The case for SQ-LNS to prevent child undernutrition

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Best Bets Webinar

The challenge: meeting nutrient requirements in 6-23 month old children

- Globally, < 30% of children 6-23 months old meet criteria for a minimally diverse diet.
- ↑ risk of growth faltering, anemia, and impaired development.
- Key barrier is lack of affordability of nutrient-rich complementary foods.

Lipid-based nutrient supplements

- Provide energy, protein, multiple micronutrients and essential fatty acids.
- Daily ration varies in size depending on whether it is designed for prevention or treatment of child undernutrition.

Prevention → Treatment

Small quantity
~120 kcal/d (~20 g/d)

Medium quantity
~270 kcal/d (~50 g/d)

Large quantity

~540 kcal/d (~100 g/d)
For treatment of moderate wasting

~500 kcal (92 g)/sachet
[# sachets/d varies]
For treatment of severe wasting

Small-quantity LNS (SQ-LNS)

- Designed for prevention of undernutrition among children 6-23 months of age
- Contain micronutrients in a dose of ~ 1 RDA.
- Ration size is small (~20 g/100-125 kcal per day) in order to:
  - Avoid displacement of breastmilk and nutrient-rich foods
  - Ensure that all targeted infants and young children can consume the entire ration in one day (thereby receiving the intended doses of micronutrients)
  - Minimize cost

Impact of SQ-LNS for children 6-23 mo

- Effect of LNS on **child mortality** 6-23 months:
  - Stewart CP, Wessells KR, Arnold CD, Huybregts L, Ashorn P, Becquey E, Humphrey JH, Dewey KG. Am J Clin Nutr 2019; 111:207-218.
  - 12 of the 13 trials in the primary analysis used SQ-LNS
  - 27% reduction in all-cause mortality 6-23 months

- Effects of SQ-LNS on **child growth, anemia, micronutrient status and development** (Individual participant data (IPD) meta-analyses):
  - Am J Clin Nutr 2021 supplement: https://academic.oup.com/ajcn/issue/114/Supplement_1
  - Am J Clin Nutr 2022 paper on severe wasting and stunting: https://academic.oup.com/ajcn/article-abstract/116/5/1314/6679556?redirectedFrom=fulltext&utm_source=etoc&utm_campaign=ajcn&utm_medium=email

SQ-LNS Individual Participant Data (IPD) Analysis

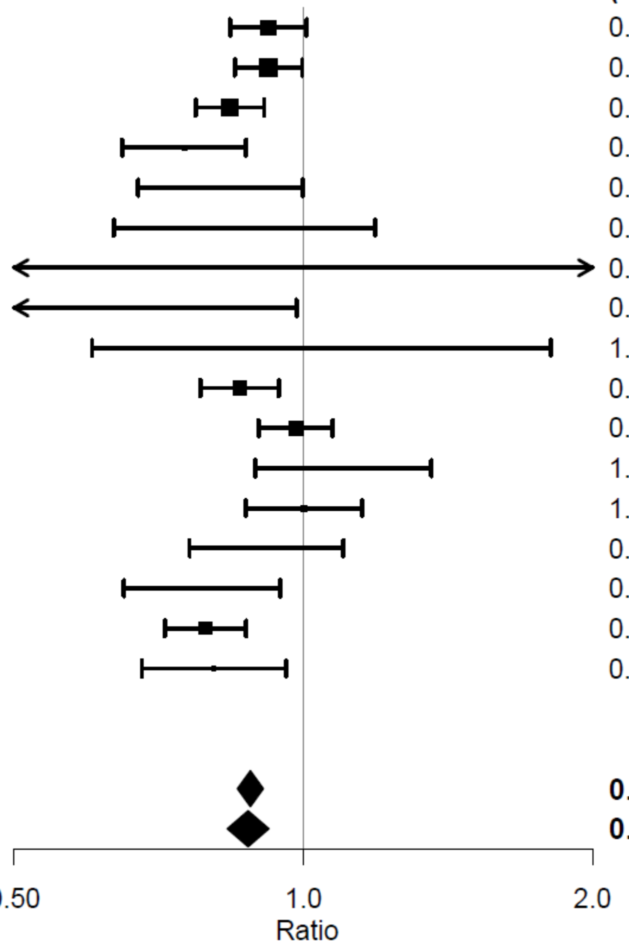
Total of 14 trials included; 9 countries; >37,000 children

Country	Author	Trial name	Age at start (mo)	Duration (mo)	Participants
Bangladesh	Christian 2015	JiVitA-4	6	12	4218
Bangladesh	Dewey 2017	RDNS	6	18	2478
Bangladesh	Luby 2018	WASH-B-B	6	18	4633
Burkina Faso	Hess 2015	iLiNS-ZINC	9	9	2626
Burkina Faso	Becquey 2019	PROMIS-BF	6	12	2651
Ghana	Adu Afarwuah 2007		6	6	194
Ghana	Adu Afarwuah 2016	iLiNS-DYAD-G	6	12	1040
Haiti	Iannotti 2014		6-11*	3-6**	300
Kenya	Null 2018	WASH-B-K	6	18	6649
Madagascar	Galasso 2019	MAHAY	6-11*	6-12**	3390
Malawi	Ashorn 2015	iLiNS-DYAD-M	6	12	664
Malawi	Maleta 2015	iLiNS-DOSE	6	12	943
Mali	Huybregts 2019	PROMIS-M	6	18	2937
Zimbabwe	Humphrey 2019	SHINE	6	12	3676
Zimbabwe	Prendergast 2019	SHINE (HIV-exp)	6	12	667

(Dewey et al. Am J Clin Nutr 2021). PROMIS, Innovative Approaches for the Prevention of Childhood Malnutrition; RDNS, Rang-Din Nutrition Study; SHINE, Sanitation, Hygiene, Infant Nutrition Efficacy Project. *Children enrolled between 6 and 11 mo of age. **Intervention duration varied between intervention groups or among children.

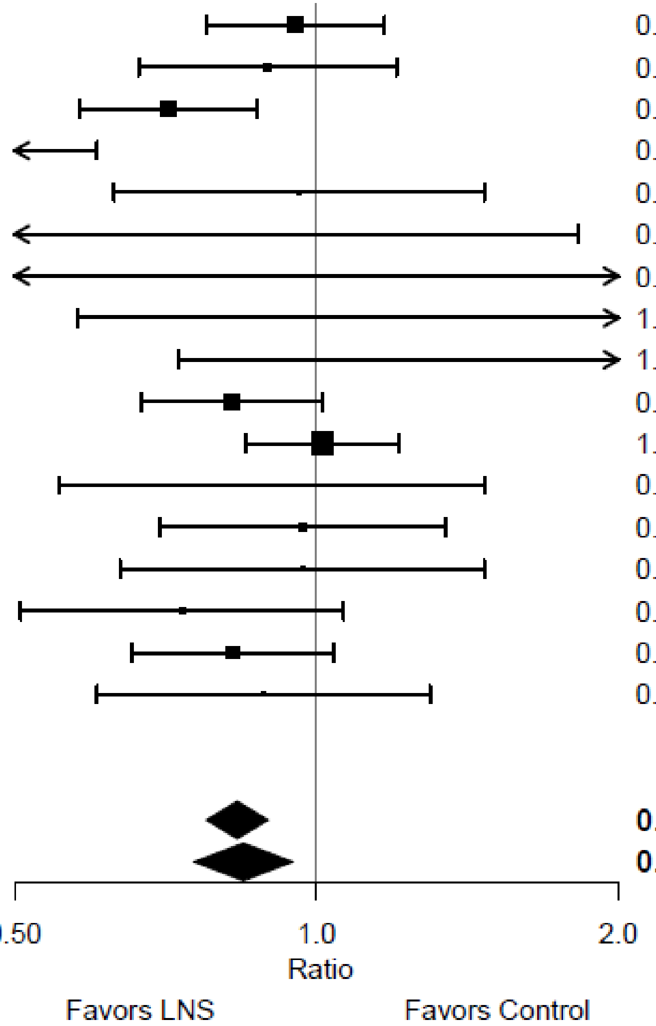
Main effects, all-trials analysis: Stunting prevalence ratio

Trial	Country	LNS N	Control N	PR (95% CI)	Fixed W	Random W
JiVitA-4	Bangladesh	2838	1244	0.92 (0.84, 1.01)	0.12	0.10
RDNS	Bangladesh	1663	815	0.92 (0.85, 1.00)	0.15	0.10
WASH-B	Bangladesh	1158	3431	0.84 (0.77, 0.91)	0.14	0.10
iLiNS-Zinc	Burkina Faso	1952	664	0.75 (0.65, 0.87)	0.04	0.06
PROMIS	Burkina Faso	863	914	0.82 (0.67, 1.00)	0.03	0.04
PROMIS CS	Burkina Faso	430	439	0.87 (0.63, 1.19)	0.01	0.02
GHANA	Ghana	98	96	0.70 (0.23, 2.13)	0.00	0.00
iLiNS-DYADG	Ghana	347	692	0.66 (0.45, 0.98)	0.01	0.01
HAITI	Haiti	149	149	1.04 (0.60, 1.81)	0.00	0.01
WASH-B	Kenya	1457	5137	0.86 (0.78, 0.94)	0.11	0.09
MAHAY	Madagascar	1702	1682	0.98 (0.90, 1.07)	0.12	0.10
iLiNS-DYADM	Malawi	220	444	1.10 (0.89, 1.36)	0.02	0.04
iLiNS-DOSE	Malawi	696	241	1.00 (0.87, 1.15)	0.05	0.07
PROMIS	Mali	506	506	0.92 (0.76, 1.10)	0.03	0.05
PROMIS CS	Mali	952	969	0.78 (0.65, 0.95)	0.03	0.05
SHINE (HIV-)	Zimbabwe	1880	1794	0.79 (0.72, 0.87)	0.10	0.09
SHINE (HIV+)	Zimbabwe	337	330	0.81 (0.68, 0.96)	0.03	0.05
Summary	**I² = 0.49, Tau² = 0.00**	**17248**	**19547**			
	Fixed			**0.88 (0.85, 0.91)**		
	Random			**0.88 (0.83, 0.92)**		

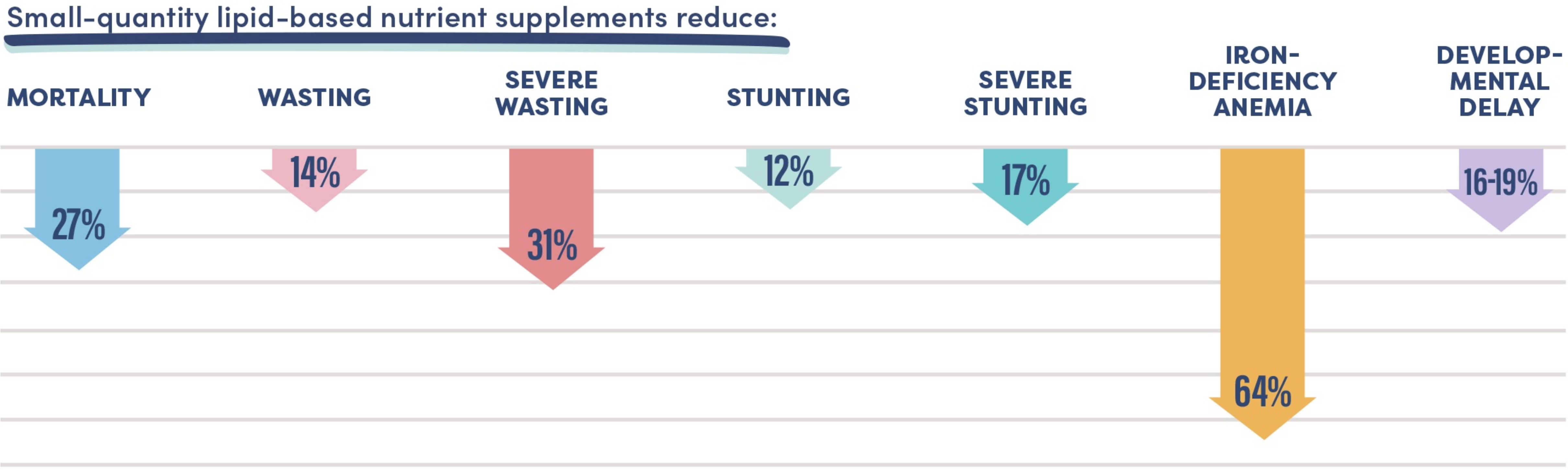


Main effects, all-trials analysis:
Severe Stunting prevalence ratio

Country	Trial	LNS N	Control N	PR (95% CI)	Fixed W	Random W
Bangladesh	JiVitA-4	2838	1244	0.95 (0.78, 1.17)	0.12	0.10
Bangladesh	RDNS	1663	815	0.89 (0.67, 1.20)	0.06	0.07
Bangladesh	WASH-B	1158	3431	0.71 (0.58, 0.87)	0.12	0.10
Burkina Faso	iLiNS-Zinc	1952	664	0.48 (0.38, 0.60)	0.10	0.09
Burkina Faso	PROMIS	863	914	0.96 (0.63, 1.47)	0.03	0.05
Burkina Faso	PROMIS CS	430	439	0.88 (0.42, 1.82)	0.01	0.02
Ghana	GHANA	98	96	0.98 (0.06, 15.43)	0.00	0.00
Ghana	iLiNS-DYADG	347	692	1.71 (0.58, 5.05)	0.00	0.01
Haiti	HAITI	149	149	1.79 (0.73, 4.42)	0.01	0.01
Kenya	WASH-B	1457	5137	0.82 (0.67, 1.01)	0.12	0.10
Madagascar	MAHAY	1702	1682	1.01 (0.85, 1.21)	0.17	0.10
Malawi	iLiNS-DYADM	220	444	0.90 (0.55, 1.47)	0.02	0.04
Malawi	iLiNS-DOSE	696	241	0.97 (0.70, 1.35)	0.05	0.06
Mali	PROMIS	506	506	0.97 (0.64, 1.47)	0.03	0.05
Mali	PROMIS CS	952	969	0.73 (0.51, 1.06)	0.04	0.06
Zimbabwe	SHINE (HIV-)	1880	1794	0.82 (0.65, 1.04)	0.10	0.09
Zimbabwe	SHINE (HIV+)	337	330	0.89 (0.60, 1.30)	0.03	0.05
I² = 0.58, Tau² = 0.02		**17248**	**19547**			
Fixed				**0.83 (0.78, 0.90)**		
Random				**0.85 (0.75, 0.95)**		



Main conclusion:
SQ-LNS have a beneficial impact on multiple outcomes



For most outcomes, evidence was graded as "high certainty"

Stewart, AJCN, 2019: https://doi.org/10.1093/ajcn/nqz262; Dewey, AJCN, 2021: https://doi.org/10.1093/ajcn/nqab278; Prado, AJCN, 2021: https://doi.org/10.1093/ajcn/nqab277; Wessells AJCN, 2021: https://doi.org/10.1093/ajcn/nqab276; Dewey, AJCN, 2022: https://doi.org/10.1093/ajcn/nqac232

Analysis of effect modifiers: who benefits most?

Study-level characteristics

- Region (Africa vs S.Asia)
- Stunting burden
- Malaria prevalence
- Community water & sanitation coverage
- Duration of supplementation
- Child age at enrollment
- Frequency of contact
- Compliance

Household, maternal, or child-level characteristics

- Household SES
- Household water or sanitation
- Household food security
- HOME environment
- Maternal age, height, BMI
- Maternal education
- Maternal depressive symptoms
- Child sex or birth order
- Season of assessment

In general, there were benefits seen across nearly all strata of community-level, household-level, and individual-level characteristics.

All children have an opportunity to benefit.

Stewart, AJCN, 2019: https://doi.org/10.1093/ajcn/nqz262; Dewey, AJCN, 2021: https://doi.org/10.1093/ajcn/nqab278; Prado, AJCN, 2021: https://doi.org/10.1093/ajcn/nqab277; Wessells AJCN, 2021: https://doi.org/10.1093/ajcn/nqab276; Dewey, AJCN, 2022: https://doi.org/10.1093/ajcn/nqac232

Effect modification by stunting burden, food security, and household SES

- In **households** with a **lower SES**, and in **communities** with a **higher stunting burden,** there were greater effects on developmental outcomes
- In **communities** with **poorer WASH conditions**, there were greater effects on severe wasting, but lesser effects on iron deficiency anemia
- In **households** with **more severe food insecurity,** there were greater percentage point reductions in acute malnutrition and underweight

Targeting on the basis of population-level SES or burden of undernutrition may be worth considering.
Such settings are also associated with greater risk of infection/inflammation, which could constrain a response on IDA. Consider co-packaging with other interventions.

Review

Effective interventions to address maternal and child malnutrition: an update of the evidence

Emily C Keats*, Jai K Das*, Rehana A Salam, Zohra S Lassi, Aamer Imdad, Robert E Black, Zulfiqar A Bhutta

Malnutrition—consisting of undernutrition, overweight and obesity, and micronutrient deficiencies—continues to afflict millions of women and children, particularly in low-income and middle-income countries (LMICs). Since the 2013 *Lancet* Series on maternal and child nutrition, evidence on the ten recommended interventions has increased, along with evidence of newer interventions. Evidence on the effectiveness of antenatal multiple micronutrient supplementation in reducing the risk of stillbirths, low birthweight, and babies born small-for-gestational age has strengthened. Evidence continues to support the provision of supplementary food in food-insecure settings and community-based approaches with the use of locally produced supplementary and therapeutic food to manage children with acute malnutrition. Some emerging interventions, such as preventive small-quantity lipid-based nutrient supplements for children aged 6–23 months, have shown positive effects on child growth. For the prevention and management of childhood obesity, integrated interventions (eg, diet, exercise, and behavioural therapy) are most effective, although there is little evidence from LMICs. Lastly, indirect nutrition strategies, such as malaria prevention, preconception care, water, sanitation, and hygiene promotion, delivered inside and outside the health-care sector also provide important nutritional benefits. Looking forward, greater effort is required to improve intervention coverage, especially for the most vulnerable, and there is a crucial need to address the growing double burden of malnutrition (undernutrition, and overweight and obesity) in LMICs.

Lancet Child Adolesc Health 2021; 5: 367–84

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See Series Lancet 2021; 397: 1388–99 and Lancet 2021; 397: 1400–18

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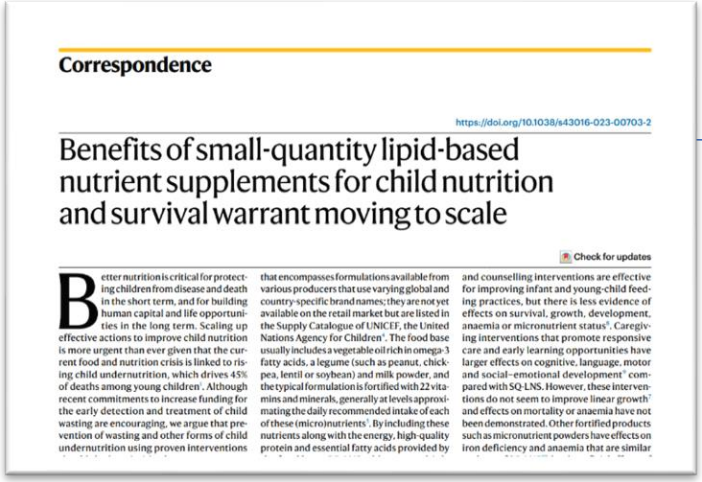

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https://doi.org/10.1038/s43016-023-00703-2

Benefits of small-quantity lipid-based nutrient supplements for child nutrition and survival warrant moving to scale

Check for updates

Better nutrition is critical for protecting children from disease and death in the short term, and for building human capital and life opportunities in the long term. Scaling up effective actions to improve child nutrition is more urgent than ever given that the current food and nutrition crisis is linked to rising child undernutrition, which drives 45% of deaths among young children[1]. Although recent commitments to increase funding for the early detection and treatment of child wasting are encouraging, we argue that prevention of wasting and other forms of child undernutrition using proven interventions

that encompasses formulations available from various producers that use varying global and country-specific brand names; they are not yet available on the retail market but are listed in the Supply Catalogue of UNICEF, the United Nations Agency for Children[4]. The food base usually includes a vegetable oil rich in omega-3 fatty acids, a legume (such as peanut, chickpea, lentil or soybean) and milk powder, and the typical formulation is fortified with 22 vitamins and minerals, generally at levels approximating the daily recommended intake of each of these (micro)nutrients[5]. By including these nutrients along with the energy, high-quality protein and essential fatty acids provided by

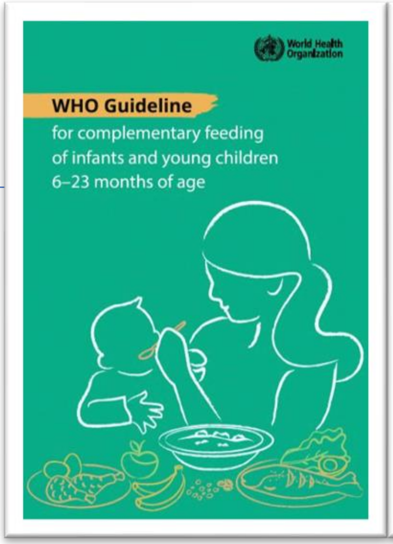
and counselling interventions are effective for improving infant and young-child feeding practices, but there is less evidence of effects on survival, growth, development, anaemia or micronutrient status[8]. Caregiving interventions that promote responsive care and early learning opportunities have larger effects on cognitive, language, motor and social–emotional development[9] compared with SQ-LNS. However, these interventions do not seem to improve linear growth[7] and effects on mortality or anaemia have not been demonstrated. Other fortified products such as micronutrient powders have effects on iron deficiency and anaemia that are similar

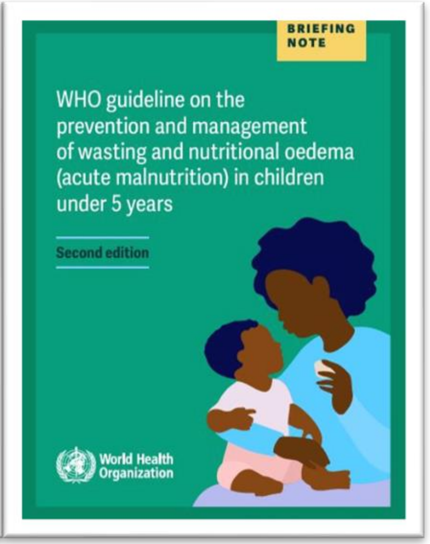
2021
SQ-LNS added to the list of evidence-based interventions to improve maternal and child nutrition in the Lancet Series on Maternal and Child Nutrition

2022
Convening of interested stakeholders in Washington, DC

2023
Representatives from UNICEF, WFP, the World Bank, USAID, the Bill & Melinda Gates Foundation, and UC Davis encourage scaling-up SQ-LNS

2023
SQ-LNS included in WHO Guidelines for complementary feeding and prevention and management of wasting





What is cost-effectiveness?

Type of economic analysis	Definition
Cost-efficiency	Estimate of the cost per unit of output (e.g., per child).
Cost-effectiveness	Estimate of the cost per unit of outcome, where the outcome is measured in natural units (e.g., deaths averted, cases of stunting averted).
Cost-utility	Estimate of the cost per disability-adjusted life year (DALY) averted.
Cost-benefit	Estimate of total cost relative to the monetary value of one or more outcomes.

DALYs reflect the current value of future **years of life lost** (YLL) and/or **years of healthy life lost due to living with disability or disease** (YLD), where the conversion of morbidity to DALYs is based on applying disease-specific weights as established by, e.g., the Global Burden of Disease.

Evidence on the cost and cost-effectiveness of SQ-LNS

- **Cost and Cost-effectiveness Working Group** of the SQ-LNS Task Force formed in 2022 to compile information from projects in several countries that had collected detailed data to estimate costs and/or cost-effectiveness of distributing SQ-LNS to children.

Country	Study	Cost-effectiveness (DALYs) based on:
Bangladesh	Modeling based on RDNS[1]	Mortality, anemia, developmental disability
Burkina Faso	PROMIS (program RCT)	Wasting & severe wasting
Madagascar	MAHAY (program RCT)	N/A
Mali	PROMIS (program RCT)	Wasting & severe wasting
Niger	ALIMA (program)	N/A
Uganda	Modeling[2]	Mortality, anemia, developmental disability

[1]Cost estimates based on adapted actual cost data collected on SQ-LNS distribution costs during the RDNS trial in Bangladesh.
[2]Cost estimates based on adapted actual cost data collected on MNP distribution costs in Uganda.

Evidence on the cost and cost-effectiveness of SQ-LNS

The total cost of providing SQ-LNS daily was ~$50 per child-year in most of the case studies, with product cost averaging 60% of that total

- Total cost for a program aimed at all age-eligible children in a given country will be high
- Product price may decline with global scale-up
- Policy-makers may choose to target to most vulnerable communities or devise cost-sharing strategies

Cost per DALY averted ranged from $253 to $1,186

- Higher cost in less efficient programs (e.g. Burkina Faso program)
- In more efficient programs, cost per DALY was < GDP per capita

Country	Bangladesh	Burkina Faso	Mali	Uganda
Cost per DALY averted (undiscounted 2021 USD)	$548-780[1]	$1,186	$826	$253-368[1]
GDP per capita (2021 USD)	$2,458	$893	$874	$884

[1]Lower and upper estimates based on assuming 27% and 18% mortality reductions, respectively.

Is SQ-LNS cost-effective?

Current evidence suggests that provision of SQ-LNS can be very cost-effective if properly implemented and integrated into an existing delivery platform

- Take advantage of existing human resources; share overhead, training and supervision costs

Cost-benefit evidence (Copenhagen Consensus analysis[1])

- Targeted to the poorest 60% of the population in the 40 LMICs with the highest rates of child stunting
- Benefit:cost ratio 13.7:1

[1]Larsen B, Hoddinott J, Razvi S. Investing in nutrition: A global best investment case. Journal of Benefit-Cost Analysis. 2023:1-20.

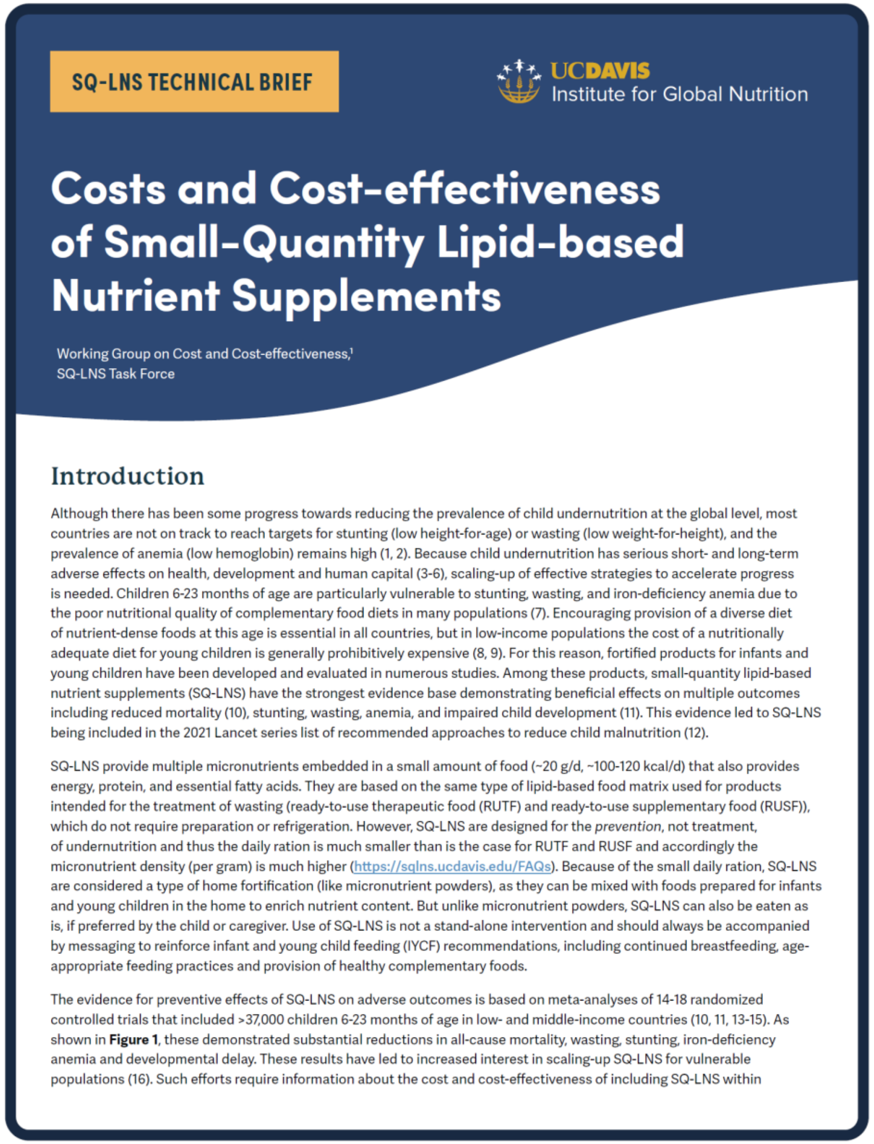
Cost and Cost-effectiveness Working Group of the SQ-LNS Task Force

- Eric Anderson (USAID)
- Rebecca Brander (IFPRI)
- Kathryn Dewey (UC Davis)
- Emanuela Galasso (World Bank Group)
- Lieven Huybregts (IFPRI)
- Grainne Moloney (UNICEF)
- Kevin Phelan (ALIMA)
- Christopher Rue (USAID)
- Gregory Sclama (WFP)

Project teams

- ALIMA and Befen teams in Niger
- Chloe Puett and the PROMIS study team
- Jacob Humber and the RDNS study team
- Mahay study team
- UC Davis Institute for Global Nutrition team

Technical brief available at:
https://sqlns.ucdavis.edu/technical-brief



SQ-LNS TECHNICAL BRIEF

UCDAVIS
Institute for Global Nutrition

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).

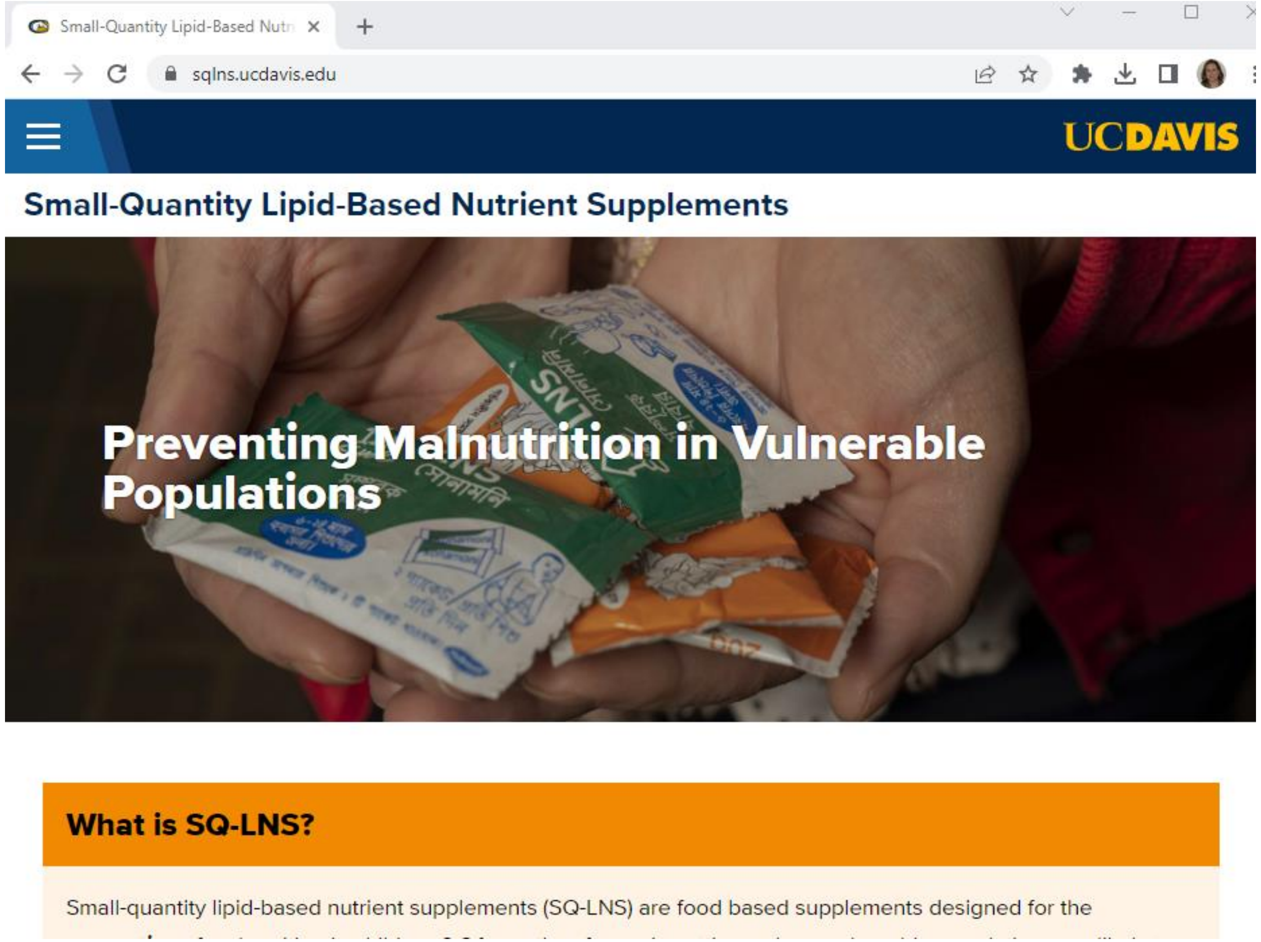
SQ-LNS provide multiple micronutrients embedded in a small amount of food (~20 g/d, ~100-120 kcal/d) that also provides energy, protein, and essential fatty acids. They are based on the same type of lipid-based food matrix used for products intended for the treatment of wasting (ready-to-use therapeutic 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

More information:

sqlns.ucdavis.edu

Website contains FAQs, research updates, and operational guidance.



Main effects, all-trials analysis: Wasting prevalence ratio[1]

Trial	Country	LNS N	Control N	PR (95% CI)	Fixed W	Random W
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WASH-B	Bangladesh	1156	3424	0.79 (0.65, 0.96)	0.16	0.16
iLiNS-Zinc	Burkina Faso	1952	664	0.69 (0.54, 0.87)	0.11	0.11
PROMIS	Burkina Faso	856	907	0.86 (0.59, 1.27)	0.04	0.04
PROMIS CS	Burkina Faso	430	436	1.03 (0.72, 1.49)	0.04	0.04
GHANA	Ghana	98	96	0.87 (0.35, 2.16)	0.01	0.01
iLiNS-DYADG	Ghana	347	692	0.84 (0.52, 1.37)	0.03	0.03
HAITI	Haiti					
WASH-B	Kenya	1455	5118	0.88 (0.53, 1.45)	0.02	0.02
MAHAY	Madagascar	1700	1682	0.96 (0.67, 1.38)	0.05	0.05
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iLiNS-DOSE	Malawi	696	241	1.37 (0.78, 2.40)	0.02	0.02
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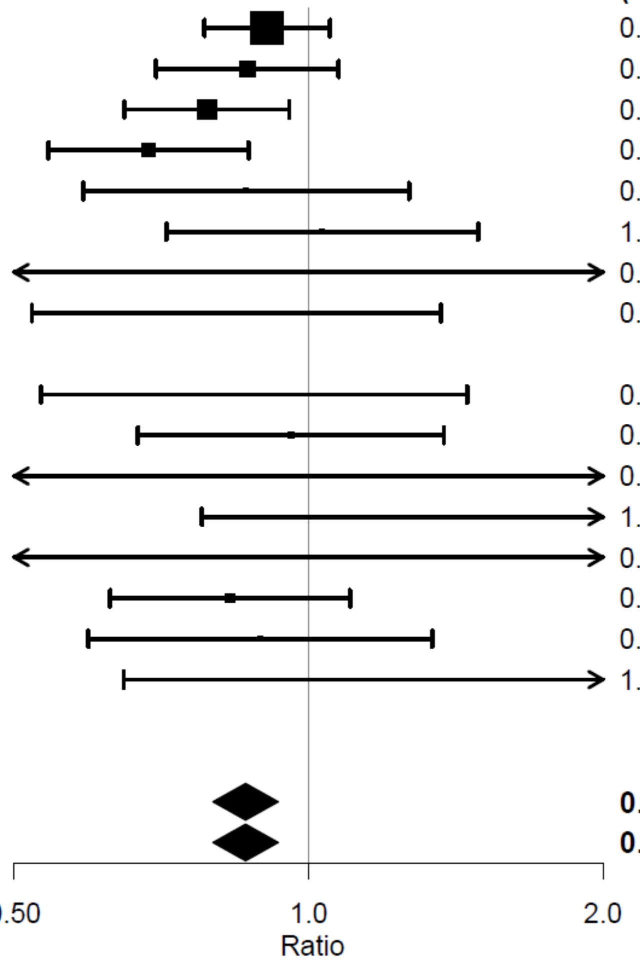
SHINE (HIV-)	Zimbabwe	1869	1784	0.89 (0.60, 1.34)	0.04	0.04
SHINE (HIV+)	Zimbabwe	336	328	1.38 (0.65, 2.96)	0.01	0.01
Summary	**I² = 0.00, Tau² = 0.00**	**17002**	**19309**			
	Fixed			**0.86 (0.80, 0.93)**		
	Random			**0.86 (0.80, 0.93)**		



[1]Cross-sectional prevalence at endline. May underestimate impact compared to longitudinal prevalence. In Mali, the SQ-LNS intervention reduced the incidence rate of acute malnutrition in the longitudinal sample by 29%.

Main effects, all-trials analysis: Severe Wasting prevalence ratio

Country	Trial	LNS N	Control N	PR (95% CI)	Fixed W	Random W
Bangladesh	JiVitA-4	2783	1217	0.90 (0.58, 1.39)	0.27	0.26
Bangladesh	RDNS	1661	815	0.70 (0.34, 1.45)	0.10	0.10
Bangladesh	WASH-B	1156	3424	0.61 (0.30, 1.25)	0.10	0.10
Burkina Faso	iLiNS-Zinc	1952	664	0.36 (0.19, 0.68)	0.13	0.13
Burkina Faso	PROMIS	856	907	1.06 (0.33, 3.38)	0.04	0.04
Burkina Faso	PROMIS CS	430	436	0.51 (0.17, 1.54)	0.04	0.04
Ghana	GHANA	98	96	3.92 (0.45, 34.42)	0.01	0.01
Ghana	iLiNS-DYADG	347	692	0.85 (0.22, 3.28)	0.03	0.03
Haiti	HAITI					
Kenya	WASH-B	1455	5118	0.27 (0.04, 1.86)	0.01	0.01
Madagascar	MAHAY	1700	1682	0.58 (0.29, 1.17)	0.10	0.10
Malawi	iLiNS-DYADM	220	444	2.02 (0.41, 9.92)	0.02	0.02
Malawi	iLiNS-DOSE					
Mali	PROMIS					
Mali	PROMIS CS	944	959	0.48 (0.21, 1.10)	0.08	0.08
Zimbabwe	SHINE (HIV-)	1869	1784	0.95 (0.38, 2.38)	0.06	0.06
Zimbabwe	SHINE (HIV+)	336	328	0.98 (0.14, 6.63)	0.01	0.01
I² = 0.01, Tau² = 0.00		**15807**	**18566**			
Fixed				**0.69 (0.55, 0.86)**		
Random				**0.69 (0.54, 0.86)**