individually randomized controlled trials are largely consistent and plausible.

As mentioned above, there are different hypotheses for the fact that two studies did not find improved TB

treatment completion [30] or ART adherence [37]. For the study by Martins et al. [30], the fact that treatment compliance and completion, before the conflict in Timor Leste, were already high (85 % treatment success and 91.4 % compliance in control group), may mean that the reasons for non-compliance in this population are very specific and not amenable to improve by food assistance. Furthermore, the enabling effect of the food assistance may have been limited because the amount of food provided was relatively small and coming to the clinic every day for the first 2 months to consume a midday meal was inconvenient for many. For the study by Posse et al. [37], which retrospectively compared data from clinics in one province that received food assistance and others in another province that did not, the receipt of food was not conditional upon clinic visits or obtaining medication, and the quality of data may have differed between the intervention and control clinics.

Conclusion

Available studies indicate that in most cases, enablers in the form of food assistance improve TB treatment outcome and/or adherence to clinic visits or treatment regimens among PLHIV when implemented among populations affected by food insecurity and poverty, particularly when the food transfers are conditional upon clinic or pharmacy visits. TB treatment usually lasts 6–9 months and

adherence is very important to avoid developing drug resistance. Therefore, in contexts where patients struggle to adhere and enablers are likely to make a difference as they support clinic visits and/or provide an in-kind transfer to compensate for lost income and increased expenses, it makes sense to support patients by providing food assistance, which can be in-kind, with vouchers or as cash. The type and size of the transfer needs to be determined locally and be selected based on its potential for enabling staying in care, adhering to treatment and possibly also for modifying risk behavior that affects infection transmission. Monitoring treatment completion before and after the introduction of the enablers or in clinics with and other without such a scheme, such as by many of the studies reviewed, will give a good idea of the difference the enabling scheme makes in the particular setting.

Furthermore, when patients receive a special nutritious food to treat malnutrition, this will also have an enabling effect, which may or may not need to be enhanced by additional food assistance. Thus, food interventions can have both a biological and a behavioural effect. Since special nutritious foods are typically provided to treat malnutrition, food assistance as enabler may have to be continued after the provision of specialized nutritious foods.

For PLHIV, once ART is started, it is for life. A critical period is the initial phase of treatment when clinical symptoms may be experienced, side effects of treatment may be difficult to tolerate, an adherence routine needs to be established, and people may have to start rebuilding their livelihoods. Supporting the start of treatment with an enabler in the form of food assistance will therefore be helpful for food insecure people, similar to the case of TB patients. However, enabling people to continue to adhere, throughout the rest of their lives, is the ultimate goal. Unfortunately, limited experience exists with that, since the focus has mainly been on getting people started on treatment rather than on retaining them in care. Furthermore, adherence has typically been defined in terms of medication possession rather than remaining in care and adhering to treatment over a number of years, and this would also not be practical as an outcome for a randomized controlled trial [38].

In certain situations, food assistance may be required for longer than possible or cannot be justified considering the needs of other vulnerable groups in the population. Integrating HIV care and support with other programs and services that provide services to vulnerable people would be an appropriate strategy, aiming to achieve longer term adherence and retention in care and rebuild livelihoods. For such integration, communities and health systems should work together to create enabling environments, both from a biological and a behavioral perspective. Based on frameworks

proposed by Mehra et al. [39], Fig. 1 shows a 2×2 matrix delineating the role of food and nutrition support as an enabler for adherence to treatment and retention in care. Here, food assistance may be part of nutrition assistance counseling and support (NACS) and/or of livelihood and resilience building activities. While the interventions under ‘health systems’ are focused on the biological aspects of food assistance, such as deciding on eligibility for therapeutic or supplementary foods, and individual assessment and counseling for good nutrition, the behavioral and some of the logistical aspects of the enabling environment created by food assistance can be implemented at the ‘community level’, closer to where PLHIV live. For communities (top right box of Fig. 1), this could mean performing tasks that are typically done in more medical environments (i.e. task shifting, [40]), for instance, assessing and tracking malnourished clients by lay community health workers (CHWs) trained for specific tasks or establishing nutrition support centers for PLHIV equipped to distribute therapeutic or supplementary foods, eligibility for which is decided by the clinician based on adherence and nutritional status. For health systems, the linkages with communities could be collaborating on the above-mentioned shift of tasks as well as referring PLHIV to HIV sensitive or HIV specific safety nets (e.g., resilience building, livelihood support) and linking them to programs for prevention of mother to child transmission and sexual and reproductive health programs implemented in the community.

Since the need for enablers and the most suitable type and transfer amount to support TB treatment and retention in HIV care and adherence to ART are context specific, varying across populations and specific subgroups among them, many valuable lessons can be learned from programs that achieve good long-term adherence and high retention rates, including how they have linked the health system and community services. It is therefore very important that programs monitor changes of key outcomes when introducing or modifying enabler schemes and use strong designs that do not only minimize the risk of bias, but also enable understanding of the specifics of program implementation, including care, treatment and enabling scheme that are provided and client perceptions of these.

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