



Symposium: Lipid nutrition – new insights

Lipid-based nutrient supplements and linear growth in children under 2 years: a review

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The prevalence of stunting remains high in low- and middle-income countries despite adoption of comprehensive nutrition interventions, particularly in low-income countries. In the present paper, we review current evidence on the acceptability and efficacy of small-quantity lipid-based nutrient supplements (SQ-LNS) on preventing stunting in children under 2 years, discuss the factors that affect their efficacy, highlight the implications of the current findings at pragmatic level and identify research priorities. Although the present paper is not a generic systematic review, we used a systematic approach to select relevant literature. The review showed that there is growing interest in the potential benefits of using SQ-LNS to prevent growth faltering. Acceptability studies showed that SQ-LNS are generally well accepted. However, results on the efficacy of SQ-LNS on improving linear growth or preventing growth faltering in infants and young children are still inconclusive. Factors that may affect efficacy include the duration of the trial, composition and dosage of SQ-LNS given, and baseline demographics and nutritional status of research participants. Future research should focus on controlled and long-term follow-up trials to obtain more conclusive results. In the long term, there will be need for studies to investigate how provision of SQ-LNS can be integrated with existing strategies to prevent stunting in low- and middle-income settings.

Lipid nutrient supplements: Stunting: Linear growth faltering: Fortification

Global context and consequences of stunting

In 2015, stunting affected approximately 159 million children under the age of 5 years worldwide and an important proportion of these children were in sub-Saharan Africa and South-central Asia⁽¹⁾. It is projected that about 127 million children under 5 years will be stunted in 2025 if no meaningful preventive actions are taken⁽²⁾. In low- and middle-income countries, stunting is a huge public health burden that has consequences on long-term health⁽³⁾. In addition, linear growth faltering has multiple causal factors⁽²⁾, and is associated with poverty and hence a critical development indicator⁽⁴⁾.

In vulnerable populations, intra-uterine growth restriction is often associated with maternal undernutrition⁽⁵⁾

and this may result in a vicious cycle of cross-generational stunting⁽⁶⁾. The incidence of stunting usually peaks around age 6–23 months as result of the transition from exclusive breastfeeding to introduction of complementary foods, which may be of poor nutritional quality^(7,8). In addition, infections can aggravate children's nutritional status and can contribute to stunting indirectly via the environmental enteric dysfunction mechanism⁽⁹⁾.

Growth retardation, reduced work capacity and poor mental and social development can occur as a result of poor dietary intake during early childhood⁽¹⁰⁾. In addition, growth faltering is also affected by several non-dietary factors that are closely linked and multifaceted⁽¹¹⁾. Nevertheless, the consequences of stunting may include

Abbreviations: LAZ, length for age z-score; LNS, lipid-based nutrient supplements; SQ-LNS, small-quantity lipid-based nutrient supplements.
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delayed cognitive development and increased morbidity and mortality⁽¹²⁾.

Strategies to reduce stunting

Actions to address multiple forms of malnutrition are described in the Comprehensive Implementation Plan on Maternal, Infant and Young Child Nutrition which was endorsed by the World Health Assembly in 2012⁽¹³⁾. Other interventions include the WHO package of effective direct nutrition interventions⁽⁸⁾, the strategies for infant and young child feeding^(7,8) and nutrition-specific and -sensitive approaches as highlighted in the 2013 *Lancet* Maternal and Child Nutrition Series^(14,15).

Improving maternal nutritional status coupled with appropriate infant and young child feeding during the critical first 1000 d (from conception to age 24 months) window can result in reduced morbidity and mortality, with notable benefits on growth and development for children⁽⁷⁾. Evidence-based, innovative and affordable interventions such as exclusive breastfeeding, appropriate introduction of complementary foods coupled with continued breastfeeding from age 6 to 23 months or beyond can help prevent growth failure^(8,16,17). This eventually may have a long-term impact on global health and development^(15,18–20). To address growth faltering and break the intergenerational cycle of undernutrition a total life-cycle approach is necessary to fully address malnutrition. Improving pre-conceptual nutritional status contributes to the prevention of intra-uterine growth restriction, which may result in lower risk for low birth weight and lower risk of stunting^(15,21).

Interventions targeting complementary feeding are usually focused on the age range of 6–23 months^(7,15). This is the period of a high incidence of growth faltering, micronutrient deficiencies and infectious illnesses in developing countries. In low-income settings, consumption of plant-based complementary foods, which are usually deficient in key micronutrients (particularly iron, zinc and vitamin B₆) often results in sub-optimum child growth and development^(7,8). Therefore, interventions that provide fortified complementary food supplements as 'point of use' or 'home' fortificants, or eaten alone as snacks have potential to improve both macronutrient and micronutrient intake^(22,23). A number of complementary food supplements have been developed, which include fortified spreads⁽²⁴⁾ water-dispersible or crushable micronutrient tablets⁽²⁵⁾, micronutrient powders⁽²⁶⁾ and small-quantity lipid-based nutrient supplements (SQ-LNS)^(27–29).

Nevertheless, it is important to note that dietary interventions during the complementary feeding period may not be sufficient, and integrated multifaceted interventions, addressing the various underlying causes of child malnutrition, are needed. Timing of these interventions are important, as maternal undernutrition increases the risk for growth restriction *in utero*; the first 1000 d is now thought to be the critical period for intervening^(14,15). This indicates the need for comprehensive nutrition action in vulnerable communities in order to

achieve the World Health Assembly target of reducing by 40 % the prevalence of stunting in children under 5 years by 2025⁽²⁾.

Small-quantity lipid-based nutrient supplements as strategy to improve linear growth

Although micronutrient interventions have received much attention as a cost-effective and promising strategy to improve child health, the results of multiple micronutrient intervention studies have been inconclusive⁽¹⁰⁾. Subsequently, lipid-based nutrient supplements (LNS) usually in form of SQ-LNS were designed to provide energy, protein, macro-minerals and essential fatty acids, in addition to micronutrients⁽²⁷⁾.

The SQ-LNS are currently at the centre of interest of academic research as a cost-effective and affordable method to ensure that children's recommended nutrient intakes are met, and further to reduce anaemia and prevent stunting in children aged 6–23 months. A broad spectrum of LNS products has been developed over the past decades. Ready-to-use therapeutic foods (100 g; 2092 kJ (500 kcal)/serving) or large-quantity LNS products such as PlumpyNut[®] were developed to treat severe acute malnutrition⁽³⁰⁾. Medium-quantity LNS or ready-to-use supplementary foods (40–50 g; 1046 kJ (250 kcal)/serving) are designed to provide more than half of daily energy requirements and are used in the nutritional management of severe acute malnutrition and moderate acute malnutrition⁽³⁰⁾. Small-quantity LNS products (such as NutriButter[®]) are designed to supply a lower energy dose (20 g; 460–628 kJ (110–150 kcal)/serving) and 50 % of recommended nutrient intakes for micronutrients and essential fatty acids. SQ-LNS are more suitable as home fortificants, for longer duration use, and are used for prevention of undernutrition in more food secure situations to fill certain nutrient gaps in the diet⁽³¹⁾. SQ-LNS products are covered by CODEX CAC/GL 8–1991, and are classified by the World Health Assembly as home fortificants and they are excluded from the guidance on ending inappropriate marketing of foods for infants and young children⁽¹⁶⁾.

A daily ration of SQ-LNS (20 g sachet) provides energy (about 460–502 kJ (110–120 kcal), protein, essential fatty acids and approximately twenty-two micronutrients, including zinc⁽³⁰⁾. SQ-LNS are cost effective compared with high-energy-dense products with similar formulations and are thus more affordable for low-income consumers⁽³⁰⁾. SQ-LNS provide low energy to ensure that breast milk intake is not compromised⁽³²⁾ and allows for higher intakes of local foods, including animal-source foods, fruit and vegetables⁽³⁰⁾. Based on experiences from previous and ongoing studies researchers from the International Lipid-based Nutrient Supplements project (<http://www.iLiNS.org>) published an overview on key issues to be considered when developing SQ-LNS for the prevention of linear growth faltering⁽³⁰⁾.

Acceptability of small-quantity lipid-based nutrient supplements

To achieve their intended benefits, SQ-LNS need to be acceptable to the target groups in terms of organoleptic properties and user-friendliness in household settings^(33,34). Poor sensory attributes of SQ-LNS^(30,33) can lead to low adherence to the supplementation regimen for the test products. Short-term studies to assess acceptability of SQ-LNS were done among 6–12 months old children and their caregivers in South Africa⁽³⁵⁾, infants and pregnant or lactating women in Ghana⁽³⁶⁾, 9–15 months old children and their mothers in Burkina Faso⁽³⁷⁾, and 8–12 months old children and their caregivers in Malawi⁽³⁸⁾. Long-term acceptability was assessed in 6–18 months old children in Malawi⁽³⁴⁾.

Although acceptability of SQ-LNS is typically assessed via sensory evaluation based on the child's willingness to consume the test meal and mother's perceived acceptance of the supplement using hedonic scales⁽³⁰⁾, different approaches were used across studies. In the Burkina Faso⁽³⁷⁾, Ghana⁽³⁶⁾, Malawi⁽³⁸⁾ and South African⁽³⁵⁾ studies, acceptability testing consisted of evaluation of a test meal (or meals) and a 2-week home trial. Acceptability was measured based on the amount of test meal consumed, the time in which the test meal was consumed, the mother's evaluation of the sensory attributes of SQ-LNS (using a hedonic scale), the mother's perception of the infant's acceptance, and ease of use at home. The results of these short-term studies showed that SQ-LNS were well accepted by children and their mothers. In one of the efficacy studies done in Malawi⁽³⁴⁾, acceptability of SQ-LNS was assessed over the 1-year intervention period. Acceptability was defined based on adherence to the feeding regimen and the mothers' experiences of feeding SQ-LNS to their children (from age 6 to 18 months). Results of this study showed that acceptability was sustained over the 12-month period. Sustained acceptability and ease of use at the household level are crucial to have impact on child growth⁽³⁴⁾, and future studies should therefore assess the acceptability of long-term use of SQ-LNS in addition to evaluating sensory attributes⁽³⁰⁾.

For SQ-LNS to have the desired nutritional impact, they should be consumed as per intended protocol. Using SQ-LNS as home fortificants should therefore not alter the taste of the usual complementary foods; for example they should not be too oily⁽³⁶⁾. Consequently, the acceptability SQ-LNS can be influenced by the effect of specific ingredients on the organoleptic properties of the final product⁽³⁰⁾. Peanut-based SQ-LNS was shown to be acceptable in African^(36–41) and non-African studies^(42–44), while a soya-based SQ-LNS was shown to be acceptable in a study in South Africa⁽³⁵⁾. Although overall acceptability of these SQ-LNS products were shown, there is still limited evidence on the mothers willingness to pay for SQ-LNS should they be commercially available⁽⁴⁵⁾.

Current evidence on efficacy of small-quantity lipid-based nutrient supplements on linear growth

There is a growing body of evidence on the efficacy of SQ-LNS on the prevention of linear growth faltering^(30,46). Although the present paper is not a generic systematic review, we employed a systematic approach, as described by Khan *et al.*⁽⁴⁷⁾ to select relevant literature. A comprehensive literature search was conducted for studies reported in the English language on PubMed, Google Scholar and Cochrane Library. The search words and phrases used included the following: stunting, lipid nutrient supplements, complementary food supplements, linear growth faltering, home fortificants, supplementation, length for age *z*-score (LAZ), children 6–23 months old. These words and phrases were used either separately or in combination. The articles appearing in reference lists of identified papers were also used for secondary search. The aim was to assess literature on the efficacy of SQ-LNS in the prevention of growth faltering in children under 2 years old. A summary of the results of these studies is given in Table 1. This section presents results of efficacy studies for SQ-LNS used for infants (from age 6 to 12 months) and for children (from age 12 to 18 months) and finally, prenatally, during pregnancy and for 6 months postnatally.

Small-quantity lipid-based nutrient supplements used for infants (age 6–12 months) and children (age 12–18 months)

Provision of SQ-LNS showed positive effects on linear growth in infants from 6 to 12 months in Haiti and Ghana^(28,29), and in children from 9 to 18 months in Burkina Faso, regardless of whether SQ-LNS contained zinc⁽²⁷⁾. In Malawi, providing SQ-LNS to children from 6 to 18 months showed limited effects. In the first study, provision of SQ-LNS showed a tendency to reduce the incidence of severe stunting, particularly in children who already showed growth faltering (LAZ < median) at baseline⁽⁴⁸⁾. Results of the second study suggest that provision of milk SQ-LNS, but not soya SQ-LNS, promotes linear growth between 9 and 12 months, but not thereafter⁽⁴⁹⁾. On the contrary, another study in Malawi failed to show any effect of SQ-LNS on linear growth in infants from 6 to 18 months regardless of whether the SQ-LNS contained milk⁽⁵⁰⁾. For the studies reviewed, results on the impact of providing SQ-LNS for infants (6–12 months old) and children (12–18 months old) on preventing stunting is still inconclusive.

Provision of small-quantity lipid-based nutrient supplements to pregnant and lactating mothers and infants from age 6 months old

SQ-LNS have also been designed to fortify maternal diets with micronutrients and essential fatty acids⁽³⁰⁾.

However, trials that have investigated the effect of providing SQ-LNS to mothers during pregnancy and for 6 months postpartum, and subsequently to the child from age 6 months onwards on birth outcomes and stunting



Table 1. Efficacy trials investigating the impact of the provision of small-quantity lipid-based nutrient supplements (SQ-LNS) on linear growth for infants/young children

Study site	Objective of study	Study population and design	Results	Observed trends/conclusions
Malawi ⁽⁵⁵⁾	To test the hypothesis that provision of SQ-LNS to mothers during pregnancy and 6 months postpartum and to their infants from 6 to 18 months of age would promote infant and child growth	Children 6–18 months (<i>n</i> 869) <i>Individually randomised, controlled, outcome assessor-blinded trial:</i> <i>Groups:</i> (1) Mother: IFA, Child: no supplement (2) Mother: MMN, Child: no supplement (3) SQ-LNS (20 g/d) (mother and child)*	At age 18 months, the mean length in the IFA, MMN and SQ-LNS groups were 77.0, 76.9 and 76.8 cm ($P = 0.90$), respectively, and the prevalence of stunting was 32.7, 35.6 and 37.9 % ($P = 0.54$), respectively	There were no differences between infant growth in groups who received maternal IFA, MMN or SQ-LNS during pregnancy and no supplement or SQ-LNS postpartum in children from 6 to 18 months of age
Malawi ⁽⁵⁰⁾	To test the hypotheses that: (1) the change in mean LAZ for infants provided with 10–40 g SQ-LNS/d from ages 6 to 18 months would be greater than that for infants receiving no dietary intervention at the same age and (2) provision of SQ-LNS that did not contain milk would be as good as milk-containing LNS in promoting linear growth	Children 6–18 months (<i>n</i> 1932) <i>Randomised controlled single-blind trial:</i> <i>Groups:</i> (1) Milk-SQ-LNS 1 (10 g/d)† (2) Milk-SQ-LNS 2 (20 g/d)† (3) Milk-SQ-LNS 3 (40 g/d)† (4) Milk-free-SQ-LNS 1 (20 g/d)† (5) Milk-free-SQ-LNS 1 (40 g/d)† (6) Control	The overall mean (sd) length and LAZ changes were 13.0 (2.1) cm and –0.45 (0.77) z-score units, respectively; with no difference between the six groups ($P = 0.66$ for length and $P = 0.74$ for LAZ). The difference in mean LAZ change in the no-milk LNS group compared with the milk LNS group was –0.02 (95 % CI –0.10, 0.06; $P = 0.72$)	SQ-LNS provided during infancy and childhood did not promote length gain or prevent stunting between 6 and 18 months of age compared to a control group
Burkina Faso ⁽²⁷⁾	To assess the impact of providing SQ-LNS with varied amounts of zinc, along with illness treatment, on zinc-related outcomes compared with standard care	Children 9–18 months (<i>n</i> 2435) <i>Placebo controlled, cluster-randomised trial:</i> <i>Groups:</i> (1) IC: 1.1 SQ-LNS without zinc (20 g/d), placebo tablet*; 1.2 SQ-LNS with 5 mg zinc (20 g/d), placebo tablet* 1.3 SQ-LNS with 10 mg zinc (20 g/d), placebo tablet* 1.4 SQ-LNS without zinc, 5 mg zinc tablet* (2) Non-intervention cluster	At age 18 months, the length was significantly greater in IC compared to non-intervention cluster (NIC) (77.7 (3.0) v. 76.9 (3.4) cm; $P < 0.001$) and stunting prevalence was significantly lower in IC (29.3 %) than NIC (39.3 %; $P < 0.0001$), but did not differ by intervention group within the IC	SQ-LNS with or without zinc, provided along with malaria and diarrhoea treatment, significantly increased growth and reduced stunting in comparison with a non-intervention cluster
Haiti ⁽²⁸⁾	To test the efficacy of a daily SQ-LNS for increased linear growth in young children	Infants 6–12 months (<i>n</i> 589) <i>Randomised controlled trial with a parallel design:</i> <i>Groups:</i> (1) 3 months SQ-LNS (20 g/d)† (2) 6 months SQ-LNS (20 g/d)† (3) Control	The LAZ (se) significantly increased in the 6 months SQ-LNS group by 0.13 (0.05) compared to the control group (adjusted for child age, $P < 0.001$)	SQ-LNS provided from 6 to 12 months resulted in increased length. The effects were sustained 6 months' post-intervention, compared to a control group

Table 1. (Cont.)

Study site	Objective of study	Study population and design	Results	Observed trends/conclusions
Malawi ⁽⁴⁹⁾	To test the hypothesis that providing lipid-based nutrient supplements (SQ-LNS) promotes linear growth and reduces the incidence of severe stunting among at-risk infants	Children 6–18 months (<i>n</i> 840) <i>Randomised assessor-blinded trial</i> : <i>Groups</i> : (1) Milk-SQ-LNS (20 g/d)‡ (2) Soya-SQ-LNS (20 g/d)‡ (3) CSB (4) Control	Between 9 and 12 months of age, the mean change in LAZ was –0.15, –0.02, –0.12 and –0.18 (<i>P</i> = 0.045) for control, milk-LNS, soya-LNS and CSB groups, respectively No between group differences at other age intervals	Exploratory analyses suggest that provision of milk-SQ-LNS, but not soya-SQ-LNS promotes linear growth among at-risk infants mainly between 9 and 12 months of age
Malawi ⁽⁶⁵⁾	To assess whether a reduction in stunting seen with 12-month SQ-LNS supplementation was sustained over a subsequent 2-year non-intervention period	Children 6–12 months (<i>n</i> 182) <i>Randomised controlled trial</i> : <i>Groups</i> : (1) CSB (2) SQ-LNS 1 (50 g/d)‡, (3) SQ-LNS 2 (25 g/d)§ (4) Control group	The cumulative 36-month incidence of severe stunting was 19.6 % in CSB, 3.6 % in SQ-LNS 1 and 10.3 % in SQ-LNS 2 groups (<i>P</i> = 0.03). Differences in LAZ observed at age 10–18 months	Provision of 50 g/d SQ-LNS from 6 to 18 months of age showed a tendency to reduce the incidence of severe stunting, particularly for children with baseline LAZ below the median
Ghana ⁽²⁹⁾	To test the hypothesis that multiple micronutrients added to home-prepared complementary foods would increase growth and that the effect would be greatest in the presence of added energy from fat	Infants 6–12 months (<i>n</i> 313) <i>Randomised controlled trial</i> : <i>Groups</i> : (1) SP (2) NT (3) SQ-LNS (Nutributter [®]) (20 g/d)† Non-randomised non-intervention group at age 12 months	At age 12 months, the SQ-LNS group had a significantly greater LAZ (–0.20 (0.54), <i>P</i> = 0.04) compared with NT (–0.39 (0.54)) groups and NT & SP combined (–0.38 (0.54))	Provision of SQ-LNS from 6 to 12 months improved linear growth

IFA, iron folic acid capsules; MMN, micronutrient capsules; LAZ, length for age z-scores; IC, intervention cluster; CSB, maize–soya blend; SP, Sprinkles powder; NT, crushable Nutritabs.

* SQ-LNS, International Lipid-Based Nutrient Supplements (iLINS) (California Davis, USA).

† SQ-LNS, Nutributter[®] (Nutriset SA, Malaunay, France).

‡ SQ-LNS, Project Peanut Butter (Blantyre, Malawi), The Nutributter[®] and iLINS formulations for infants/young children, pregnant and lactating women compared to WHO/FAO⁽⁶⁶⁾ Recommended Nutrient Intakes were presented in detail by Arimond *et al.*⁽³⁰⁾.



have produced mixed results^(51–55). Efficacy trials in Ghana showed that providing SQ-LNS for 6 months prenatally and a further 6 months postpartum to mothers and to children from age 6 to 18 months had positive effects on birth outcomes and linear growth in children^(51,54). In Bangladesh, SQ-LNS given for 6 months prenatally and a further 6 months postpartum to mothers and to children from age 6 to 18 months improved birth outcomes⁽⁵²⁾. However, in Gambia provision of SQ-LNS prenatally did not show significant benefits on preventing intra-uterine growth restriction which is associated with childhood stunting⁽⁵³⁾. The lack of intervention effect was also observed in the Malawi trial⁽⁵⁵⁾.

Differences in duration of trials, composition and dosage of SQ-LNS, and baseline demographics and nutritional status of participants make it difficult to directly compare studies. During a recent technical meeting to review evidence and pragmatic issues on provision of SQ-LNS as a preventative strategy for undernutrition, it was recommended that contextual factors and study design should be considered in the implementation of results of SQ-LNS trials⁽⁴⁶⁾. Nevertheless, further research is required to understand the potential growth-promoting effect of SQ-LNS and certain ingredients in SQ-LNS, such as milk powder and essential fatty acids⁽³¹⁾. At pragmatic level as part of integrated nutrition interventions, behaviour change communication may be necessary to ensure appropriate utilisation of SQ-LNS and subsequent impact on linear growth^(41,56).

Factors affecting efficacy of small-quantity lipid-based nutrient supplements on linear growth

Although efficacy trials are carried out under ideal and controlled conditions⁽⁵⁷⁾, the differences in the study design and settings across different trials may partly explain the mixed results on the impact of SQ-LNS on linear growth. Therefore, the interpretation of results from efficacy trials depends on the study population, setting and design^(46,57,58). This is particularly important for complementary feeding interventions that are expected to have impact for children 6–23 months old. Complementary feeding interventions usually report small to medium effects on child growth as there are many factors that influence child growth besides dietary intake⁽⁵⁹⁾. The efficacy of complementary food supplements such as SQ-LNS on child growth is influenced by factors that include but are not limited to the following: the characteristics of the target group (i.e. baseline nutritional status, age, withdrawal rates); the study setting (socioeconomic status, infections) and design (adherence calculation, control group, duration of intervention)⁽⁵⁹⁾. These factors can affect the internal and subsequent external validity of results of efficacy trials, and this makes it difficult to assess the impact of the intervention in the absence of the baseline prevalence of stunting. The internal validity of trial results can also be a factor of robust inclusion criteria, randomisation and blinding, baseline nutritional and socioeconomic status of participants and data quality

management, adherence monitoring and duration of the intervention^(30,46).

A study in Malawi showed that the provision of milk-SQ-LNS, but not soya-SQ-LNS promotes linear growth among at-risk infants aged between 9 and 12 months, but not from 12 to 18 months⁽⁴⁹⁾; overall evidence on an intervention effect of provision of SQ-LNS on stunting prevalence was inconclusive. Mangani *et al.*⁽⁴⁹⁾ reasoned that the observed prevalence of stunting across study groups in the Malawi study could have been influenced by the high incidence and prevalence of morbidity and associated environmental enteropathy⁽⁹⁾ or poor prenatal and maternal nutritional status⁽⁶⁰⁾. In addition, the researchers hypothesised that the constant dose of 20 g/d may not be sufficient as the children get older and have increased nutrient requirements. Results from a recent trial in Malawi also reported no effect of SQ-LNS supplementation prenatal and postpartum to women and their children⁽⁵⁵⁾. The researchers attributed the lack of effect on stunting on some technical difficulties in supply of SQ-LNS to participants, high attrition rate, low-energy dose of the SQ-LNS regimen, low compliance to intervention protocol and low adherence for SQ-LNS for children (77.1%). In addition, the results also suggested possible effect of underlying infections that may indirectly restrict linear growth⁽⁹⁾.

Another trial in Malawi showed no effect of SQ-LNS on linear growth in children aged 6–18 months⁽⁵⁰⁾. This finding could have been influenced by high rate of attrition or mobility, technical difficulties in supply of SQ-LNS to participants, inability to verify self-reported supplement consumption (self-reported adherence of 92.9% *v.* reported consumption rate of 71.6%). The lack of standardised methods of calculating adherence makes it difficult to make comparisons across studies.

Another probable reason why SQ-LNS efficacy trials report low impact on linear growth could be that the usual 20 g/d may not be sufficient for older children as their nutrient requirements do increase with age⁽⁴⁹⁾. There are also indications that LAZ may not be an appropriate indicator to assess changes in length over time compared with height-for-age difference (child's height compared to reference height, expressed in centimetres)⁽⁶¹⁾. There may be need to investigate the use of height-for-age difference *v.* LAZ in assessing the intervention effects of SQ-LNS on linear growth⁽⁶¹⁾.

The factors discussed earlier highlight the importance of appropriate study design and data quality on the interpretation of trial results to ascertain impact of SQ-LNS on linear growth.

Therefore, future studies should be designed to accurately assess total nutrient intake, utilise reliable indicators of estimating actual consumption of SQ-LNS, maintain acceptability of SQ-LNS and based on comprehensive situation analysis in the context of target communities⁽⁶²⁾.

In summary, there is inconclusive evidence on the efficacy of SQ-LNS supplementation on improving linear growth in infants and children and more trials are required to provide insight into this area. Therefore, there is need for pragmatic trials to assess the impact of

integrating SQ-LNS with already existing interventions targeted at girls and women of child bearing age, such as availability of safe drinking-water, basic sanitation and hygiene, malaria and infection control in different contexts. Behaviour change communication may be necessary to ensure appropriate utilisation of SQ-LNS and associated impact on linear growth^(41,56).

Recommendations for future research

There is evidence that linear growth faltering affects children beyond the first 1000 d in low-and middle-income countries⁽⁶³⁾ and the implications of this on the timing for interventions to reduce stunting still needs to be explored. Therefore, there will be need for SQ-LNS trials with longer follow-up to assess if the benefits can be maintained beyond age 2 years. These studies can also investigate the use of height-for-age difference *v.* LAZ to assess the intervention effects of SQ-LNS interventions on linear growth⁽⁶¹⁾. Trials in Malawi have shown that there is need to explore the impact of the enteropathy mechanism on child growth in low-income settings^(50,55). Iannotti *et al.*⁽²⁸⁾ highlighted the need for SQ-LNS effectiveness studies. The contribution of SQ-LNS to the prevention of growth faltering is still unclear and more research needs to be done to produce more conclusive results. There is need for standardised methods to assess adherence in community-based supplementation trials⁽⁶⁴⁾. This will enable accurate accountability of SQ-LNS utilisation and enable possible interpretation of study outcomes across studies.

Future studies can also explore how to maintain optimum dosage (>20 g/d) for children as they get older⁽⁴⁹⁾. Accurately recording of morbidities that commonly occur during this critical period of development (age 6–23 months) should further improve the interpretation of infant growth and development outcomes. Overall there is great need for providing SQ-LNS as part of integrated and comprehensive nutrition interventions and to ascertain the cost and comparative cost-effectiveness of different integrated strategies⁽³¹⁾ to prevent stunting in low-income settings.

Conclusions

The results of the studies reviewed showed inconclusive evidence on the efficacy of SQ-LNS to improve linear growth in children under 2 years. To be effective there is need to critically consider contextual factors and to integrate the provision of SQ-LNS with existing interventions aimed at addressing growth faltering in low-income settings.

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References

1. United Nations Children's Fund (2015) *Levels and Trends in Child Malnutrition: Key Findings of the 2015 Edition*. New York, USA: United Nations Children's Fund, World Health Organization, and World Bank Group.
2. World Health Organization (2014) *Global Nutrition Targets 2025: Stunting Policy Brief*. Geneva: World Health Organization.
3. Prendergast AJ & Humphrey JH (2014) The stunting syndrome in developing countries. *Paediatr Int Child Health* **34**, 250–265.
4. Kraemer K (2016) Making stunting a development indicator. *Sight Life* **30**, 10.
5. Dewey KG & Begum K (2011) Long-term consequences of stunting in early life. *Matern Child Nutr* **7**, 5–18.
6. Victora CG, Adair L, Fall C *et al.* (2008) Maternal and child undernutrition: consequences for adult health and human capital. *Lancet* **371**, 340–357.
7. World Health Organization, United Nations Children's Fund (2003) *Global Strategy for Infant and Young Child Feeding*. Geneva: World Health Organization.
8. World Health Organization (2013) *Essential Nutrition Actions: Improving Maternal, Newborn, Infant and Young Child Health and Nutrition*. Geneva: World Health Organization.
9. Prendergast A, Rukobo S, Chasekwa B *et al.* (2014) Stunting is characterized by chronic inflammation in Zimbabwean infants (620.4). *FASEB J* **28**, 620–624.
10. Souganidis E (2012) The relevance of micronutrients to the prevention of stunting. *Sight Life* **26**, 10–18.
11. United Nations Children's Fund (1990) *Strategy for Improved Nutrition of Children and Women in Developing Countries*. New York, USA: United Nations Children's Fund.

12. Victora CG, de Onis M, Hallal PC *et al.* (2010) Worldwide timing of growth faltering: revisiting implications for interventions. *Pediatrics* **125**, e473–e480.
13. World Health Organization (2014) *Comprehensive Implementation Plan on Maternal, Infant and Young Child Nutrition*. Geneva: World Health Organization.
14. Ruel MT & Alderman H (2013) Nutrition-sensitive interventions and programmes: how can they help to accelerate progress in improving maternal and child nutrition? *Lancet* **382**, 536–551.
15. Bhutta ZA, Das JK, Rizvi A *et al.* (2013) Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet* **382**, 452–477.
16. World Health Organization (2016) *Ending the Inappropriate Promotion of Foods for Infants and Young Children: a Primer on WHO Guidance. Sixty-ninth World Health Assembly A69/7*. Geneva: World Health Organization.
17. United Nations Children's Fund (2006) *1990–2005. Celebrating the Innocenti Declaration on the Protection, Promotion and Support of Breastfeeding: Past Achievements, Present Challenges and Priority Actions for Infant and Young Child Feeding*. New York, USA: United Nations Children's Fund.
18. Gruszfeld D & Socha P (2013) Early nutrition and health: short- and long-term outcomes. *World Rev Nutr Diet* **108**, 32–39.
19. World Health Organization, Food and Agriculture Organisation (2014) *Second International Conference on Nutrition (ICN2): Framework for Action*. Geneva: World Health Organization.
20. Haddad LJ, Hawkes C, Achadi E *et al.* (2015) *Global Nutrition Report 2015: Actions and Accountability to Advance Nutrition and Sustainable Development*. Washington, DC, USA: International Food Policy Research Institute.
21. Nabarro D (2013) Global child and maternal nutrition – the SUN rises. *Lancet* **382**, 666–667.
22. Maternal, Infant and Young Child Nutrition Working Group (2009) Formulations for fortified complementary foods and supplements: review of successful products for improving the nutritional status of infants and young children. *Food Nutr Bull* **30**, S239–S255.
23. Dewey KG (2013) The challenge of meeting nutrient needs of infants and young children during the period of complementary feeding: an evolutionary perspective. *J Nutr* **143**, 2050–2054.
24. Briend A (2001) Highly nutrient-dense spreads: a new approach to delivering multiple micronutrients to high-risk groups. *Br J Nutr* **85**, S175–S179.
25. Gross R (2000) *Micronutrient Supplementation Throughout the Life Cycle*. New York, USA: United Nations Children's Fund.
26. Wang Y, Chen C, Wang F *et al.* (2007) Effects of nutrient fortified complementary food supplements on growth of infants and young children in poor rural area in Gansu Province. *Wei Sheng Yan Jiu = J Hyg Res* **36**, 78–81.
27. Hess SY, Abbeddou S, Jimenez EY *et al.* (2015) Small-quantity lipid-based nutrient supplements, regardless of their zinc content, increase growth and reduce the prevalence of stunting and wasting in young burkinabe children: a cluster-randomized trial. *PLoS ONE* **10**, e0122242.
28. Iannotti LL, Dulienci SJ, Green J *et al.* (2014) Linear growth increased in young children in an urban slum of Haiti: a randomized controlled trial of a lipid-based nutrient supplement. *Am J Clin Nutr* **99**, 198–208.
29. Adu-Afarwuah S, Lartey A, Brown KH *et al.* (2007) Randomized comparison of 3 types of micronutrient supplements for home fortification of complementary foods in Ghana: effects on growth and motor development. *Am J Clin Nutr* **86**, 412–420.
30. Arimond M, Zeilani M, Jungjohann S *et al.* (2013) Considerations in developing lipid-based nutrient supplements for prevention of undernutrition: experience from the International Lipid-Based Nutrient Supplements Project. *Matern Child Nutr* **11**, 1–31.
31. Dewey KG & Arimond M (2012) Lipid-based nutrient supplements: how can they combat child malnutrition? *PLoS Med* **9**, 1–2.
32. Giugliani ER, Horta BL, Loret de Mola C *et al.* (2015) Effect of breastfeeding promotion interventions on child growth: a systematic review and meta-analysis. *Acta Paediatr* **104**, 20–29.
33. DePee S (2015) Special nutritious solutions to enhance complementary feeding. *Matern Child Nutr* **11**, i–viii.
34. Ashorn U, Alho L, Arimond M *et al.* (2015) Malawian mothers consider lipid-based nutrient supplements acceptable for children throughout a 1-year intervention, but deviation from user recommendations is common. *J Nutr* **145**, 1588–1595.
35. Rothman M, Berti C, Smuts M *et al.* (2015) Acceptability of two lipid-based complementary food supplements in a peri-urban South African community. *Food Nutr Bull* **36**, 455–466.
36. Adu-Afarwuah S, Lartey A, Zeilani M *et al.* (2011) Acceptability of lipid-based nutrient supplements among Ghanaian infants and pregnant or lactating women. *Matern Child Nutr* **7**, 344–356.
37. Hess SY, Bado L, Aaron GJ *et al.* (2011) Acceptability of zinc-fortified, lipid-based nutrient supplements prepared for young children in Burkina Faso. *Matern Child Nutr* **7**, 357–367.
38. Phuka J, Ashorn U, Ashorn P *et al.* (2011) Acceptability of three novel lipid-based nutrient supplements among Malawian infants and their caregivers. *Matern Child Nutr* **7**, 368–377.
39. Tripp K, Perrine CG, de Campos P *et al.* (2011) Formative research for the development of a market-based home fortification programme for young children in Niger. *Matern Child Nutr* **7**, 82–95.
40. Ickes SB, Jilcott SB, Myhre JA *et al.* (2012) Examination of facilitators and barriers to home-based supplemental feeding with ready-to-use food for underweight children in western Uganda. *Matern Child Nutr* **8**, 115–129.
41. Paul KH, Muti M, Chasekwa B *et al.* (2012) Complementary feeding messages that target cultural barriers enhance both the use of lipid-based nutrient supplements and underlying feeding practices to improve infant diets in rural Zimbabwe. *Matern Child Nutr* **8**, 225–238.
42. Heidkamp RA, Stoltzfus RJ, Fitzgerald DW *et al.* (2012) Growth in late infancy among HIV-exposed children in urban Haiti is associated with participation in a clinic-based infant feeding support intervention. *J Nutr* **142**, 774–780.
43. Matias SL, Chaparro CM, Perez-Exposito AB *et al.* (2011) *Acceptability of a Lipid-based Nutrient Supplement Among Guatemalan Infants and Young Children*. FHI 360/FANTA-2. Washington, DC, USA: Food and Nutrition Technical Assistance.
44. Mridha M, Chaparro C, Matias S *et al.* (2012) *Acceptability of Lipid-based Nutrient Supplements and Micronutrient Powders Among Pregnant and Lactating Women and Infants and Young Children in Bangladesh and their Perceptions about Malnutrition and Nutrient*



- Supplements. FHI 360/FANTA-2. Washington, DC, USA: Food and Nutrition Technical Assistance.
45. Segrè J, Winnard K, Abrha TH *et al.* (2015) Willingness to pay for lipid-based nutrient supplements for young children in four urban sites of Ethiopia. *Matern Child Nutr* **11**, 16–30.
 46. Food and Nutrition Technical Assistance III Project (2015) *Meeting Highlights: Evidence and Programmatic Considerations for the Use of Small Quantity Lipid-Based Nutrient Supplements for the Prevention of Malnutrition*. FANTA/FHI 360. Washington, DC, USA: Food and Nutrition Technical Assistance.
 47. Khan KS, Kunz R, Kleijnen J *et al.* (2003) Five steps to conducting a systematic review. *J R Soc Med* **96**, 118–121.
 48. Phuka JC, Maleta K, Thakwalakwa C *et al.* (2008) Complementary feeding with fortified spread and incidence of severe stunting in 6-to 18-month-old rural Malawians. *Arch Pediatr Adolesc Med* **162**, 619–626.
 49. Mangani C, Maleta K, Phuka J *et al.* (2013) Effect of complementary feeding with lipid-based nutrient supplements and corn-soy blend on the incidence of stunting and linear growth among 6- to 18-month-old infants and children in rural Malawi. *Matern Child Nutr* **11**, 132–143.
 50. Maleta KM, Phuka J, Alho L *et al.* (2015) Provision of 10–40 g/d lipid-based nutrient supplements from 6 to 18 months of age does not prevent linear growth faltering in Malawi. *J Nutr* **145**, 1909–1915.
 51. Adu-Afarwuah S, Lartey A, Okronipa H *et al.* (2016) Small-quantity, lipid-based nutrient supplements provided to women during pregnancy and 6 mo postpartum and to their infants from 6 mo of age increase the mean attained length of 18-mo-old children in semi-urban Ghana: a randomized controlled trial. *Am J Clin Nutr* **104**, 797–808.
 52. Mridha MK, Matias SL, Chaparro CM *et al.* (2016) Lipid-based nutrient supplements for pregnant women reduce newborn stunting in a cluster-randomized controlled effectiveness trial in Bangladesh. *Am J Clin Nutr* **103**, 236–249.
 53. Johnson W, Darboe MK, Sosseh F *et al.* (2016) Association of prenatal lipid-based nutritional supplementation with fetal growth in rural Gambia. *Matern Child Nutr* [Epublication ahead of print version].
 54. Adu-Afarwuah S, Lartey A, Okronipa H *et al.* (2015) Lipid-based nutrient supplement increases the birth size of infants of primiparous women in Ghana. *Am J Clin Nutr* **101**, 835–846.
 55. Ashorn P, Alho L, Ashorn U *et al.* (2015) Supplementation of maternal diets during pregnancy and for 6 months postpartum and infant diets thereafter with small-quantity lipid-based nutrient supplements does not promote child growth by 18 months of age in rural Malawi: a randomized controlled trial. *J Nutr* **145**, 1345–1353.
 56. Kodish S, Aburto N, Hambayi MN *et al.* (2015) Identifying the sociocultural barriers and facilitating factors to nutrition-related behavior change formative research for a stunting prevention program in Ntchisi, Malawi. *Food Nutr Bull* **36**, 138–153.
 57. Gartlehner G, Hansen RA, Nissman D *et al.* (2006) *Criteria for Distinguishing Effectiveness from Efficacy Trials in Systematic Reviews*. Technical Reviews, No. 12 Report no. 06-0046. Rockville, MD: Agency for Healthcare and Quality.
 58. Singal AG, Higgins PDR & Waljee AK (2014) A primer on effectiveness and efficacy trials. *Clin Trans Gastroenterol* **5**, e45.
 59. Dewey KG & Adu-Afarwuah S (2008) Systematic review of the efficacy and effectiveness of complementary feeding interventions in developing countries. *Matern Child Nutr* **4**, 24–85.
 60. Christian P, Lee SE, Donahue Angel M *et al.* (2013) Risk of childhood undernutrition related to small-for-gestational age and preterm birth in low- and middle-income countries. *Int J Epidemiol* **42**, 1340–1355.
 61. Leroy JL, Ruel MT & Habicht J-P (2015) *Using Height-for-age Difference Instead of Height-for-age Z-scores for the Meaningful Measurement of Catch-up Growth in Children Less than 5 Years of Age*. Washington, DC, USA: International Food Policy Research Institute.
 62. Kodish S, Rah JH, Kraemer K *et al.* (2011) Understanding low usage of micronutrient powder in the Kakuma Refugee Camp, Kenya: findings from a qualitative study. *Food Nutr Bull* **32**, 292–303.
 63. Leroy JL, Ruel M, Habicht J-P *et al.* (2014) Linear growth deficit continues to accumulate beyond the first 1000 days in low-and middle-income countries: global evidence from 51 national surveys. *J Nutr* **144**, 1460–1466.
 64. Abbeddou S, Hess SY, Yakes Jimenez E *et al.* (2015) Comparison of methods to assess adherence to small-quantity lipid-based nutrient supplements (SQ-LNS) and dispersible tablets among young Burkinabé children participating in a community-based intervention trial. *Matern Child Nutr* **11**, 90–104.
 65. Phuka JC, Maleta K, Thakwalakwa C *et al.* (2009) Postintervention growth of Malawian children who received 12-mo dietary complementation with a lipid-based nutrient supplement or maize-soy flour. *Am J Clin Nutr* **89**, 382–390.
 66. World Health Organization/Food and Agriculture Organisation (2004) *Vitamin and Mineral Requirements in Human Nutrition*, 2nd ed. Geneva: World Health Organization.