

## Supplementary File

Table 1. Summary of Ethiopia studies on therapeutic foods: Ready-to-Use Therapeutic Foods (RUTF)

Citation	Objective	Design	Study population (# of subjects, age, population)	Type of therapeutic food	Key results	Observed trends/ remarks/ conclusions
<b>RUTF use in non-HIV population</b>						
Chaiken et al. 2006	-To compare the effectiveness of the community-based therapeutic care (CTC) strategy in combination with conventional treatments for acute malnutrition.	-Case study; -Program impact evaluation based on secondary data.	-Children (6-59 months) with severe acute malnutrition in Sidama Zone of south Ethiopia.	-RUTF: Plumpy'Nut®	Key findings indicated the CTC model for SAM with the use of RUTF (Plumpy'Nut®) had comparable rate of recovery with international standard and far higher coverage compared to the traditional center-based treatment; -Families and communities became key participants in the rehabilitation of their children, and benefited from the increased knowledge base of the local health workers.	-Study concludes that CTC with the use of RUTF was effective in addressing nutritional emergencies; -Effectiveness of CTC is the result of local capacity building, timely & sufficient delivery of supply, coordinated effort between non-governmental organizations (NGO) and local and national governments.
Belachew & Nekatibeb, 2007	-To document the experiences for rolling out of the outpatient program (OTP) service at the wider scale with the aim of assessing the strengths and weaknesses of the project and suggest recommendations for future programming.	-Qualitative method: Focus group discussion, observation & in-depth interview of key informants.	-36 key informants; a total of 30 Focus Group Discussion participants in three regions (Southern, Nations, Nationalities and People's Region (SNNPR), Addis Ababa & Oromia).	RUTF: Plumpy'Nut®.	-Enhanced utilization of health services (such as use of Plumpy'Nut®), resulting in faster recovery of malnourished children in OTP; -An understanding by providers that malnourished children can be treated without being admitted to health facilities.	-OTP was shown to be successful but irregularity and incompleteness of supply availability of Plumpy'Nut® was noted as one of the limiting factor.
Chandani et al. 2012	-To understand supply chain related factors that affect the availability of products at the community level; -To improve supply chains for better community level management of pneumonia and other childhood illnesses.	-Survey design and observation.	-Community health workers and their health product supply chain.	RUTF—no specific information on exact type#.	-Limited product availability in Ethiopia: More than half Community health workers reported stock-outs of at least one product on the day of the assessment.	-Five products considered including RUTF; -lowest product availability in Ethiopia.
Tekeste et al. 2012	-To determine the average cost of treatment of a severely malnourished child in-patient Therapeutic Feeding Centre (TFC) and Community-based Therapeutic Care (CTC) in SNNPR; - To determine the effectiveness of TFC and CTC as measured by the clinical outcomes and; -To determine and compare the cost effectiveness of the two programs.	-Qualitative & quantitative approach: Employed societal perspective (considers costs (of CTC & TFC) to all sectors of the society).	-Sectors considered: Save the Children USA, UNICEF, government health facilities; -306 caretakers of children treated in the program (to estimate cost to parents).	-RUTF/ Milk based formula#.	-Cure rates were high at ~95% for both the CTC and TFC treatment programs; -Average cost per child was \$285 in TFC and \$135 in CTC; -Institutional cost per child treated in TFC was \$262 (of this, 47% was personnel cost), while it was \$129 in the CTC (and 43% of this went into procuring more RUTF); -Opportunity cost per caretaker in TFC was \$21 but only \$6 in CTC.	-Community-based treatment care of SAM children was less than half as costly as in-patient care in the setting studied; -Study also suggested local production of RUTF could further reduce cost of CTC of SAM children as RUTF accounted the highest cost.
Yebo et al. 2013	-To assess the outcomes (recovery, default, non-responder and mortality rates) and estimating the length of intervention period to reach the minimum sphere standard recovery rate among the cohort of 6-59 months age SAM children relying on their individual OTP record cards in Tigray region, Northern Ethiopia.	-Retrospective cohort study.	-628 Children (6-59 months of age) admitted to OTP programs due to SAM in 12 Health Posts and 4 Health Centers.	-RUTF: Plumpy'Nut®.	-Rates of recovery, defaulter, mortality and weight gain were 61.78%, 13.85%, 3.02% and 5.23 gm/kg/day, respectively; -Median recovery time was 7 weeks.	-Plumpy'Nut® had positive effect on time to recovery (every additional Sachet of Plumpy'Nut® increased recovery rate by 4%) -Children admitted into the program without complication had higher likelihood of fast recovery; -Recovery rate was below *Sphere minimum.

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<b>RUTF use in non-HIV population</b>						
Ryan et al. 2014	-To develop a comprehensive linear programming (LP) tool to create novel RUTF formulations for Ethiopia, thereby to minimize the ingredient cost of RUTF for the case of Ethiopia.	-Systematic survey of national and international crop and animal food databases.	-Local and international databases search for possible ingredients for RUTF in Ethiopia; -Modeling of ingredients for RUTF.	-Novel RUTF for Ethiopia by using the LP tool.	-LP tool found around 32 formulations that were predicted to be feasible for creating a paste, and these were prepared in the laboratory. -Final palatable formulations include, ingredients such as fish, different dairy powders, and various seeds, grains, and legumes; - The LP tool also ensured micronutrient contents within <10% from the laboratory analysis.	-LP tool can be used to develop new RUTF formulations that make more use of locally available ingredients; - LP tool has a potential to develop affordable RUTF formulation, increasing access for more children.
Puett & Guerrero, 2014	-To understand and compare the primary barriers households face when accessing OTP treatment for cases of childhood severe acute malnutrition (SAM) in different cultural settings with different types of implementing agencies (an NGO and a Health Ministry).	-Comparative qualitative analysis involving group and individual interviews.	-Beneficiary communities (households of children who recovered from SAM or defaulted from the program) and staff of SAM treatment services in Tigray Region, Ethiopia (and Sindh in Pakistan); -Three program sites in each country (with a minimum of 10 beneficiaries consulted/site).	-RUTF: Plumpy'Nut®.	-Common barriers identified to accessing SAM services include • Distance • high opportunity costs • knowledge of services • knowledge of malnutrition and • child's refusal of ready-to-use foods	-The selected programs were relatively well established in each country; however, households/ beneficiaries still faced various barriers to accessing the SAM services; -The study recommends that programs should focus on minimizing the identified barriers by modifying service delivery mechanisms (e.g. doorstep delivery, awareness creation in remote areas, integrating SAM service with other community services).
Tadesse et al. 2015	-To examine caregivers' and health workers' perceptions of usages of RUTF in a chronically food insecure area in South Ethiopia.	-Qualitative design (Focus group discussions and individual interviews).	-Caregivers (n=103) of SAM children and Community Health Workers (n=9).	RUTF: Plumpy'Nut®.	-RUTF was perceived and used as an effective treatment of SAM -Sometimes, caregivers also sold RUTF products for income of the household; and hence expected prolonged provision/ supply of the product; -Caregivers also attempted to alter identities of SAM children to have them readmitted at a different facility just to get more RUTF supply; -Health Workers applied various control measure.	-The effectiveness of the community based management of acute malnutrition program has been endangered by the fact that caregivers desired the RUTF product for collective benefits of the household; -Study suggested that intervention on SAM & MAM should also consider addressing the broader needs of poor households to ensure effective use of RUTF for the intended purpose.
Tadesse et al. 2016	-To determine challenges in implementing the critical steps in community-based Therapeutic Care (CTC) programs and caregivers' perceptions of service provision in southern Ethiopia.	-Prospective cohort study.	-1048 caregivers of SAM children (6-59months of age) and 175 Community Health Extension Workers (HEW) from 94 Health Posts from four districts in south Ethiopia.	-RUTF: Not specified#.	-SAM children who received recommend amount of RUTF were only 46.6% and only 19% received antibiotics; -Only 35% of admitted children had uninterrupted supply of recommended RUTF ration (supply was limited at distribution centers, in part, due to lack transportation); -Only 40% of the children who exited the program met the national guideline for exit criteria; -2/3 of all children in the program did not receive home visits from HEWs during their stay in the program as per the national guideline; -Significant proportion of caregivers (43%) and Health Extension Workers (37%) indicated that RUTF products were being sold at market.	-The study noted the existence of inadequate provision of RUTF, unintended use of RUTF products, inappropriate exit from the treatment program; -Ensuring provision of supplies, proper training of providers and supportive supervision have been recommended.
Mengesha et al. 2016	-To assess treatment outcome and factors affecting time to recovery in children with Sever Acute Malnutrition (SAM) treated at Outpatient Therapeutic Care Program (OTP) (in south Ethiopia).	-A retrospective cohort study.	-A total of 348 children (6-59 months) with SAM from 12 Health Posts in Shebedino district -165 (47%) kwashiorkor & 183 (53%) marasmic cases.	- RUTF (Plumpy'Nut®).	-Higher recovery in kwashiorkor (89%) than marasmic (69%) children; -Overall recovery was ~79%; -Median time of recovery was 35 days in kwashiorkor and 49 days in marasmic children; -From the total admissions, 22% were readmitted cases; -delayed recovery were noted in marasmic children, children >3yrs and those <0.24mm/day MUAC gain.	-The study noted that overall recovery rate met the international minimum standard but treatment duration was longer than recommendation (i.e., < 4 weeks); - Factors with positive effect on time to recover were admission weight and rate of MUAC gain; -Older age & type of SAM (marasmus) had negative effect.

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<b>RUTF use in non-HIV population</b>						
Kabalo and Seifu, 2017	-To assess treatment outcomes of SAM and identify factors associated among children treated at Outpatient Therapeutic Program (OTP) in Wolaita Zone, South Ethiopia.	-Retrospective facility-based cross-sectional study design	-A total of 794 children (age 6-59 months) treated in 24 health posts in 2014	-Type of RUTF not specified but Plumpy'Nut* is likely;	-Recovery rate (from SAM) was 64.9%; -Death rate, default rate, weight gain, and length of stay was 1.2%, 2.2%, 4.2 g/kg/day, and 6.8 weeks, respectively. -Children within 25minutes from the treatment site had 1.53 higher odds of recovery than those living >25mintues; -Children with Kwashiorkor had 2.6 higher likelihood of recovery than those with Marasmus; -Children provided with amoxicillin had 1.52 higher odds of recovery than those who did not receive it.	-Recovery rate was below the recommended minimum >75%; -Strengthening capacity of OTP providers was recommended.
Weber et al. 2017	-To determine whether new formulations of RUTF produced using locally available ingredients were acceptable to young children in Ethiopia, Ghana, Pakistan and India.	-4 two-arm, crossover, site-randomized food acceptability trials.	-50 children 8-24 months of age (25/site) with moderate wasting in each country (n~200) were enrolled in the 2-week study.	-An alternative RUTF formula (developed by the linear programming tool) compared with the standard peanut-based RUTF containing powdered milk.	-In Ethiopia, Ghana and India, the local RUTF was tolerated well without increased reports of rash, diarrhoea or vomiting; -Children consumed similar amounts of the local and standard RUTF and preferred them similarly; -Only in Pakistan, mothers perceived children did not enjoy the local RUTF as much as the standard one though the children consumed similar quantities of each product.	-The ingredient cost of all of the RUTFs was about 60% of standard RUTF; -The study recommends further investigation of local RUTFs and suggest that local RUTFs may be of lower cost.
<b>RUTF use in HIV positive patients</b>						
aKebede & Haidar, 2014	-To assess factors influencing adherence to the Food by Prescription (FBP) program among adult HIV positive patients in Addis Ababa, Ethiopia; (adherence to RUF was measured using the Morisky 8-item Medication Adherence Scale (MMAS-8))	-A facility-based, cross-sectional design with quantitative and qualitative approach.	-Adult HIV + patients (n=630); -Age ranged from 18 y -76 y; -Sex: Male = 43%; female = 57%.	-Ready-to-Use Foods (both RUTF and RUSF); - Patients with SAM (BMI <16kg/m2) received 4 sachets of RUTF (Plumpy'Nut*): 2000kcal. - Patients with MAM (≥16 to <17 kg/m2) received 2 sachets of RUSF (RUSF, not specified).	-Level of adherence was found to be 36.3% with a 95.0% response rate; -No significant effect of socio-demographic variables on adherence except educational status (more education, better adherence); - Those who knew about the FBP program 1.78 times more likely to adhere to the nutrition therapy; -Patients not informed about treatment duration; those prescribed >2 sachets/day and had been taking RUF for >4 month were less likely to adhere; - Main reasons for non-adherence: disliking the taste of the RUF and missing follow-up appointments; stigma, sharing and selling food were other reasons.	-Overall, low adherence to the FBP program; -low level of education, poor knowledge on the benefits of RUF, longer program duration, consuming >2 prescribed sachets of RUF/day, and not being informed about treatment duration: key reasons for low adherence; - The study suggests counseling patients on the program's benefits, including the treatment plans to improve adherence.
Bhagavathula et al. 2016	To assess the retention and outcomes of under-nutrition treatment program (for HIV patients involving Ready-to-use Therapeutic Food) in Gondar University Hospital, Ethiopia.	-A retrospective cross-sectional study.	-A total of 636 HIV patients (adults and children) with SAM (240) or MAM (396); -Male and female patients were 49.7% & 50.3%, respectively; -Age group: <18years (62.6%) & >18 years (37.4%).	-RUTF (Plumpy'Nut*)	-44.2% achieved MUAC measures ≥ 125 mm for children and ≥ 21 cm for adults at 4 and 6 months; -70% of those who achieved recovery were children while 29.9% were adults; -Rapid initial response in MUAC to RUTF noted in children (at 2nd month of treatment) while response in adults was at the 4th & 6th months of initiating treatment; -significant association between younger age and MAM to recovery.	- Recovery was only 44%, below Sphere Minimum Standard; - High default (25%), non-responder (19%) and relapse (12%) rates were noted and were higher in adults (>18yrs). -The study speculated that the lower recovery rate/delayed response in adults could be because adults share or sell the RUTF products.

\*The study deals with HIV positive patients with SAM or MAM and involves the use of both RUTF (Plumpy'Nut\*) and RUSF products. However, the study is summarized in Table 1 for convenience;

\*Sphere Minimum Standard is an internationally set minimum standards by humanitarian organizations for humanitarian response/assurances (key indicators in management of acute malnutrition include <10% death in SAM/<3% in MA\*M, <15% default and >75% recovery rates at discharge) (53);

#Not specified but likely Plumpy'Nut\*

Table 2. Summary of Ethiopia studies on supplementary foods: Ready-to-Use Supplementary Foods (RUSF) and Lipid-based Nutrient Supplements (LNS).

Citation	Objective	Design	Study population (# of subjects, age, population)	Type of therapeutic food (RUSF/LNS)	Key results	Observed trends/ remarks/ conclusions
<b>RUTF use in non-HIV population</b>						
Chaiken et al. 2006	-To compare recovery rates of children with moderate acute malnutrition in supplementary feeding programs by using the newly recommended ration of ready-to-use supplementary food (RUSF) and the more conventional ration of corn-soya blend (CSB) in Ethiopia.	-Cluster-randomized effectiveness trial; -Two clusters (districts) randomly assigned to receive CSB or RUSF ration for 16 weeks.	-Children aged 6–60 months (n=1125) with MAM from 10 Health Centers in northern Sidama Zone, south Ethiopia.	-300g Corn-Soya Blend (CSB) plus 32g vegetable oil per child per day; -92g Ready-to-Use Supplementary Food (RUSF) (also known as Supplementary Plumpy; Nutriset) per child per day.	-There was a 15% lower recovery rate in the CSB than RUSF group ( $P = 0.039$ ), (Hazard Rate for CSB children of 0.85 (95% CI: 0.73, 0.99)), -Recovery rates of children at the end of the 16-wk treatment period trended higher in the RUSF group (73%) than in the CSB group (67%) ( $P = 0.056$ ).	-Treatment of MAM with RUSF resulted in higher recovery rates in children, despite larger ration size and higher energy content of conventional CSB ration; -recovery rates for both was below minimum*.
Segrè et al. 2015	-To determine the willingness to pay (WTP) for a week's supply of Nutributter* through typical urban Ethiopian retail channels.	-Survey and experimental design (market simulation), as well as qualitative methods (qualitative interview with participants)	-128 parents of children 6-24 months of age from four urban sites (Central Addis Ababa, peripheral Addis Ababa, Hawassa and Mekelle cities).	-LNS: Nutributter*	-Nearly all (96%) of the respondents had a positive WTP, -Stated WTP was not predictive of actual WTP (there was no association); - Only 25% were willing to pay the equivalent of at least \$1.05 (estimated to be the likely minimum, unsubsidised Ethiopian retail price of 1 week supply of Nutributter*/child; -Those willing to pay \$1.05 for a week's supply of Nutributter* per child included men and women from all wealth categories; -Estimated initial market size for Nutributter* was \$500,000 for all the 4 cities combined.	-The study was indicative of the potential retail distribution of LNS products in Ethiopia and why initial market would be too small for profit oriented food manufacturers.
Tekele et al. 2015	-To assess sensory acceptability of locally-produced chickpea-based ready-to-use supplementary foods (RUSF) among moderately malnourished children (6-59 months).	-“Quantitative descriptive” (cross-sectional survey design)	-Mother-child pairs (n=140) from a total of 10 study sites in 5 districts (from Oromia, SNNPR, Amhara, Somali and Tigray Regions) -Children were 6-59 months with MAM, but no illness.	-Four locally produced chickpea based RUSF (i.e., (chickpea), (chickpea + maize), (chickpea + maize + soy) and (chickpea + soy).	-Children from 48-59months of age consumed more RUSF than children who were 6-11 months; -regional differences were seen in the acceptance of “chickpea only” and “chickpea + maize + soy” RUSF products -Mothers’ perception of appearances and overall acceptability of the products (chickpea and chickpea + maize + Soy?) were mostly similar; -Overall, the chickpea only product was rated higher than the other three for taste, texture and appearance by the mothers of the participating children.	-Study recommends that the WFP's purchase for progress (P4P) program can utilize this opportunity to encourage agricultural cooperatives to produce more chickpeas for the market.
Karakochuk et al. 2015	-To evaluate food sharing practices in households receiving corn-soya blend (CSB) and ready-to-use supplementary food (RUSF) in southern Ethiopia.	-Cluster randomized effectiveness trial (31)	-MAM children 6–60 months (n=1125) from 10 supplementary feeding sites in two Districts of Sidama zone, south Ethiopia.	-Corn-Soya Blend (CSB) flour and RUSF (Nutriset supplementary Plumpy or Plumpy'Sup™) (children received either product depending on which district they were from).	-CSB was shared with greater number of family members and with greater quantity than RUSF; -Higher recovery rates were observed in the RUSF group -At the end of 16 weeks, recovery rates were 67% in the CSB 73% in the RUSF group.	-Study noted presence of significant sharing of food and suggested strengthening the nutrition education component of supplementary feeding program emphasizing prescribed foods are medicine and are meant to treat sick children.
<b>RUSF use in HIV positive patients</b>						
Olsen et al. 2013	-To explore the use, perceptions, and acceptability of Ready-to-Use Supplementary Food (RUSF) among adult HIV patients in Jimma, Ethiopia.	-Qualitative method: 24 in-depth interviews of participants and direct observation	- HIV infected adults (n=24) initiating ART	-RUSF: Plumpy'Sup™.	-The RUSF was generally well accepted and thought beneficial by participants; -RUSF was considered to fill the nutrition gap, build the body and protect the body from the negative effect of ART drugs; -The supplement was considered as having “medicinal qualities” and hence, was exempt from social and religious restrictions -Main concerns related to RUSF use was the risk of HIV disclosure and its social consequences;	-Study recommends that nutrition support programs should consider social context to minimize unintended consequences (stigma and discrimination) to beneficiaries and improve treatment outcomes.

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<b>RUSF use in HIV positive patients</b>						
Olsen et al. 2014	-To determine the effects of lipid based nutritional supplements with either whey or soy protein in patients with HIV during the first three months of antiretroviral treatment (ART) and to explore effects of timing by comparing supplementation at the start of ART and after three months delay.	-Randomized controlled trial	-Adults (age ≥18y) with HIV eligible for ART with body mass index (BMI) >16 (n=318; women= 210)	-LNS containing 32g of either whey protein concentrate 80%, or soy protein isolate, developed based on the Plumpy'Sup™ formula by Nutriset, France; -Participants received 200g/day (4600 kJ).	-Increased lean body mass by (whey group 0.85 kg; soy group 0.97kg) more than control group, at three months; -increased gain of grip strength of 0.68 kg (-0.11 kg to 1.46 kg) for the whey supplement group and 0.93 kg (0.16 kg to 1.70 kg) for the soy supplement group; -Total weight gain increased by 2.05 kg and 2.06 kg for the whey and soy groups, respectively; -whey supplement group overall CD3 counts improved by 150 cells/μL; -effect on immune recovery in the soy group was not significant.	-Lipid based nutritional supplements improved gain of weight, lean body mass, and grip strength in patients with HIV starting ART; -Supplements containing whey were associated with improved immune recovery.
Abdissa et al. 2015	-To assess/evaluate the effect of LNSs on the plasma concentrations of the nonnucleoside reverse transcriptase inhibitors (NNRTIs) efavirenz (EFV) and nevirapine (NVP) in HIV-infected adults initiating ART in Ethiopia.	-Randomized control trial; -Participants randomly assigned in three groups (i.e., LNS whey protein group, LNS soy protein group and no supplement group)	-HIV infected adults (n=282, with BMI >17 and n=36, with BMI of 16-17) eligible for ART in Jimma University Hospital, Jimma Health Centre & Agaro Health Centre	-LNS product containing whey protein (LNS/w) or LNS product containing soy protein (LNS/s) -LNS dose: 200gm/day	-Nevirapine concentrations in patients with BMI > 17 kg/m2 were lower in the LNS/w and LNS/s groups by a median of -2.3 μg/mL and, -2.1 μg/mL, respectively, compared with the no supplement group. -Plasma efavirenz concentration: not affected by LNS -Adherence to LNS: ~28% poor adherence to LNS products (i.e., <75% consumption of daily supplement) and adherence did not differ between whey and soy groups;	-LNS was associated with lower plasma nevirapine concentrations: possible drug-LNS interactions (clinical relevance, not clear) -22 subjects excluded from the study because they disliked the LNS products.
Tesfaye et al. 2016	-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.	-A randomized controlled trial (within public Health facilities in Jimma, S. West Ethiopia)	-People living with HIV (PLHIV) eligible to start ART (body mass index >17 kg/m2); -n=282 and 186 (66.0%) were women.	-LNS, daily supplements of 200 g containing whey or soya either during the first 3 months or the subsequent months of ART.	-At 3 months, participants who received LNS showed better quality of life than those who only received ART without LNS; -At 6 months, no difference in total quality-of-life score between early and delayed supplementation groups; -The early supplementation group showed higher scores on the social and spirituality domains than the delayed group.	-LNS given during the first three months of ART improves the quality of life of PLHIV.
Yilma et al 2016	-To compare the levels of serum 25-hydroxyvitamin D (25OHD) in HIV-positive and HIV-negative persons, and investigate the role of nutritional supplementation and antiretroviral treatment (ART) on serum 25OHD levels.	-A randomized nutritional supplementation trial (Jimma University Specialized Hospital, Ethiopia)	-HIV patients: A total of 348 HIV-positive and -100 HIV- negative persons were recruited; -Age ≥18y and BMI>16kg/m2; -Not pregnant or lactation & no current use of nutritional supplementation.	- LNS: 200 g/d (with whey (LNS/w) or soya (LNS/s) protein) v. no supplementation during the first 3 months of ART; -The LNS contained 10μg/200g day vitamin D3 (twice the recommended intake).	-Median baseline serum 25OHD level was higher in HIV-positive than in HIV-negative persons; - Supplemented group had a 4-1 nmol/l increase in serum 25OHD and -Non-supplemented group had a 10-8 nmol/l decrease in serum 25OHD level after 3 months of ART.	-Vitamin D containing nutritional supplementation prevented a reduction in serum 25(OH)D levels in HIV-positive persons initiating ART; -The study suggests vitamin D replenishment may be needed to prevent reduction in serum 25OHD levels during ART.

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