

Costs and Cost-effectiveness of Small-Quantity Lipid-based Nutrient Supplements

Working Group on Cost and Cost-effectiveness,¹ SQ-LNS Task Force

Introduction

Although there has been some progress towards reducing the prevalence of child undernutrition at the global level, most countries are not on track to reach targets for stunting (low height-for-age) or wasting (low weight-for-height), and the prevalence of anemia (low hemoglobin) remains high (1, 2). Because child undernutrition has serious short- and long-term adverse effects on health, development and human capital (3-6), scaling-up of effective strategies to accelerate progress is needed. Children 6-23 months of age are particularly vulnerable to stunting, wasting, and iron-deficiency anemia due to the poor nutritional quality of complementary food diets in many populations (7). Encouraging provision of a diverse diet of nutrient-dense foods at this age is essential in all countries, but in low-income populations the cost of a nutritionally adequate diet for young children is generally prohibitively expensive (8, 9). For this reason, fortified products for infants and young children have been developed and evaluated in numerous studies. Among these products, small-quantity lipid-based nutrient supplements (SQ-LNS) have the strongest evidence base demonstrating beneficial effects on multiple outcomes including reduced mortality (10), stunting, wasting, anemia, and impaired child development (11). This evidence led to SQ-LNS being included in the 2021 Lancet series list of recommended approaches to reduce child malnutrition (12).

SQ-LNS provide multiple micronutrients embedded in a small amount of food (~20 g/d, ~100-120 kcal/d) that also provides energy, protein, and essential fatty acids. They are based on the same type of lipid-based food matrix used for products intended for the treatment of wasting (ready-to-use therapeutic food (RUTF) and ready-to-use supplementary food (RUSF)), which do not require preparation or refrigeration. However, SQ-LNS are designed for the *prevention*, not treatment, of undernutrition and thus the daily ration is much smaller than is the case for RUTF and RUSF and accordingly the micronutrient density (per gram) is much higher (https://sqlns.ucdavis.edu/FAQs). Because of the small daily ration, SQ-LNS are considered a type of home fortification (like micronutrient powders), as they can be mixed with foods prepared for infants and young children in the home to enrich nutrient content. But unlike micronutrient powders, SQ-LNS can also be eaten as is, if preferred by the child or caregiver. Use of SQ-LNS is not a stand-alone intervention and should always be accompanied by messaging to reinforce infant and young child feeding (IYCF) recommendations, including continued breastfeeding, age-appropriate feeding practices and provision of healthy complementary foods.

The evidence for preventive effects of SQ-LNS on adverse outcomes is based on meta-analyses of 14-18 randomized controlled trials that included >37,000 children 6-23 months of age in low- and middle-income countries (10, 11, 13-15). As shown in **Figure 1**, these demonstrated substantial reductions in all-cause mortality, wasting, stunting, iron-deficiency anemia and developmental delay. These results have led to increased interest in scaling-up SQ-LNS for vulnerable populations (16). Such efforts require information about the cost and cost-effectiveness of including SQ-LNS within



programs in various settings. To address this need, the Cost and Cost-effectiveness Working Group of the SQ-LNS Task Force (<u>https://sqlns.ucdavis.edu/taskforce</u>) compiled information from projects in several countries that had collected data to estimate costs and/or cost-effectiveness. This technical brief first presents the SQ-LNS cost estimates, and then describes information on cost-effectiveness, contextual factors that may influence cost-effectiveness, benefit-cost estimates, research needs, and policy implications.



FIGURE 1

Costs of SQ-LNS

Costs for a given intervention can be estimated based on a societal perspective (i.e., accounting for all resources required to provide and access the intervention for all stakeholders), or a narrower financial perspective (e.g., limited to the costs incurred only by implementers). The societal perspective includes all costs, regardless of who incurs them, including the estimated value of inputs that are not paid for, such as volunteer community health worker time or caregiver time to participate (i.e., opportunity costs). Studies based only on financial costs do not include opportunity costs. This may lead to different cost estimates for the same intervention.

Table 1 provides cost information for the projects identified by the Working Group that included detailed costing information for the distribution of child SQ-LNS and associated activities. Three of these case studies used a societal costing perspective, and 3 used a government or non-government organization (NGO) perspective. For 5 of the 6 case studies, cost data were collected using an "ingredients", activity-based, approach (17). The target age range for SQ-LNS was 6-18 or 6-23 mo. The number of recipients per year ranged from 3,250 to 14,550 in the 4 case studies that were based on the actual numbers of children receiving SQ-LNS in the programs. For the other 2 case studies, modeling was used to extrapolate the cost of providing SQ-LNS to all rural, age-eligible children in Uganda (18) and Bangladesh (19). For Uganda, costs were adapted from a detailed costing study of an actual micronutrient powder program in Uganda. Costs in the Bangladesh case study were based on a community health program implemented in 2 rural northwest districts, Rangpur and Dinajpur, that incorporated the distribution of SQ-LNS. Because these two districts were similar to the national average in population density and other characteristics (20), national coverage with similar community health programs is very high, and the number of households per community health worker was typical of such programs (21), costs were extrapolated to a scenario in which target-age children in all rural unions in Bangladesh would be provided with SQ-LNS. In 4 case studies the delivery platform was a community-based health worker program and in the



other 2 case studies it was health clinics. Two case studies involved distribution of SQ-LNS directly to households either monthly (Bangladesh) or every 3 months (Uganda). In the other 4 case studies, participants received SQ-LNS when they attended regular community meetings or came to the health clinic, usually monthly. Intended duration of supplementation was 12 months in 4 case studies and up to 18 months in 2 case studies. Coverage ranged from 37% in Burkina Faso to 95-97% in 3 of the programs; for Uganda and Bangladesh modeling, hypothetical coverage was assumed to be 100%. Coverage was low in Burkina Faso due in part to low attendance at preventive well-baby clinics organized at the first-line health facilities, the platform used to distribute SQ-LNS. All programs included services other than provision of SQ-LNS, usually health and nutrition services and behavior change communication (BCC)/nutrition counseling. In general, personnel costs for including SQ-LNS in these programs were based on the estimated share of staff time spent on SQ-LNS distribution to caregivers.

TABLE 1 – SQ-LNS COST FOR 6 CASE STUDIES

Country	Uganda ¹	Madagascar ²	M	ali ³	Burkin	a Faso ⁴	Niger ⁵	Bangladesh ⁶
Costing perspective and time horizon	Societal 2021-2031 ⁷	Government 2014-2016	Societal 2014-2016		Societal 2014-2016	I NGO/ Government 16 2023-2024		NGO/ Government 2022-2031 ⁸
Costing approach	Ingredients, activity- based	Product cost + sensitivity analysis for programmatic costs ⁹	Ingredients, based	activity-	Ingredients, activity- based		Ingredients, activity- based	Ingredients, activity- based
Target age range	6-18 mo	6-18 mo	6-23 mo		6-23 mo		6-23 mo	6-18 mo ¹⁰
Average # recipients/y	1,118,34011	3,250	14,550		2,283		13,674 (10,256 person years)	1,669,74211
Delivery platform	CHW program	CHW program	CHW progra	m	Health centers		Health centers	CHW program
Mode & frequency of distribution	To households every 3 mo	To communities every week	To participar monthly me	nts at etings	To participants at monthly well-baby visits		To participants at monthly screenings	To households every month
Intended duration of supplementation per child	12 mo	12 mo	Up to 18 mo		Up to 18 mo		9 mo	12 mo ⁹
Actual coverage	Assumed 100%	Ever: 95% Previous month: 89%	Average: 60% Plateau: ~68	%; %	Average: 37%; Plateau: ~51%		N/A	97%
Other program services	Health services, BCC	Health and nutrition services, BCC	Screening & acute malnu	referral for trition; BCC	Screening & referral for acute malnutrition; BCC		Health services; BCC for IYCF; family MUAC; screening and referral for acute malnutrition	Health services, BCC
Shared costs	Based on share of staff time spent on SQ-LNS delivery		Based on sh time spent o activity relat SQ-LNS deliv	are of staff n each ed to very	Based on share of staff time spent on each activity related to SQ-LNS delivery		Costs below are those directly linked to transport, storage and distribution of SQ-LNS	Costs below are those directly linked to delivery of SQ-LNS and related BCC for participants
Annual costs (2021 USD per child):			Observed costs ¹²	Modeled costs ¹³	Observed costs ¹²	Modeled costs ¹³		
Product only (SQ- LNS)	23	47	32	32	46	46	26	34
Total product procurement	35	50	45	45	49	49	33	39
Total non-product program costs	20		11	8	47	22	13	10
Total costs	55	50 ⁹	56	53	96	71	46	48

BCC, behavior change communication; CHW, community health worker; IYCF, infant and young child feeding; MUAC, mid-upper arm circumference; USD, U.S. dollars

¹Adams KP, Vosti SA, Arnold CD, Engle-Stone R, Prado EL, Stewart CP, et al. The cost-effectiveness of small-quantity lipid-based nutrient supplements for prevention of child death and malnutrition and promotion of healthy development: Modelling results for Uganda. Public Health Nutrition. 2023:1-13.



TABLE 1 continued

²Integration of nutrition counseling, nutrition supplementation and parenting support into Madagascar's national nutrition program: The Mahay clusterrandomized effectiveness trial, Endline Impact Evaluation Report, Strategic Impact Evaluation Fund

³Huybregts, L., le Port, A., Becquey, E., Zongrone, A., Barba, F. M., Rawat, R., Leroy, J. L., & Ruel, M. T. (2019). Impact on child acute malnutrition of integrating smallquantity lipid-based nutrient supplements into community-level screening for acute malnutrition: A cluster-randomized controlled trial in Mali. PLoS Medicine, 16(8). <u>https://doi.org/10.1371/journal.pmed.1002892</u>. Costing study publication in progress.

⁴Becquey, E., Huybregts, L., Zongrone, A., le Port, A., Leroy, J. L., Rawat, R., Touré, M., & Ruel, M. T. (2019). Impact on child acute malnutrition of integrating a preventive nutrition package into facility-based screening for acute malnutrition during well-baby consultation: A cluster-randomized controlled trial in Burkina Faso. PLoS Medicine, 16(8). <u>https://doi.org/10.1371/journal.pmed.1002877</u>. Costing study publication in progress.

⁵These costs represent a real-life budget for an SQ-LNS distribution program in Dakoro, Niger, through USAID's International Food Relief Program (IFRP). The SQ-LNS distributions are integrated into ALIMA-supported Ministry of Health nutrition and health programs in which many positions and activities are already routinely financed. Health centers are chosen to participate according to whether the number of children in a health zone aligns with the maximum amount of SQ-LNS available in the IFRP request for proposals.

⁶Costs adapted from Humber J, Vosti SA, Cummins J, Mridha MK, Matias SL, Dewey KG. 2017. The Rang-Din Nutrition Study in Rural Bangladesh: The Costs and Cost-Effectiveness of Programmatic Interventions to Improve Linear Growth at Birth and 18 Months, and the Costs of These Interventions at 24 Months. Washington, DC: FHI 360/FANTA.

⁷Cost estimates adapted and extrapolated from cost data collected in 2016 (see Schott W, Richardson B, Baker E, D'Agostino A, Namaste S, Vosti SA. Comparing costs and cost-efficiency of platforms for micronutrient powder (MNP) delivery to children in rural Uganda. Annals of the New York Academy of Sciences. 2021;1502(1):28-39).

⁸Cost estimates adapted and extrapolated from cost data collected in 2012-2015 (see Humber et al.).

⁹Programmatic costs (not included in the analysis) would include salary for CHWs, materials for site, NGO supervision, training (\$3.33 per child per year, with an average site having 200 children 0-24 mo). Imputing 15% of the total cost to SQ-LNS would imply an annual programmatic cost that is attributed to SQ-LNS of \$0.5 per child per year.

¹⁰For cost analysis; actual project provided supplements beginning at 6 mo of age and continuing until 23 mo of age

¹¹Hypothetical, for modeling

¹²Observed costs are the costs that correspond to the observed level of SQ-LNS distribution coverage (37% in Burkina Faso and 60% in Mali)

¹³Modeled costs assume that the SQ-LNS distribution coverage was 100%. For this purpose, variable costs were increased to the amount needed to cover all eligible children, whereas fixed costs were divided by the number of eligible children. Costs of overhead, indirects, startup, annualized capital, community sensitization, and capacity building were considered fixed. Costs of product, shipping, handling, storage, and beneficiary costs were considered variable.

Product costs were based on the cost to purchase SQ-LNS at the time of each costing study. When expressed in 2021 USD, these ranged from 23 to 47 USD per child-year. Total product procurement cost (including shipping and handling, customs, and storage), ranged from 33 to 50 USD per child-year across the 6 case studies. In September 2023 the cost of one carton (600 sachets) of SQ-LNS was 58.77 USD, equivalent to 0.098 USD per sachet. For a 12-month supply, the cost at that price would be ~36 USD per child. The UNICEF Supply Catalogue provides current prices: https://supply.unicef.org/s0000323.html.

Non-product costs can vary widely due to differences in program design and delivery platform, and costs required for setup. Integrating SQ-LNS into an existing health infrastructure or social protection platform is likely to reduce some costs, particularly capital costs and management overheads. In the early stages of program implementation, cost per child may be higher than is the case after the program has been operating for some time, due to fixed start-up costs and lags in increasing coverage. Non-product costs are likely to decrease as programs scale-up and increase coverage, as fixed costs do not vary with the number of beneficiaries and operational efficiencies may be achieved over time. On the other hand, some nonproduct costs may increase as programs scale-up, if harder to reach populations are covered in later stages of program implementation. In these case studies, the costing time horizon was generally only 2-3 years (except for the Uganda model, which included one year of start-up and 10 years of implementation and the Bangladesh modeling, which used a 10-year costing time horizon), so potential longer-term efficiencies are not reflected in the estimates. Non-product costs generally ranged from 8 to 22 USD per child-year, but observed costs were considerably higher in Burkina Faso (47 USD per child-year), where program coverage was below 40% and associated overhead costs were significantly larger than in the other sites.

Total costs ranged from 46 to 56 USD per child-year in 5 of the 6 case studies. In Burkina Faso, total costs were much higher for the reasons explained above.



Cost-effectiveness of SQ-LNS

Cost-effectiveness of a given intervention can be estimated based on a single outcome, such as cost per life saved, or cost per case of stunting, wasting, or anemia averted. However, when an intervention has effects on multiple outcomes, it is useful to include a cost-effectiveness estimate that captures those combined effects, such as the cost per disability-adjusted life years (DALYs) averted. DALYs combine burden of mortality and burden of other health conditions (diminished quality of life) into one number. Averting one DALY is the same as gaining one healthy life year (HLY). "HLYs gained" is the preferred terminology in recent WHO-CHOICE publications (22), but to avoid confusion we retain the term DALYs in this brief.

DALYs can be calculated as the sum of years of life lost due to mortality plus years lived in disability due to other adverse outcomes (such as anemia or developmental disability). Estimating disability due to adverse outcomes is usually based on Global Burden of Disease (GBD) disability weights (23). However, certain outcomes (e.g., stunting) are not included in the GBD list, and for others (e.g., moderate wasting, mild anemia), the disability weights are zero or close to zero.

Cost-effectiveness calculations, regardless of the metric used, require estimates of the impact of the intervention on the outcome or outcomes. To calculate DALYs averted, the assumed time frame for the impact on each outcome (i.e., duration of disability) also needs to be specified. In addition, estimates are needed for the prevalence of each outcome in the target population, and the relevant population size. In some cost-effectiveness studies, the estimated impact of the intervention has been based on direct evidence from randomized trials or meta-analyses of that specific intervention (e.g., for anemia, (24)). In others (25), the estimated impact is modeled indirectly via the effects of the intervention on diseases and intermediary outcomes that are linked to the outcome(s) of interest (e.g., mortality). For example, the Lives Saved Tool (LiST) estimates the impact of complementary feeding interventions on child mortality via various pathways based on how those interventions affect specific diseases (e.g., diarrhea, respiratory infections) as well as stunting and wasting (26). To estimate lives saved, this requires data on how the intervention affects those specific diseases, and assumptions about the links between the intermediary outcomes and child mortality.

For mortality, the impact is permanent and the number of years of life lost can be modeled based on the country-specific life expectancy. For other outcomes included in calculations of DALYs, the estimated duration of disability may be relatively short (e.g., anemia) or life-long (e.g., developmental disabilities). Data on prevalence of each outcome, and the relevant population size of the target population, should be specific to the country or setting for which cost-effectiveness is being estimated.

Cost-effectiveness calculations may or may not apply discounting to the costs or benefits of a given intervention. Discounting is based on the assumption that costs and benefits incurred in the future have a lower value than those same costs and benefits incurred in the present. There is a lack of consensus on the use of discounting in such analyses (27, 28). For this reason, the current WHO-CHOICE methodology includes two discounting scenarios, one that applies a 3% discount rate to costs and a zero-discount rate to benefits, and another that uses a 3% discount rate for both costs and benefits (27).

Variation in the approach taken and the data used to calculate cost-effectiveness means that estimates from different studies may not be comparable. For SQ-LNS interventions, the Cost and Cost-effectiveness Working Group collected information from several case studies (Uganda, Mali, Burkina Faso, and Bangladesh) and documented the methods used for each. **Table 2** provides the details for each of these case studies.



TABLE 2 – SQ-LNS COST-EFFECTIVENESS FOR 4 CASE STUDIES

Country	Uganda	Mali	Burkina Faso	Bangladesh
Targeting	All rural districts	Bla and San health districts in Segou region of eastern Mali; rural area (58 health center catchment areas)	Gourcy health district of Zondoma province in Northern Burkina Faso; rural area (30 health center areas)	All rural unions
Prevalence of stunting (length-for-age < -2 SD) in target population	42%	34%	22%	36%
Cross sectional prevalence of wasting (weight-for-length < -2 SD) in target population	7.8%	15%	12%	8.2%
Disabilities included in DALY calculation	Mortality, anemia, developmental disability	Wasting (WHZ<-2 or MUAC<125mm or edema), severe wasting (WHZ<-3 or MUAC<115mm or edema)	Wasting (WHZ<-2 or MUAC<125mm or edema), severe wasting (WHZ<-3 or MUAC<115mm or edema)	Mortality, anemia, developmental disability
Other assumptions	Assumed 27% and 18% relative reductions in mortality based on Stewart et al. ¹ Relative reductions in anemia and developmental disability based on Wessells et al. ² and Prado et al. ³	CEA modeled effect size and 95% CI of effects on wasting incidence and treatment coverage. SQ-LNS was delivered as a package with behavior change communication and wasting screening.	CEA modeled effect size and 95% Cl of effects on wasting incidence and treatment coverage. SQ-LNS was delivered as a package with behavior change communication and wasting screening.	Assumed 27% and 18% relative reductions in mortality based on Stewart et al. ¹ Relative reductions in anemia and developmental disability based on Wessells et al. ² and Prado et al. ³
Cost per DALY averted (undiscounted 2021 USD)	\$253-3684	\$826	\$1,186	\$548-7804
Cost per DALY averted (2021 USD discounted at 3%)	\$432-6104	N/A	N/A	\$1,068-1,4784
Cost per death averted (2021 USD) [same estimates whether undiscounted or discounted]	\$16,662-24,9934	N/A	N/A	\$44,195-66,2944

DALY, disability-adjusted life year; MUAC, mid-upper arm circumference; SD, standard deviations; USD, U.S. dollars, WHZ, weight-for-height z-score.

¹Stewart C.P., Wessells K.R., Arnold C.D., Huybregts L., Ashorn P., Becquey E., ... Dewey K.G. (2019). Lipid-based nutrient supplements and all-cause mortality in children 6–24 months of age: A meta-analysis of randomized controlled trials. The American Journal of Clinical Nutrition, 111, 207-218. doi: 10.1093/ajcn/nqz262. ²Wessells K.R., Arnold C.D., Stewart C.P., Prado E.L., Abbeddou S., Adu-Afarwuah S., ... Dewey K.G. (2021). Characteristics that modify the effect of small-quantity lipid-based nutrient supplementation on child anemia and micronutrient status: An individual participant data meta-analysis of randomized controlled trials. The American Journal of Clinical Nutrition, 114, 68S-94S. doi: 10.1093/ajcn/nqab276.

³Prado E.L., Arnold C.D., Wessells K.R., Stewart C.P., Abbeddou S., Adu-Afarwuah S., . . . Dewey K.G. (2021). Small-quantity lipid-based nutrient supplements for children age 6–24 months: A systematic review and individual participant data meta-analysis of effects on developmental outcomes and effect modifiers. The American Journal of Clinical Nutrition, 114, 43S-67S. doi: 10.1093/ajcn/nqab277.

⁴Lower and upper estimates based on assuming 27% and 18% mortality reductions, respectively.

As mentioned above, Adams et al. (18) developed a cost model to estimate the annual total societal cost and cost per child of providing SQ-LNS in rural Uganda. They then developed a cost-effectiveness model to translate the effects of SQ-LNS, based on the meta-analysis results described above (for mortality, anemia, and developmental disability), into cost per DALY averted, per death averted, and per case of anemia, developmental disability, stunting, and wasting averted. These models were used to generate hypothetical SQ-LNS cost-effectiveness estimates for Uganda, using Uganda-specific estimates of baseline mortality and the prevalence of stunting, wasting, anemia, and developmental disability. Estimates were based on providing SQ-LNS for 12 months (from 6 to 18 months of age) to all young children residing in rural districts of Uganda, delivered via an existing community health worker program (see **Table 1**). Costs and effects were modeled over the period 2021-2031. Cost-effectiveness estimates were \$242 per DALY averted (undiscounted 2020 USD) or \$413 per DALY averted with costs and effects discounted



at 3%. For individual outcomes, undiscounted cost-effectiveness estimates were \$366 per case of moderate-to-severe anemia averted, \$374-863 per incident case of wasting averted, \$1,051 per case of stunting averted, and \$15,914 per death averted.

For the PROMIS studies in Burkina Faso (29) and Mali (30), investigators developed a Markov model to estimate costeffectiveness of the PROMIS package relative to standard care. This intervention package integrated a BCC intervention and SQ-LNS into platforms for wasting screening in Burkina Faso (preventive well-baby clinics) and Mali (village-based group meetings organized by community health volunteers). Standard of care consisted of BCC and wasting screening only. The authors used empiric cost data collected in the PROMIS study and modeled the effect sizes and 95% confidence intervals observed in the PROMIS impact evaluations in both Burkina Faso and Mali, which were a statistically non-significant 10% reduction in moderate wasting (defined as middle upper arm circumference, MUAC, between 115 and < 125 mm, or weightfor-height z-score between -3 and -2) and severe wasting (defined as MUAC < 115 mm, or weight-for-height z-score < -3, or presence of bilateral pitting edema) incidence in Burkina Faso, and 30% and 40% reduction in moderate and severe wasting incidence, respectively, in Mali. Costs and effects were modeled over the length of the study period, which corresponded to 12 months (children ages 6-17 months) in Burkina Faso and 18 months (6-23 months) in Mali. The authors did not employ age-weighting or discounting, and the Markov cycle length was 1 month. The cost-effectiveness estimates used the intent-totreat impact estimates, i.e., the mean impact of the program across all eligible children whether or not they actually received the intervention. The outcomes contributing to DALYs were moderate and severe wasting incidence and the modeled effects of wasting incidence on mortality, as well as the modeled effects of wasting treatment coverage on recovery and mortality. The PROMIS intervention cost \$1,073 per DALY averted in Burkina Faso and \$747 in Mali (2017 USD). Sensitivity analyses suggest that the results were most sensitive to the effect size of the PROMIS package on treatment coverage and SAM incidence, the cost per child-contact of the PROMIS intervention, and wasting incidence in the absence of intervention.

For Bangladesh, the cost-effectiveness model developed for the Uganda case study (18) was adapted to estimate costeffectiveness, using Bangladesh-specific estimates of baseline mortality, anemia, and developmental disability (paper in preparation). Estimated impact of SQ-LNS on those outcomes was based on the same meta-analysis results as described above (10). Costs and effects were modeled over the period 2022-2031. Cost-effectiveness estimates were \$548-780 per DALY averted (undiscounted 2021 USD), depending on which mortality reduction estimate was used, or \$1,068-1,478 per DALY averted with costs and effects discounted at 3%. Cost per death averted ranged from \$44,196 to \$66,294 (Table 2).

The cost per DALY averted (undiscounted) in the case studies described above ranges from \$253 in Uganda to \$1,186 in Burkina Faso (2021 USD). These estimates vary for several reasons. First, the outcomes included in DALY calculations differed across case studies (e.g., some included mortality as a direct effect of SQ-LNS, others did not). Second, the baseline prevalence of adverse outcomes differed across sites. Third, distribution coverage (and thus efficiency of the program) ranged from a low of 37% in Burkina Faso to an assumed 100% in the models for Uganda and Bangladesh. Fourth, the platform used for distribution differed across studies (for example, a health center platform in Burkina Faso, a community platform in Uganda, Mali, and Bangladesh), as did other contextual, country-specific factors that impact costs.

The first of these reasons, inclusion of a direct estimate of all-cause mortality reduction due to SQ-LNS, plays a large role in the calculation of DALYs averted and thus the cost per DALY averted. It is somewhat unique to have such an estimate from a published meta-analysis, and this may be a superior approach compared to relying on indirect estimates of effects on cause-specific mortality via various pathways, as has been done for other types of child nutrition interventions (25, 26). However, the estimated overall 27% reduction in all-cause mortality due to SQ-LNS is based on data from a combination of efficacy trials (7 estimates) and programmatic settings (5 estimates) (10). Although the median relative risk reduction was similar between these two types of studies, there was greater heterogeneity in the programmatic trials, and thus there is some uncertainty in the estimate when extrapolating to programs because context-specific elements may interfere with optimal implementation. In the Uganda and Bangladesh modeling studies, one of the sensitivity analyses used a lower mortality reduction estimate (18%), which increased cost per DALY averted. Cost per DALY averted is also strongly influenced by the baseline child mortality rate: even



though the estimated cost per child was lower in Bangladesh than in Uganda (\$48 vs \$55 per child-year), the child mortality rate is substantially higher in Uganda than in Bangladesh (31, 32), and thus the number of deaths potentially averted is large, leading to a lower cost per DALY averted in Uganda than in Bangladesh. For the PROMIS estimates of cost-effectiveness, no direct impact on mortality was modeled, only a reduction in mortality through reductions in wasting. Although wasting and severe wasting are strongly associated with mortality, this approach may underestimate the impact of SQ-LNS on all-cause mortality.

For the reasons explained above, direct comparisons of estimated cost per DALY averted across these case studies is not warranted. However, these estimates can be interpreted based on published cost-effectiveness thresholds. Although there is no universal consensus on such thresholds (27), the World Health Organization has suggested that interventions with a cost per DALY averted that is less than the gross domestic product (GDP) per capita can be considered "very cost-effective" (33). The per capita GDP in the case study countries in 2021 was \$884 for Uganda, \$893 for Burkina Faso, \$874 for Mali and \$2458 for Bangladesh. Based on that threshold, these case study estimates would be rated as "very cost-effective" for Uganda, Mali, and Bangladesh but not Burkina Faso (due to low coverage and high overhead costs, as explained above). However, a threshold based on per capita GDP has been criticized for being impractically high in LMICs (34-36). Moreover, being categorized as "very cost-effective" does not ensure that an intervention is affordable or feasible for a particular target population. As discussed in the final section of this brief, total costs for a scaled-up program that includes SQ-LNS could be high relative to a country's total health budget or to resources that are available. Thus, strategies for reducing and/or sharing costs should be considered.

Programmatic and contextual factors that may influence cost-effectiveness of SQ-LNS

Targeting programs that include SQ-LNS to high-risk settings (e.g., districts or communities with high child mortality rates or prevalence of stunting and/or wasting) is one strategy that could enhance cost-effectiveness. First, limiting the target population that is eligible to receive SQ-LNS will reduce total costs due to lower amounts of SQ-LNS procured and a smaller geographic area to be reached. Second, targeting SQ-LNS to children in the most vulnerable communities could enhance effectiveness for certain outcomes. In the SQ-LNS meta-analyses, the relative reductions in adverse outcomes (developmental delay, iron deficiency, severe wasting, and severe stunting) due to SQ-LNS were greater among children with a higher burden of undernutrition or lower socio-economic status (13, 14), or in populations with poor water quality and similar indicators (15). Third, if the baseline prevalence of adverse outcomes such as mortality, stunting, or wasting is high, the absolute numbers of adverse outcomes averted due to SQ-LNS will be higher than in lower-burden areas. On the other hand, programs in high-risk settings may face higher costs related to security, inaccessibility, and other constraints.

Program efficiency is a key element that will influence cost-effectiveness. Issues such as over-procurement of SQ-LNS relative to actual achieved distribution coverage, high overhead costs, and centralized vs. decentralized distribution (see BOX), can affect program efficiency.

Distribution coverage should not be confused with compliance among participants in consuming SQ-LNS once supplements have been received. Compliance has been defined in very different ways across SQ-LNS studies (11). In general, reported compliance to consuming child SQ-LNS is high, ranging from 74% to 97% when distribution coverage has been adequate. It should be noted that the estimated impact of SQ-LNS on adverse outcomes used in the modeled cost-effectiveness calculations is not based on 100% compliance or distribution coverage, because there was a wide range in actual receipt/ consumption of supplements among the trials included in the meta-analyses (from 37% to 97%). Average study-level compliance generally did not modify the effects of SQ-LNS on adverse outcomes. This implies that compliance is not likely to be a major factor affecting cost-effectiveness estimates.



Duration of supplementation (i.e., months of supplementation per child) will certainly affect costs and may also influence effectiveness of SQ-LNS. In the costing case studies (Table 1), intended duration of supplementation was 12 months in 3 studies and up to 18 months in 2 studies. In most of the randomized trials in the SQ-LNS meta-analyses, supplementation started at 6 months of age and was continued for at least 12 months (i.e., to \geq 18 months of age), so the estimated impact of SQ-LNS is most relevant to this scenario. In some programs, children may begin receiving SQ-LNS later than 6 months of age, and duration of supplementation might vary. There is some evidence that the benefits of SQ-LNS are greatest when supplementation begins at 6 months of age (37). Further research is needed on both costs and effectiveness of SQ-LNS provided for durations of less than 12 months (e.g., for 6-9 months, starting as close as possible to 6 months of age).

The type of delivery platform and frequency of delivery of SQ-LNS can have an important impact on non-product costs. In the Uganda-based model (18), the assumption was that community health workers would deliver SQ-LNS every 3 mo. More frequent delivery (e.g., monthly) would increase costs to some extent, but may also limit the likelihood of caregivers sharing or selling the product. To adequately deliver SQ-LNS, some community-based programs may need to be strengthened, which could increase costs. The overall impact of this on cost-effectiveness depends on the degree to which there is cost-sharing of program components that go beyond procurement and distribution of SQ-LNS. In the Bangladesh case study, monthly home visits by community health workers were already an expected component of the existing program, so adding delivery of SQ-LNS did not have a large impact on workload (21). One key consideration is that the addition of a supplement to be provided by community health workers may enhance their performance - e.g., in Bangladesh, addition of SQ-LNS to the program led to a higher percentage of caregivers who reported being visited by a CHW in the previous month: >90% in intervention communities vs. <25% in control communities (21). Additionally, when delivery occurs via health centers or existing community health platforms, SQ-LNS distribution may have other spillover effects, potentially incentivizing caregiver attendance and participation in wasting screening, well-child visits, immunizations, and behavior change counseling (29, 30). Increased attendance at screenings for child malnutrition may increase the number of children identified as eligible for treatment. Early detection and treatment of child wasting can shorten children's exposure to wasting, thereby reducing both the prevalence of wasting and the associated DALYs, leading to better cost-effectiveness. All of these aspects of program design and function can impact both costs and effectiveness, and further work is needed to document these effects.

The importance of distribution coverage and demand from participants

In the PROMIS Burkina Faso case study, SQ-LNS distribution coverage was only 37% because caregivers did not always show up at preventive wellbaby clinics organized at the health center. Because the distribution was organized by health staff, there was very little SQ-LNS product leakage.

In the sister trial in Mali, monthly group sessions were organized by community health volunteers to offer the integrated PROMIS intervention package consisting of screening children for wasting, delivering BCC, and distributing SQ-LNS. Distribution coverage via these sessions was 47%. However, if these sessions were not organized by CHVs or caregivers did not attend, many caregivers sought to obtain the SQ-LNS from the CHV outside of the program's activities, increasing total monthly distribution coverage to 73%.

Decentralized distribution is more difficult to supervise and can lead to unintended consequences, whereas more centralized distributions require caregivers to cover larger distances to obtain the SQ-LNS which can lead to lower distribution coverage.



Benefit-cost estimates for SQ-LNS

Benefit-cost analyses differ from cost-effectiveness analyses because the former require assigning a monetary value to the benefits of the intervention of interest (such as the value of a life saved). For benefit-cost analyses, estimates of benefits are based on various assumptions such as the value of a "statistical life year" (e.g., in relation to gross domestic product) and the increases in lifetime income associated with certain outcomes such as reduced stunting (e.g., via links to increased cognitive development and/or schooling). In a recent Copenhagen Consensus assessment of the most cost-effective maternal and child nutrition interventions (38), the authors estimated a benefit to cost ratio of 13.7 for preventive SQ-LNS for children 6-23 months of age, when targeted to the poorest 60% of the population in the 40 low- and lower middle-income countries with the highest rates of child stunting. For those estimates, the authors assumed a 27% reduction in all-cause mortality due to SQ-LNS based on the meta-analysis (10). The value of deaths averted was pegged at 1.55 times the GDP per capita in 2022, rising to 2.9 times GDP per capita in 2090, and cases of stunting averted were assumed to increase lifetime income by 30% (based on initial socio-economic status).

For the project in Madagascar (37, 39) (see **Table 1**), the analysis focused only on benefits from reduced stunting, without accounting for the value of mortality reduction or valuing the benefits on other outcomes such as wasting or anemia. The estimated impact on stunting was based on children with full exposure to SQ-LNS (12 months of supplementation, between 6 and 18 months of age). A benefit-cost ratio of 6:1 was estimated for child SQ-LNS based on the net present value (imputed per capita) of future earnings gains from the estimated reduction in stunting. Stunting reduction in childhood is modeled to improve lifetime income through higher years of schooling, better cognitive skills and increased height in adulthood, all of which have returns after the child joins the labor force. Under very conservative assumptions of doubling the cost and halving the estimated benefits of the program, the benefit-cost ratio would be 3:1, with benefits still largely outweighing the costs.

Research needs

Additional documentation of the costs and cost-effectiveness of programs that include child SQ-LNS is needed, in particular to understand variation by context, duration of supplementation, program platform, and joint delivery with a larger package of interventions. The Working Group identified several key topics to be addressed:

- Effectiveness and cost-effectiveness for scenarios in which the age at beginning of supplementation and duration of access to SQ-LNS vary.
- Potential cost savings associated with effects of SQ-LNS on reduced need for treatment for moderate or severe acute malnutrition and for hospitalization. Cost of treatment for acute malnutrition and impact on DALYs was included in the PROMIS case studies in Mali and Burkina Faso, but more such analyses of programs that combine food-based prevention and treatment components are needed. In Niger, blanket provision of SQ-LNS was associated with reduced hospitalization among children identified with acute malnutrition (40), but this needs confirmation in other settings.
- Costs and cost-effectiveness of providing SQ-LNS as an incentive to attend health clinics and/or nutrition counseling sessions, with regard to potentially increased uptake of non-nutrition services such as immunizations.
- 4 Cost and cost-effectiveness implications of targeting SQ-LNS to high-risk populations or individuals, and in humanitarian contexts.



5 Costs based on local production and/or modified formulations or packaging of SQ-LNS. Local production of SQ-LNS is occurring in several countries (<u>https://sqlns.ucdavis.edu/FAQs</u>), although costs may or may not be lower than the cost of importing the product (41). Local manufacturers face multiple challenges including taxes on imported ingredients, high interest rates, long cash conversion cycles, technical requirements, limited access to quality testing laboratories, and limited benefits to local economies.

6 Estimates of how the unit costs vary with scale.

Conclusions and policy implications

The total cost of providing SQ-LNS daily was ~\$50 per child-year in most of the case studies described above, with product cost averaging 60% of that total. The cost-effectiveness estimates suggest that provision of SQ-LNS can be a very cost-effective intervention if properly implemented using a suitable delivery platform with appropriate support and supervision. The benefit to cost ratio from the Copenhagen Consensus analysis (38) was 13.7, indicating that the potential economic benefits greatly outweigh the costs.

Nonetheless, it should be recognized that the total cost for a program aimed at all age-eligible children in a given country will be high. This is also the case for other food-based interventions that are designed for prevention of malnutrition, such as blanket provision of complementary foods (42). For this reason, decision-makers may choose to target provision of SQ-LNS to the most vulnerable communities, such as those with high levels of child wasting, stunting, mortality, or household food insecurity.

When SQ-LNS is incorporated into an existing program platform, it is likely that there will be economies from cost-sharing and piggybacking on an existing infrastructure of human resources, overhead, training, and supervision. These cost savings, generally referred to as economies of scope, are one of the major reasons for integrating programs. There also might be synergies of integrating with regard to effectiveness, if the provision of SQ-LNS enhances the take-up of an existing package of services. The choice of program platform is thus a key element in scaling-up SQ-LNS in any context, and proper care should be taken in carefully measuring the additional costs of inputs that are necessary for integrating SQ-LNS into an existing intervention or package of interventions.

In the long-run, beneficiary households may be able to bear some of the cost of SQ-LNS. Several studies have assessed household willingness-to-pay for SQ-LNS in low- and middle-income countries (43-46). In most of these settings, average willingness-to-pay exceeded the product cost (not including non-product costs). However, it is likely that the unsubsidized price of SQ-LNS would be unaffordable for a substantial proportion of households, especially in the most vulnerable populations. Moreover, requiring some payment may reduce uptake among households most in need (47), thereby reducing the cost-effectiveness of the intervention. Further investigation is needed to determine the feasibility and cost-effectiveness of a cost-sharing distribution strategy in which higher-income households are expected to pay while poorer households are provided SQ-LNS free of charge.

Although it is useful to understand how much households might be willing to pay for SQ-LNS, these types of studies generally do not take into account the future economic benefits to them or to society. Given the high return to investment expected from interventions that include child SQ-LNS, these programs are likely to have a favorable benefit:cost ratio regardless of how much the beneficiaries are willing to pay.

Members of the Working Group on Cost and Cost-effectiveness: Katherine Adams (University of California, Davis), Eric S. Anderson (United States Agency for International Development), Rebecca Brander (International Food Policy Research Institute), Kathryn Dewey (University of California, Davis), Emanuela Galasso (World Bank Group), Lieven Huybregts (International Food Policy Research Institute), Grainne Moloney (United Nations International Children's Emergency Fund), Kevin Phelan (ALIMA, The Alliance for International Medical Action), Christopher Rue (United States Agency for International Development), Gregory Sclama (World Food Programme)



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