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Commentary

Why small-quantity lipid-based nutrient supplements should be integrated into comprehensive strategies to prevent child undernutrition in nutritionally vulnerable populations: response to Gupta et al.'s commentary

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We write in response to the commentary by Gupta et al. (2023) on small-quantity lipid-based nutrient supplements (SQ-LNS) for infants and young children 6 to 24 months of age, which was prompted by the recent brief guidance note from UNICEF (2023) explaining when, why and how SQ-LNS are being prioritized as part of their package of preventive actions to combat early childhood malnutrition. The UNICEF document was disseminated shortly after publication of a correspondence in Nature Food (Aguayo et al. 2023), authored by nutrition leaders from several organizations, that summarized the evidence on the benefits of SQ-LNS and called for this intervention to be scaled up and integrated into programs for populations in which child undernutrition is prevalent and dietary quality is very poor.

We agree with Gupta et al. that child malnutrition is the result of many factors and there is no single "quick fix" or "magic bullet". In fact, the above-cited documents state clearly and frequently that provision of SQ-LNS is not a stand-alone intervention and must be integrated into comprehensive strategies to improve infant and young child feeding (IYCF), including the promotion of dietary diversity, as well as other actions needed to prevent malnutrition. SQ-LNS are intended for vulnerable populations who lack access to an affordable, nutritionally adequate complementary feeding diet and have high rates of stunting, wasting and mortality. In such populations, we agree with Gupta et al. that IYCF messages alone are not enough. This is precisely why SQ-LNS were originally developed.

RATIONALE FOR DEVELOPMENT OF SQ-LNS

Inadequate intakes of key nutrients from 6 to 24 months of age are highly prevalent (Beal et al. 2021; White et al. 2021). While improved dietary adequacy through the intake of nutrient-rich complementary foods is the first priority (UNICEF 2020), it is very difficult to meet needs for nutrients such as iron (in the absence of fortification) without substantial intakes of animal-source foods (e.g., liver)

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(Zlotkin and Dewey 2021). As a result, the cost of a nutritionally adequate diet during this age interval is out of reach for a large proportion of households in low- and middle-income countries (LMICs) (World Food Programme 2022; Ryckman, Beal, Nordhagen, Chimanya, et al. 2021; Ryckman, Beal, Nordhagen, Murira, et al. 2021). Fortified products such as SQ-LNS should never replace a diverse complementary food diet, but they can help meet the needs for certain limiting nutrients (such as iron, zinc and calcium) and thus improve the availability and affordability of a nutritionally adequate diet (World Food Programme 2022; Ferguson et al. 2018; Dewey and Vitta 2013). Even in high-income countries, fortified foods for infants play an important role in reducing the risk of micronutrient deficiencies in this age group (Ramakrishnan and Yip 2002). As a matter of equity, we believe that infants and young children in LMICs also deserve access to high-quality fortified products. In the long term, we hope that ongoing efforts to reduce poverty and transform food systems will make healthy, diverse and nutritionally adequate diets accessible and affordable for all. We are committed to working towards that goal, but in the meantime, there is an urgent need to reduce child undernutrition and save lives in vulnerable populations around the world.

SQ-LNS were not designed primarily to fill an "energy gap" as implied by Gupta et al., but to fill key intake gaps for micronutrients and essential fatty acids, and provide a small amount of energy and high-quality protein (Arimond et al. 2015). As explained elsewhere (https://sqlns.ucdavis.edu/FAQs) (Dewey, Stewart, et al. 2021), the quantity of food included in SQ-LNS – only 4 teaspoons per day - is deliberately small for several reasons: a) to avoid displacing breast milk and leave room for other nutritious foods, b) to make it easy for a child to consume the daily ration and thereby receive the intended doses of nutrients, c) to make it possible for SQ-LNS to be mixed with other foods or consumed as is, allowing for flexibility in feeding practices, and d) to minimize cost. SQ-LNS meet the definition of home fortification used by the Home Fortification Technical Advisory Group (2023): "Home-fortification consists of adding specialized, nutrient-filled products such as multiple micronutrient powders (MNP) or food-based complementary food supplements (CFS) such as small-quantity lipid-based nutrient supplements (SQ-LNS) and full-fat soy flour (and soy protein isolate) with a vitamin-mineral mix to foods prepared at home." As implied by that definition, there is no hard line between products for home fortification and fortified complementary foods, as SQ-LNS and products such as Ying Yang Bao (Huo 2017) are food-based. SQ-LNS thus also fall under the CODEX definition of Fortified Complementary Foods (Joint FAO/WHO Codex Alimentarius Commission 1991): "Formulated Complementary Foods for Older Infants and Young Children means foods that are suitable for use during the complementary feeding period. These foods are specifically formulated with appropriate nutritional quality to provide additional energy and nutrients to complement the family foods derived from the local diet by providing those nutrients which are either lacking or are present in insufficient quantities."

EVIDENCE BASE FOR SQ-LNS

The evidence for efficacy of SQ-LNS is very strong. Individual participant data (IPD) meta-analyses of 14 randomized trials in 9 countries, with a total of more than 37,000 children, showed a reduced risk of multiple adverse outcomes including severe wasting (by 31%), severe stunting (by 17%), iron deficiency anemia (by 64%), and developmental delay (by 16–19%) between 6 and 23 months of age (Aguayo et al. 2023; Dewey, Wessells, et al. 2021; Prado et al. 2021; Wessells et al. 2021). In addition, evidence from an earlier meta-analysis of LNS, in which 12 of the 13 trials in the primary analysis used SQ-LNS, indicated that child mortality was reduced by ~27% in this age range (Stewart et al. 2020). Gupta et al. criticize the study designs of the trials because the control groups were not provided with "diverse adequate food as a positive control", and argue that "it is likely that many other well -designed interventions including adequate and diverse diet will work". However, a program that would provide ingredients to households to prepare nutritionally adequate complementary food diets, using only unfortified foods, would be far more expensive (and much less feasible) than enriching the home-based diet with MNPs, SQ-LNS or a fortified complementary food, as explained above. We are unaware of any studies in which a complete, diverse diet of nutritionally adequate unfortified complementary foods has been provided as the intervention, perhaps because researchers recognize that such a diet would not meet all micronutrient needs of infants and young children unless it contained large amounts of iron-rich animal-source foods (especially at 6-11 months of age), which would make it too costly for widescale real-world implementation. Nonetheless, we welcome research evaluating such an approach. At present, however, evidence of the efficacy or feasibility of such interventions is lacking. In fact, there is very little evidence from randomized trials of the impact of providing unfortified complementary foods in general – in a recent review of provision of complementary foods (Tong et al. 2022), only 3 studies were cited in the category of "local foods", which varied widely in the type of food offered (caterpillar cereal, egg, or dry milk + cooking oil) and impact on growth, with no significant effects overall.

Gupta et al. express concern that use of SQ-LNS will undermine IYCF practices, but in programmatic contexts SQ-LNS is always accompanied by reinforcement of recommended IYCF practices, including a diverse diet with healthy foods from the key food groups. The evidence indicates that there have been no harmful effects on breastfeeding, complementary feeding practices, or dietary diversity, and in some settings provision of SQ-LNS had positive effects on feeding frequency and consumption of animal-source foods (https://sqlns.ucdavis.edu/FAQs) (Arimond et al. 2016). In addition, several trials conducted in real-world programs suggest that provision of SQ-LNS may enhance participation in nutrition education activities (Matias et al. 2017; Becquey et al. 2019; Huybregts et al. 2019), with potentially beneficial spillover effects on IYCF practices.

The commentary by Gupta et al. also suggests that an energy-dense food might lead to overweight. In fact, infants and young children need a relatively energy-dense diet (Michaelsen, Grummer-Strawn, and Bégin 2017), and in this age group there is no evidence that high-fat or energy-dense foods contribute to overweight (Patro-Gołąb et al. 2016; Michaelsen, Grummer-Strawn, and Bégin 2017; Abbeddou et al. 2022; Fabiansen et al. 2017). In the randomized trials, no short- or long-term adverse effects of SQ-LNS on child fatness, BMI or food preferences have been observed (https://sqlns.ucdavis.edu/FAQs).

CONFLICT OF INTEREST

Gupta et al. state that "there were conflicts of interest in at least 10 out of the 23 trials". We are puzzled by this statement because there were 14 SQ-LNS trials in the IPD meta-analyses, not 23. More importantly, none of those 14 trials was funded by industry (one trial was supported by the Nestlé Foundation, but that foundation is independent of the Nestlé Company). Only one of those trials received "in-kind" support in the form of donated SQ-LNS from a company. Detailed information on the funding of each trial is available in Supplemental Table 5 of Dewey, Wessells, et al. (2021). Industry had no role or input in the analysis or interpretation of the trial results. We stand by the integrity and independence of the 70+ co-authors involved in the meta-analyses, many of whom have a long track record of research that has contributed to improvements in infant and young child feeding globally.

REGULATORY, SAFETY AND ENVIRONMENTAL ISSUES

Gupta et al. state that SQ-LNS are ultra-processed foods (UPF), but we note that there is inconsistency in the definition of UPFs and in the examples of foods listed as UPFs (Gibney 2019). Gupta et al. describe UPFs as "industrial formulations of substances derived from food ingredients but containing little or no whole food", but the first ingredient of SQ-LNS in their text box is peanuts, which is a whole food. The FAO description of UPFs states that they are "formulations of ingredients, mostly of exclusive industrial use..." (https://www.fao.org/publications/card/en/c/CA5644EN/), which is not the case for SQ-LNS. Apart from a legume such as peanuts, the other key ingredients in SQ-LNS are oil, milk powder and vitamins and minerals (World Food Programme 2020). Because SQ-LNS includes polyunsaturated vegetable oils and high concentrations of certain nutrients that can cause oxidation of those oils (such as iron), certain ingredients may be added during processing to prevent spoilage and ensure a minimum shelf life of 24 months (World Food Programme 2020), such as small amounts of fully hydrogenated vegetable oil. Fully hydrogenated vegetable oil does not lead to creation of trans fat (the type of harmful fat that can be created when using partially hydrogenated fats); partially hydrogenated fats are prohibited in products for infants and young children, but fully hydrogenated fats are not (Joint FAO/WHO Codex Alimentarius Commission 1981). To prevent separation of the oil in SQ-LNS, an emulsifier (such as vegetable lecithin) may be added, which is also safe for infants and young children (Joint FAO/WHO Codex Alimentarius Commission 1981).

The World Food Programme specification for SQ-LNS (World Food Programme 2020) and the CODEX guidelines for formulated complementary foods for older infants and young children (Joint FAO/WHO Codex Alimentarius Commission 1991) ensure the safety of SQ-LNS.

SQ-LNS for children generally include 22 vitamins and minerals, and do not provide more than the recommended daily intake of each nutrient. The potential for toxicity was carefully considered when they were developed (Arimond et al. 2015; Chaparro and Dewey 2010). The values provided by Gupta et al. are the maximum allowed, and the actual recommended micronutrient fortification levels are lower than that (and account for degradation over time). However, we note that children should not be provided with both SQ-LNS and MNPs, as this could result in excessive intakes of certain nutrients such as vitamin A.

Gupta et al. express concern that the advice to use SQ-LNS within 24 hours of opening the sachet, consume it within 2 hours if mixed with other food, and store sachets in a clean, cool place is unrealistic. However, similar food safety recommendations would exist for any type of complementary food for young children, and for other types of LNS (e.g., ready-to-use therapeutic foods) that have been used safely in many settings. SQ-LNS are as safe or safer than home-prepared complementary foods. Gupta et al. repeatedly promote the provision of a "home-cooked diet", but do not address safety concerns for such diets, nor implications regarding the time availability of caregivers. Anecdotally, caregivers indicate that they value the convenience of a pre-prepared product that does not need refrigeration and saves time because it does not require cooking or fetching water.

SQ-LNS, as specified by the World Food Programme (2020), are not currently available for direct purchase by the public, as they are intended to be integrated into health/nutrition programs. In the future, if SQ-LNS are made available for direct purchase, we agree that guidelines need to be in place to ensure the adequacy and safety of such products and guard against inappropriate marketing.

We also agree that environmental issues are an important concern, although we note that they are not unique to SQ-LNS. We support the development of novel, more environmentally-sustainable packaging/delivery options such as recyclable and compostable materials. Some of these are currently in development.

COST AND SUSTAINABILITY

The SQ-LNS Task Force has summarized the costs of SQ-LNS interventions in 5 studies (https://sqlns.ucdavis.edu/FAQs). These estimates include non-product costs such as training and staffing based on real-world scenarios. Cost-efficiency and cost-effectiveness (e.g., cost per disability-

adjusted life year (DALY) averted) have also been estimated using various approaches (Adams et al. 2022). Because of the demonstrated benefits on multiple outcomes, including mortality, SQ-LNS meets international criteria for being "very cost-effective". In fact, in a recent assessment of the most cost-effective maternal and child nutrition interventions for the Copenhagen Consensus (Larsen, Hoddinott, and Razvi 2023), the authors estimate a benefit to cost ratio of 13.7 for preventive SQ-LNS for children 6–23 months of age, targeted to the poorest 60% of the population in the 40 low- and lower middle-income countries with the highest rates of child stunting. Sustainability of interventions that include SQ-LNS will depend on the commitments of governments and funders to ensure stable financing for comprehensive efforts to prevent child malnutrition. In our view, it is not an "either/or" choice between promoting SQ-LNS and assisting national governments to make healthy diets more affordable and accessible. These actions can and should be mutually supportive and integrated into strategies targeting nutritionally vulnerable populations.

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CONFLICT OF INTEREST

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